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Aims and Scope

This Journal is a multidisciplinary publication devoted to all field of Natural and Technical Sciences. The Editor of AJNTS invites original contributions which should comprise previously unpublished results, data and interpretations. Types of contributions to be published are: (1) research papers; (2) shorts communications; (3) reviews; (4) discussions; (5) book reviews;(6) announcements

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PREFACE ON THE 3RD INTERNATIONAL CONFERENCE ON PUBLIC HEALTH AND ENVIRONMENT
A Global and Interdisciplinary Dialogue

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Preface

The 3rd International Conference on Public Health and Environment, held on June 30 – July 1, 2025, at the Albanian Academy of Sciences, brought together researchers, academics, public health experts, clinicians, environmental scientists, and policy experts from Albania, Italy, the United States, Kosovo, North Macedonia and other regional and international institutions. The conference was organized by the Albanian Academy of Sciences, in close partnership with George Mason University and Collegium Ramazzini. The two-day program offered a rich and comprehensive scientific agenda, including plenary sessions, oral presentations, and poster communications, reflecting both the steady maturation of the conference since its launch in 2023 and its expanding significance as an international platform for advancing environmental health science, interdisciplinary exchange, and policy-relevant research. Featuring more than 50 oral and poster contributions, the event addressed a wide range of critical themes—including air quality, food safety, water resources, population health, environmental policy, and emerging contaminants—thereby highlighting the multifaceted nature of environmental health challenges and the shared determination of the scientific community to confront them through rigorous inquiry, cross-sector collaboration, and practical solutions.

Designed to address the pressing challenges at the nexus of environmental change and human health, the conference has proved to be a unique platform to address the global challenges at the nexus of environmental health and fostering collaboration among researchers. So, researchers from Italy, Kosovo, North Macedonia, the United States, Brazil, and other countries presented alongside Albanian scientists, creating a forum where local environmental health issues were analyzed within a broader global framework. This diversity fostered robust comparative analyses—whether on the health effects of air pollution from open waste burning in Albania, or the prevalence of respiratory and cardiovascular diseases in industrial regions, or the environmental determinants of early-onset dementia in Northern Italy.

Air Quality and Health

Air quality emerged as a central unifying theme across multiple sessions. Presentations addressed the epidemiology of pollution-related diseases, including rheumatoid arthritis, allergic conditions, tuberculosis and malignancies, illustrating the complex ways in which environmental exposures intersect with chronic and infectious disease pathways. Several speakers emphasized the urgent need to strengthen environmental monitoring infrastructure and to translate scientific evidence into effective and enforceable air quality standards. Discussions underscored the risks posed by both conventional sources, such as industrial emissions, and emerging threats, including open waste burning and the combined effects of pollen and urban air pollutants.

Food Safety and Nutritional Health

The session on food quality and safety addressed a wide range of issues, from the effect of food additives and environmental contaminants on the immune function, to the high prevalence of lactose intolerance in Albania, and the physicochemical and antimicrobial properties of locally cultivated blueberries. This session highlighted the critical interface between environmental exposures, nutrition, and immune health, while reinforcing the need for coordinated strategies that intersect agricultural practices, food processing, and public health nutrition policies.

Water Quality and Environmental Protection

The water quality session drew attention to both acute and chronic challenges, including spills of strong inorganic acids into marine environments, chemical and microbial contamination of surface and bathing waters, and the persistence of pollutants such as detergents and heavy metals. Innovative remediation approaches, including the use of natural clays and bioreporting bacteria, demonstrated the capacity of regional scientists to develop context-specific and practical solutions. Wastewater-based epidemiology was also presented as an emerging tool for monitoring infectious diseases and antimicrobial resistance, offering a promising addition to Albania’s environmental health surveillance framework.

Population Health, Policy, and Emerging Environmental Hazards

The sessions on population health and policy broadened the discussion to include pesticide exposure on reproductive health, management of chronic non-communicable diseases, pharmaceutical waste disposal practices, and the occupational and environmental health implications of European integration. Presentations also address the environmental-genetic interplay in autism, methodological advances in modern environmental epidemiology, and the toxicological effects of glyphosate-based herbicides. Collectively, these sessions illustrated the essential relationship between scientific evidence and public governance, as well as the importance of sustained dialogue among researchers, institutions, policymakers, and communities.

Thematic Threads and Collaborative Spirit

Throughout the conference, three major themes consistently emerged:

1. Interdisciplinary Collaboration – Many contributions reflected cross-institutional and cross-national partnerships, demonstrating the tangible value of the scientific networks fostered through previous editions of the conference.
2. Evidence-Based Policy Engagement – Presentations repeatedly linked research findings with policy implications, underscoring the conference's broader aim of transforming scientific evidence into actionable public health measures.
3. Capacity Building – From early-career researchers presenting innovative methodologies to broader discussions on education and professional development, the conference emphasized the importance of cultivating a new generation of creative, committed, and scientifically rigorous environmental health professionals.

Building on a Shared Vision for the Future

In the closing remarks, the conference leadership—including Dr. Melissa Perry of George Mason University, Acad. Genc Sulcebe of the Academy of Sciences of Albania, and their colleagues—outlined a shared vision for the next five years of collaboration. This forward-looking perspective includes:

- Within one year: dissemination of conference proceedings in a peer-reviewed publication; development of national five-year collaborative plans focused on air and water quality; and structured engagement with public institutions, agencies, and policymakers.
- Within three years: expansion of international participation; implementation of multi-site demonstration projects; and increased production of joint publications and conference presentations in English-language venues.
- Within five years: measurable improvements in air and water quality in Albania, supported by substantial national and international investment; and the advancement of policies and standards that align more closely with European environmental and public health norms, potentially including regulatory measures such as an asbestos ban.

A Model for Regional and Global Impact

The Third International Conference on Public Health and Environment stands as a testament to what sustained collaboration can achieve. Since 2023, the partnership between the Albanian Academy of Sciences, the George Mason University College of Public Health, and the Collegium Ramazzini has strengthened scientific exchange while also creating a durable structure for research, education, and policy influence. By fostering networks that bridge disciplines, institutions, and national borders, the conference is helping to advance environmental health solutions whose relevance extends beyond Albania to wider region and international scientific community.

Commitment to the Next Generation

Central to this vision is a strong commitment to supporting the next generation of environmental health leaders—scientists who combine rigorous inquiry with a passion for stewardship of the planet. By integrating research opportunities, mentorship, and international exposure into its framework, the conference is helping to train experts who will carry forward the mission of safeguarding human and ecological health in an era of rapid environmental change.

CONCLUSIONS

The 2025 conference unequivocally demonstrated that safeguarding environmental and public health demands more than scientific excellence alone; it requires perseverance, innovation, institutional courage, and a deeply shared sense of responsibility across disciplines and borders. As environmental challenges grow in complexity and urgency, the conference has emerged as an increasingly important forum where evidence is transformed into dialogue, dialogue, dialogue into collaboration, and collaboration into pathways for meaningful change. Its growing international profile, remarkable interdisciplinary scope, and strategic forward-looking vision confirm its evolution into a recognized hub for knowledge exchange and collaborative problem-solving. Yet, the defining strength of the conference lies not only in the quality of its scientific contribution, but in the authenticity of the engagement it fosters—active participation, sincere partnership, and concrete cooperation among scientists, health professionals, academic institutions, and public stakeholders, all united by the common aim of serving society. The robust partnerships underpinning this initiative, affirm Albania's rising role as a regional leader in environmental health dialogue and action. Grounded in science, enriched by international solidarity, and guided by a commitment to the well-being of present and future generations, the conference is shaping a durable framework for research, policy influence, and societal impact. Ultimately, the 2025 conference stands as a powerful example of how science, when coupled with vision and collaboration, can transcend the boundaries of academia to become a transformative force for a healthier, more sustainable, and more just world.

Melissa J. Perry ScD, MHS

HOUSEHOLD PHARMACEUTICAL WASTE MANAGEMENT IN ALBANIA: EVALUATING PUBLIC PERCEPTION, PHARMACY PRACTICE AND REGULATORY GAPS

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Research

Subject Category: Applied Sciences subject area: Environmental management/policy

ABSTRACT

The quantity of pharmaceutical waste generated at the household level has steadily increased owing to societal changes and expansion of pharmaceutical production. Consequently, the management of household pharmaceutical waste (HPW) has become a growing environmental and public health challenge. Improper disposal practices, particularly the landfilling of antibiotics and other hazardous medicines, pose significant risks to ecosystems and human health. This study provides a comparative assessment of HPW management in Albania relative to practices adopted in selected European countries and proposes recommendations for establishing a functional national HPW management system in the country. Public awareness and pharmacists' perceptions are key factors in achieving sustainable waste management outcomes. A survey was conducted among pharmacists in the Municipality of Tirana between January and March 2024; questionnaires administered via Google Forms collected responses from 150 citizens and 50 pharmacists. The sample consisted predominantly of females (73%), primarily within the 20–40 age group, with 97% of respondents holding higher education qualifications. The results here reported indicate that the quantity of pharmaceutical waste stored in households is relatively low. Approximately 86% of participants preferred receiving information through digital and print media, while 55% identified consultation with physicians and pharmacists as the most effective communication approach. Among the pharmacists, 86% reported refusing expired or unused medicines from patients, despite minimal public demand. Furthermore, 88% of respondents indicated an unwillingness to bear the costs associated with HPW management. The findings reveal that Albania's legislative and regulatory framework for HPW is fragmented, leading to ambiguity regarding institutional responsibilities, competencies, and administrative roles. Strengthening regulatory coherence, improving stakeholder engagement, and enhancing public education are essential steps toward establishing an effective household pharmaceutical waste management system.

Keywords: Pharmaceutical waste, expired drugs, unused drugs, pharmaceutical disposal, household hazardous waste

1. INTRODUCTION

The consumption of pharmaceuticals has expanded to an industrial scale, resulting in their widespread presence in households, frequently in surplus or unnecessary quantities. Beyond households, pharmaceuticals are ubiquitous in workplaces and public spaces, as well as in institutions where their use is foundational, ranging from pharmaceutical supply chain entities to tertiary hospital centers. Household pharmaceutical waste (HPW) is classified as household hazardous waste and encompasses a broad spectrum of materials with diverse hazardous properties. The formal definition of waste is established in Article 3 of the Waste Framework Directive (WFD) 2008/98/EC, as amended by Directive (EU) 2018/851 under the Circular Economy Waste Package.

The study was conducted in the Municipality of Tirana, the most populous region in Albania, accounting for approximately 32% of the national population (INSTAT, 2023). Tirana generates the highest share of hospital waste nationwide, representing approximately 60% of the total (State of the Environment Report, 2024). As hazardous waste,pharmaceutical waste must be treated exclusively by operators licensed by the National Environmental Agency in accordance with harmonize national standards.

This study aimed to identify existing mechanisms for the collection, processing, and disposal of household pharmaceutical waste (HPW) in Tirana, as well as legislative and regulatory gaps, through a comparative analysis with European Union (EU) best practices. The methodology involved the collection of qualitative and quantitative data, an audit of legislative documents, and structured interviews with citizens and pharmacists in the municipality of Tirana. Preliminary findings revealed substantial discrepancies between Albanian practices and EU standards. According to the Environmental Protection Agency (EPA, 2015), the production of 1 kg of herbal pharmaceutical products generates an environmental factor (E-factor) of approximately 100 kg of waste across the lifecycle. While the majority of this waste is non-hazardous, approximately 20% (Meçaj *et al.* 2021), is classified as hazardous.

In Albania, no district-level system exists for managing HPW. Consequently, such waste is frequently disposed of via improper routes, such as sewage discharge (flushing) or co-mingling with municipal solid waste. Conversely, pharmacies are mandated to follow regulated hazardous waste protocols via annual contracts with licensed providers, as stipulated in Chapter IV, Articles 12–13 of the Hazardous Waste Management Regulation (MMR, 2006). These contracts typically cover a baseline of 20 kg annually; however, implementation remains inconsistent across municipalities. These contracts typically cover up to 20 kg of waste annually, with additional charges for excess quantities. However, the implementation of these provisions remains partial and inconsistent across municipalities.

The release of pharmaceutical residues into the biosphere poses significant risks to human health and ecosystems (Aliko *et al.* 2021). Active pharmaceutical ingredients (APIs) enter aquatic systems through human excretion, direct disposal, and hospital effluents—the latter being a primary point source of pollution (Kümmerer, 2009).

Monitoring of pharmaceutical residues in Albanian surface and groundwater remains sparse, although research into hospital wastewater is increasing. According to the World Health Organization (WHO, 2023), untreated antibiotics and cytotoxic medicines can contaminate drinking water sources and enter the food chain (Sahu, 2024). While incineration is the preferred final treatment, unsafe practices like open burning release hazardous atmospheric pollutants and contaminate soil via ash deposition.

Despite international recognition of these risks, Albania lacks a systematic framework for managing household pharmaceutical waste (HPW). While environmental and health hazards are well documented, comprehensive, standardized, and accessible mechanisms for the separate collection and safe treatment of HPW are absent. In practice, expired or unused medicines are routinely disposed of through municipal waste streams or wastewater systems, increasing the risk of environmental contamination. This gap reflects shortcomings in regulatory enforcement, public awareness, and infrastructure, as well as the absence of clearly defined Extended Producer Responsibility (EPR) throughout the pharmaceutical supply chain.

The determination of antibiotic concentrations in water samples is a critical analytical component. Antimicrobial resistance (AMR) has been a global concern for over a decade (WHO, 2020), as bacteria exposed to sub-lethal concentrations of antibiotics in sludge or aquatic environments can develop resistance. Healthcare facilities continuously release a spectrum of compounds, including antibiotics, sedatives, antipyretics, and antineoplastic agents. Simultaneously, medications administered to humans and animals—such as hormones and analgesics—have been detected in potable water supplies (Kümmerer, 2009). Significant quantities of pharmaceuticals enter the biosphere through effluent discharge, sewage sludge application, and the use of organic fertilizers.

Several studies in Albania have documented specific pharmaceutical groups, such as antibiotics and beta-blockers, in river systems (Nuro *et al.* 2016) and their associated impacts on aquatic biota (Aliko *et al.* 2019). During the COVID-19 pandemic, elevated concentrations of pharmaceutical residues were detected in water bodies and algal communities (Tahiri *et al.* 2023). Further investigations indicate that antidepressants and anti-inflammatory drugs adversely affect amphibian development by delaying metamorphosis and reducing body mass, while studies on fish in lotic ecosystems have revealed neurotoxicity and altered swimming behavior (Aliko *et al*. 2021). These findings support the utilization of these species as sentinel bioindicators of pharmaceutical contamination.

1.1 Legal and Regulatory Framework for Pharmaceutical Waste Management

The Republic of Albania currently lacks specific primary or secondary legislation that regulates pharmaceutical waste as an independent category (Kuvendi i Republikës së Shqipërisë, 2004). Instead, pharmaceutical waste is categorized as a specialized subset of healthcare risk waste (Kuvendi i Republikës së Shqipërisë, 2006) and is addressed within the broader legislative framework governing clinical waste and medicinal products (Kuvendi i Republikës së Shqipërisë, 2009; 2011).

The primary regulatory instruments include:

Decision of the Council of Ministers (DCM) No. 798 (29.09.2010)

This instrument ratified the "Regulation on the Management of Hospital Waste," which provides the following technical definitions:

1. **Pharmaceutical waste:** Includes expired or unused medicinal products; residues from spills or environmental exposure; surplus medications; vaccines and sera; and ancillary materials used during handling, such as primary packaging (tubes, vials) and Personal Protective Equipment (PPE).
2. **Hazardous waste:** Includes infectious, pathological, and sharps waste; pharmaceutical residues; cytotoxic substances; chemical and radioactive materials; and contaminated solvents or aqueous effluents.

Decision No. 402 (30.06.2021)

This legislative act, "On the Approval of the Waste Catalog," established a classification system harmonized with the European Waste Catalogue (EWC). Under this framework, pharmaceutical waste is classified under Chapter 18 ("Wastes from Human or Animal Healthcare and/or Related Research"), specifically:

- 18 01 08*: Cytostatic and cytotoxic medicinal products (classified as hazardous waste).
- 18 01 09: Medicinal products other than those mentioned in 18 01 08 (non-hazardous).

Furthermore, the National Guide for the Safe Management of Hospital Waste, adopted via Ministerial Order No. 17 (12.01.2012), provides supplementary technical protocols for healthcare institutions and licensed waste management operators.

A household pharmaceutical waste survey was conducted in the Municipality of Tirana—the largest administrative division in Albania—

to assess citizen behaviors regarding waste generation and pharmacists' perspectives on its management. Two distinct surveys were administered: one targeting private citizens and the other targeting licensed pharmacists.

The citizen survey targeted respondents likely to generate HPW who were accessible via digital platforms. The pharmacist survey included practitioners within Tirana, selected for their central role in the pharmaceutical supply chain and their potential integration into future take-back schemes.

2.1 *The public questionnaire*

A survey assessing attitudes toward expired and unused medicines was conducted during the first quarter (Q1) of 2024. Data were collected via a semi-structured questionnaire comprising 12 questions, administered to 175 residents of Tirana through Google Forms and distributed via REC Albania social media channels.

The questionnaire was designed as a validated instrument to address key dimensions: environmental awareness, waste typology, disposal habits, willingness to participate in formal collection, and perceptions of institutional responsibility. A quantitative research approach using non-probability convenience sampling was applied. The instrument was reviewed and adapted with expert input from the Order of Pharmacists of Albania to reflect local consumption patterns.

2.2 *The pharmacist questionnaire*

A concurrent survey was conducted between February and March 2024 among 50 pharmacists. Using a quantitative approach and supported by the Order of Pharmacists of Albania, a semi-structured questionnaire of eight questions was developed, organized into two thematic sections:

1. **Operational Perceptions:** Existing waste management practices and preferred management models.
2. **Regulatory Literacy:** Knowledge of the legal framework and professional evaluation of current infrastructure.

Pharmacists were queried on their acceptance of returned medicines, annual waste volumes, predominant pharmaceutical categories, and fiscal responsibility for waste management.

2.3 *Pilot point methodology*

The methodology included an initial six-month preparatory phase encompassing legal analysis, stakeholder consultations, and inter-institutional coordination.

A pilot scheme was subsequently implemented across five public health centers (HC No. 1, 4, 6, 7, and 10), selected in coordination with the Ministry of Health and Social Protection. A dedicated 1 m^2 area within each facility's main hall was allocated for controlled HPW collection.

A licensed hazardous waste management company was contracted for the transportation, storage, and final disposal (valorization or incineration). Sites were equipped with compliant healthcare waste containers, awareness posters, and signage specifying that the bins were restricted to expired or unused household medications.

1. 3. RESULTS AND DISCUSSION

3.1 Results of public' opinions

Among the 175 respondents, 73% were female. While gender was not a primary variable for assessing awareness, this demographic skew suggests that female participants may demonstrate a higher propensity for engagement with pharmaceutical waste management issues. The majority of participants were aged between 20 and 40 years. This distribution likely reflects the sampling bias inherent in digital dissemination; social media platforms are predominantly utilized by younger cohorts, whereas older populations—who may have higher medication consumption rates—are more effectively reached through traditional media or clinical settings. In terms of educational attainment, 97% of respondents reported holding a university degree, indicating a highly educated sample.

Regarding disposal behaviors, 92% of respondents reported discarding expired or unused medicines with municipal solid waste (MSW) (Figure 1), citing convenience as the primary driver. A small cohort reported disposing of liquid or crushed medications via sanitary sewer systems (toilets), under the erroneous perception that this method was secure. Alternative disposal methods, such as open combustion or the use of designated pharmaceutical collection bins, were negligible. The latter is attributable to the systemic lack of specialized collection infrastructure in Albania, outside of isolated pilot initiatives.

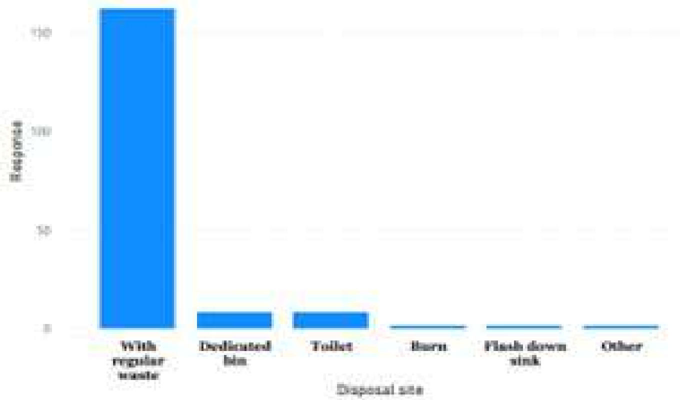

Fig. 1. Disposal methods of expired/unused pharmaceutical products by citizens of Tirana.

Regarding the volume of expired or unused medicinal products stored in households, 86% of respondents reported generating "minimal quantities" (fewer than ten units), while 12% reported "moderate quantities" (approximately twelve units), and only 2% indicated volumes exceeding twelve units. These results align with anticipated household-level HPW generation patterns; however, while individual quantities remain low, they constitute a significant aggregate waste stream when scaled to the municipal level.

In terms of therapeutic classification, antipyretics and analgesics were the most frequently discarded medications, representing 53% of the total, followed by vitamins at 24%. Notably, antibiotics accounted for 16% of the reported waste—a significant finding given the associated risks of antimicrobial resistance. Other categories were less prevalent, with antihistamines and antacids accounting for 6% and 1% of the responses, respectively (Figure 2).

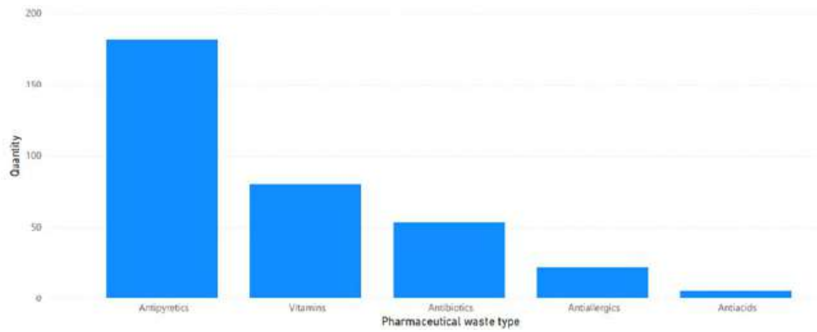

Fig. 2. Types of household pharmaceutical waste generated by interviewed citizens.

Regarding awareness of the environmental and public health implications of improper disposal, the respondent pool was nearly evenly divided: 51% reported being moderately informed, while 49% indicated a complete lack of knowledge regarding the potential ecological and health consequences.

In the absence of a dedicated HPW management system in Albania, respondents demonstrated significant ambiguity concerning appropriate disposal pathways. When queried on the ideal disposal method, 51% identified pharmacies as the preferred point of collection, whereas 47% favored source-separated municipal waste collection (Figure 3). A small minority (3%) perceived aqueous discharge (flushing) as an acceptable method, highlighting persistent behavioral misconceptions and the urgent need for targeted public health communication regarding the risks of pharmaceutical residues in water systems.

The deficit in public awareness regarding the risks of improper HPW disposal represents a challenge comparable in magnitude to the logistical problem of disposal itself. Consequently, bridging knowledge gaps regarding regulatory collection pathways and hazardous waste management is essential. When queried on preferred outreach strategies, 64% of respondents identified mass communication channels (including digital platforms and informational leaflets) as the most effective, while 55% favoured clinical counselling provided by physicians and pharmacists.

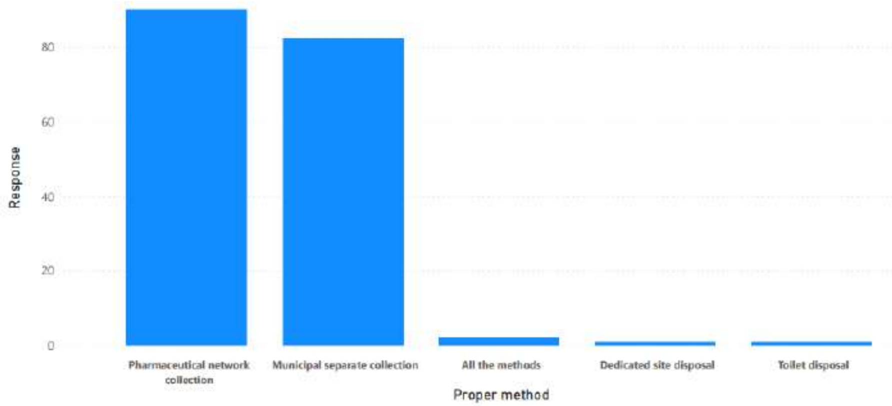

Fig. 3. The opinion of citizens about the best method for pharmaceutical waste disposal.

Regarding participation, 77% of respondents expressed a readiness to cooperate with a dedicated management system, with 21% remaining neutral. Notably, 99% of participants supported the establishment of collection points, provided they are geographically accessible (proximate to their residences).

3.2 Results of pharmacists' opinions

A total of 51 pharmacies participated in the survey, representing approximately 18% of the 281 facilities registered with the Compulsory Health Care Insurance Fund (SDKSH) in the Municipality of Tirana. A significant majority (86%) of pharmacists reported that they do not facilitate take-back services for patients. The 14% who did accept returns reported doing so despite the unsubsidized financial burden incurred.

In terms of public demand, 59% of pharmacists reported that return requests occur "almost never," while 31% described them as "rare." Only 10% noted frequent requests. Regarding institutional waste, 75% of pharmacies reported that their internal waste generation did not exceed the 20 kg annual threshold stipulated in their hazardous waste contracts.

Regarding fiscal responsibility, 69% of pharmacists asserted that management costs should be borne by state institutions, while 23%

identified pharmaceutical wholesalers as the responsible party (Figure 4). Only a negligible proportion (2.5%) believed citizens should pay. Critically, 88% of pharmacists expressed opposition to assuming these costs, citing the absence of a legal mandate or an Extended Producer Responsibility (EPR) framework.

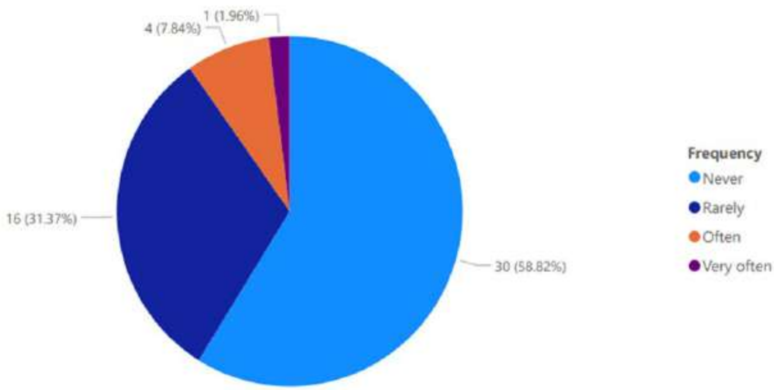

Fig. 4. The frequency with which pharmacies are asked to accept pharmaceutical products.

Public awareness regarding the risks of improper HPW disposal remains insufficient. As pharmacies constitute the primary interface between the healthcare system and the public, pharmacists are uniquely positioned as frontline interlocutors for disposal inquiries. Approximately 82% of respondents emphasized that enhancing patient literacy is critical for a functional waste management system. An additional 8% deemed it "somewhat important," while 10% viewed it as "unimportant."

Regarding regulatory literacy, 69% of pharmacists reported being informed of the Albanian legal framework, while 31% identified as uninformed. However, only 41% of the total sample perceived the framework as "clear." Within this subgroup, a significant majority (33% of the total sample) characterized the regulations as "clear but operationally challenging," while only 8% described them as "clear and feasible." The remaining respondents expressed structural concerns: 23% categorized the framework as incomplete, 10% as vague/unclear, 10% as inappropriate for the local context, and 16% reported informational insufficiency.

3.3 Results of the piloting process on four pilot points

During the four-month monitoring period, HPW collection at the pilot health centers remained minimal, ranging from 0.8 kg to 1.2 kg per facility (Table 1). While these quantities are modest, they establish a critical empirical baseline for evaluating the longitudinal effectiveness of future interventions. Public awareness of standardized disposal protocols was consistently low across all pilot locations, emphasizing the necessity for targeted social marketing and communication strategies.

All monitored health centers exhibited non-segregated waste streams, indicating a failure in source separation and primary storage protocols. Implementation challenges included low staff compliance regarding the introduction of specialized disposal units, primarily driven by concerns over occupational safety and operational ergonomics. Additional barriers included ambiguous procedural guidelines and a deficit in specialized staff training.

Overall, the pilot findings demonstrate sub-optimal system efficiency and underscore the requirement for continuous monitoring, enhanced public education, expanded staff capacity-building, and robust inter-institutional coordination to ensure the long-term operational viability and sustainability of the HPW management system.

Table 1. First-month results of pharmaceutical waste monitoring from Tirana citizens at four pilot sites.

Healthcare centers	**Amount of pharmaceutical waste (kg)**	**Public awareness**	**Variety of pharmaceutical waste**	**Challenges faced**
HC-1	1.1 kg	Low	Mix	Other Waste
HC-4	0.8 kg	Low	Mix	Other Waste
HC-4	0.9 kg	Low	Mix	Other Waste
HC-4	1.2 kg	Low	Mix	Other Waste

This study highlights the marked divergence between pharmaceutical waste management in Albania and established European benchmarks. Significant progress is required, as a comprehensive national framework remains largely absent. In many European jurisdictions, expired or unused medicines are returned directly to community pharmacies, where reverse logistics are coordinated by economic operators and subsidized by competent public authorities.

In Albania, however, substantial ambiguity persists regarding the competencies and administrative roles of institutional actors. While HPW is classified as hazardous under Law No. 9537 (On the Management of Hazardous Waste), applying identical regulatory requirements to households as to tertiary healthcare institutions exposes a significant structural implementation gap. This disparity reflects a lack of infrastructural capacity and institutional support throughout the domestic pharmaceutical supply chain.

Pharmacies occupy a strategic yet precarious position in this landscape. As the primary interface between the public and medicinal products, they are ideally situated as collection nodes. Nevertheless, private pharmacies demonstrate systemic resistance to assuming the operational and fiscal burdens of HPW. This is not merely behavioral but structural, stemming from a lack of cost-sharing mechanisms and regulatory clarity. Current arrangements for managing obsolete inventory through private contracts do not account for the additional volumes generated by the public, leading to increased liability and operational uncertainty for pharmacists.

From a policy perspective, this tension underscores the limitations of a "compliance-only" approach that ignores economic feasibility. To address this imbalance, Albania must prioritize:

1. Extended Producer Responsibility (EPR): Redistributing costs to manufacturers and importers.
2. Incentive-based Governance: Providing financial compensation or tax offsets for pharmacies acting as collection points.
3. Regulatory Harmonization: Aligning the draft national waste management law with EU Circular Economy principles.

The pilot implementation at health centers yielded minimal recovery, likely due to lower public accessibility compared to retail pharmacies. Consequently, this study concludes that community pharmacies represent the most viable alternative for HPW collection, provided they are supported by a clear legal mandate and a functional state-funded reclamation system. Without such alignment, environmental and public health risks will persist, and the gap between regulatory intent and on-the-ground implementation will continue to widen.

Ethics. Formal ethical approval was deemed not applicable for this study as it did not involve clinical interventions. All survey participants provided informed consent regarding anonymity. No data subject to Law No. 10/2023 ("On Information Classification") or Law No. 9887 ("On the Protection of Personal Data") were compromised, disclosed, or otherwise breached.

Data sharing statement. Data supporting the findings and conclusions are available upon request from the corresponding author.

Authors' contributions. M.Q., and N.M: conceptualization; M.Q.: methodology; N.M.: investigation, and resources; M.Q., and N.M.: drafting- data collection and reporting, formal analysis; M.Q.: supervision.

Both authors agreed with the results and conclusions.

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AI statement. A Large Language Model (ChatGPT 5.0) was utilized exclusively for **linguistic refinement** and improving the quality of the English text. The authors maintain full responsibility for the data interpretation, scientific content, and final wording of the manuscript.

Declaration of interest. The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

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RESIDUAL CHLORINE DEFICIENCY AND WATERBORNE DISEASE PATTERNS IN A MUNICIPAL WATER SUPPLY SYSTEM: A ONE-YEAR ASSESSMENT

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ABSTRACT

Effective disinfection is essential for maintaining drinking water quality and protecting public health from waterborne diseases. This study presents a one-year assessment of the disinfection process in the municipal water supply of Vlora, focusing on residual chlorine levels and treatment effectiveness in relation to health outcomes. A total of 8,029 water samples were analyzed for residual chlorine, microbiological indicators, and physicochemical parameters. Results showed that 4.5% of samples had critically low residual chlorine levels (0–0.1 mg/L), with simultaneous occurrences across all sampling points on certain dates, indicating systemic disinfection failures. Although laboratory results for *Escherichia coli* and key physicochemical parameters (NH_4^+, NO_2^-, NO_3^-, turbidity, and pH) remained within regulatory limits, epidemiological data revealed increased waterborne illnesses, particularly gastroenteritis. Cases peaked in August (1,117 cases; 33.5%) and July (752 cases; 22.6%). This discrepancy highlights the limitations of relying solely on conventional indicators for water safety assessment. The coexistence of low residual chlorine levels and increased disease incidence suggests gaps in disinfection performance. Overall, the findings emphasize the need for improved treatment technologies and stronger management strategies to ensure safe drinking water and support long-term public health protection.

Keywords: drinking water quality, disinfection, residual chlorine, waterborne diseases, public health, water treatment

1. INTRODUCTION

Ensuring access to microbiologically safe drinking water remains a fundamental pillar of public health (WHO, 2017). Disinfection is a critical component of water safety, essential for controlling waterborne pathogens and mitigating the risk of disease outbreaks. Despite advancements in infrastructure and treatment technologies, the effectiveness of disinfection is often compromised by operational shortcomings, inconsistent chlorine dosing, and challenges within the distribution systems.

Residual chlorine is widely recognized as a key indicator of effective disinfection due to its ability to maintain microbial control throughout the distribution network. In some countries, alternative disinfection methods, such as ozonation, are also employed, particularly in systems where reducing chemical by-products or improving taste and odor is a priority. Ozone is a powerful oxidant capable of inactivating a broad range of pathogens, including viruses, bacteria, and protozoa. However, due to its lack of residual disinfectant effect and the high cost of implementation, its use is typically limited to high-capacity urban systems or as a pre-treatment stage combined with secondary chlorination (Bartram and Hunter, 2015). Nonetheless, chlorine-based disinfection remains the most widely used method globally because of its cost-effectiveness and ability to provide lasting residual protection.

However, the effectiveness of chlorine can be affected by factors such as ageing infrastructure, environmental variability, operational failures, and increasing population demands. These factors may compromise disinfection performance and increase vulnerability to contamination.

Although routine monitoring often shows compliance with microbiological and physicochemical standards, epidemiological data have revealed public health risks linked to undetected weaknesses in water treatment and distribution systems (Payment and Hunter, 2001; Craun *et al.* 2010). This is particularly evident in developing contexts, where operational and infrastructural limitations frequently undermine disinfection efficacy (Montgomery and Elimelech, 2007).

This study presents a one-year technical assessment of disinfection performance in the public water supply system of Vlora, a coastal city in southern Albania. The analysis focuses on residual chlorine levels, their correlation with microbiological contamination, and associated health outcomes. The study aims to highlight limitations of standard monitoring approaches and emphasize the importance of integrating technical assessments with operational surveillance in managing drinking water quality.

The aim of this study is to technically assess the disinfection performance of a public drinking water supply system through the analysis of residual chlorine levels, their spatial and temporal variations, and their correlation with microbiological contamination and reported health outcomes over a one-year monitoring period in Vlora, Albania.

Ensuring access to microbiologically safe drinking water remains a fundamental pillar of public health, as emphasized by the World Health Organization (WHO, 2017). Disinfection represents a critical component of water safety management, playing a central role in controlling waterborne pathogens and preventing disease outbreaks. Among available methods, chlorination remains the most widely applied approach globally due to its cost-effectiveness and its ability to maintain a residual disinfectant throughout the distribution system (Bartram and Hunter, 2015).

Residual chlorine is widely recognized as a key indicator of disinfection performance, as it reflects the capacity to sustain microbial control within water distribution networks. However, several studies have demonstrated that residual chlorine levels may fluctuate due to ageing infrastructure, operational deficiencies, environmental variability, and changes in water demand, potentially compromising the integrity of the disinfection barrier (Montgomery and Elimelech, 2007). Such variability may increase vulnerability to contamination, even in systems that are otherwise considered compliant.

Although alternative disinfection methods, such as ozonation, have been introduced in some settings to improve water quality and reduce disinfection by-products, their lack of residual effect and higher operational costs limit their widespread implementation. As noted by Bartram and Hunter (2015), ozone is primarily used as a pre-treatment stage, typically followed by secondary chlorination to ensure residual protection within the distribution system.

Importantly, compliance with routine microbiological and physicochemical standards does not always guarantee protection of public health. Evidence from epidemiological investigations indicates that outbreaks of waterborne diseases may occur even when conventional regulatory parameters remain within acceptable limits (Payment and Hunter, 2001; Craun *et al.* 2010). This discrepancy highlights the limitations of relying exclusively on standard laboratory indicators to assess water safety, particularly in systems affected by operational and infrastructural constraints (Montgomery and Elimelech, 2007).

Despite extensive research on drinking water quality, a key gap remains in the limited integration of technical monitoring data with epidemiological evidence in real-world municipal systems. Previous studies have often examined disinfection performance and disease outcomes separately, fewer have systematically evaluated their relationship over time (Bartram *et al*. 2014). Addressing this gap is essential for improving understanding of how disinfection deficiencies may translate into measurable public health risks.

This study addresses this gap by providing a one-year integrated assessment of disinfection performance in the public water supply system of Vlora, Albania. By analyzing residual chlorine levels alongside microbiological, physicochemical, and epidemiological data, this study aims to identify systemic weaknesses in the disinfection process and their implications for public health. In particular, it contributes to the limited body of research examining residual chlorine dynamics in relation to health outcomes in real-world municipal distribution systems, especially in transitional infrastructure settings. Furthermore, it evaluates the discrepancy between compliance with physicochemical parameters—such as nitrites, nitrates, and ammonium—and the occurrence of waterborne disease. In this context, the present study contributes by providing an integrated assessment of disinfection performance and epidemiological patterns over a one-year period, highlighting the limitations of conventional monitoring approaches in fully capturing public health risks.

2. MATERIALS AND METHODS

Study Area

The present study was carried out in Vlora, a coastal city in southern Albania, characterized by a significant seasonal influx of tourists during the summer months. The city has a centralized water supply network that provides drinking water to both permanent residents and seasonal visitors.

Sampling and Water Quality Analysis

Between January and December 2023, a total of 8029 water samples were collected from various points within the municipal water distribution system. Sampling locations included main supply lines, storage reservoirs, and peripheral consumer endpoints. Each sample was analyzed for:

- Residual chlorine levels (mg/L),
- Microbiological indicators (*Escherichia coli*),
- Physicochemical parameters including ammonium (NH_4^+), nitrite (NO_2^-), nitrate (NO_3^-), turbidity, and pH.

All the analytical procedures were conducted in accordance with the national drinking water legislation of Albania (CoM, 2016) and aligned with international regulatory frameworks (Directive (EU) 2020/2184; EPA, 2022). Once collected, samples were analyzed for residual chlorine levels using portable chlorine meters. Microbiological analyses were conducted using the membrane filtration method for the enumeration of *Escherichia coli*, in accordance with the relevant ISO standard (ISO, 2014). When membrane filtration could not be applied, the multiple-tube fermentation technique was used as an alternative. Laboratory examination of physicochemical parameters employed the Standard Methods for the Examination of Water and Wastewater (APHA, 2017).

Epidemiological Data Collection

Epidemiological data on waterborne diseases were obtained from the Regional Health Directorate of Vlora. Specifically, monthly reported cases of acute gastroenteritis were collected and analyzed in parallel with water quality indicators. These data were used to assess temporal trends and potential correlations between disinfection performance and disease incidence.

Epidemiological Data Collection

Epidemiological data on waterborne diseases, specifically monthly reported cases of acute gastroenteritis, were obtained from the Vlora Regional Health Directorate. These data were collected on a monthly basis and analyzed in parallel with water quality indicators to assess temporal trends and potential relationships between disinfection performance and disease incidence.

Water Sampling and Frequency

Water samples were routinely collected from multiple fixed sampling points distributed throughout the municipality's water supply network. Sampling was performed regularly throughout the study period, with frequency varying according to operational monitoring protocols. In total, 8029 water samples were analyzed during the 12-month period, ensuring comprehensive spatial and temporal coverage of the distribution system.

Laboratory Analysis and Quality Control

All water samples were analyzed at the regional public health laboratory in accordance with standard methods for drinking water analysis and relevant regulatory guidance, including the WHO Guidelines for Drinking-water Quality (WHO, 2017). Residual chlorine was measured using standard colorimetric methods.

Quality control procedures included the use of calibrated instruments, routine analysis of blank and duplicate samples, and adherence to the laboratory's internal quality assurance protocols for the accuracy and reproducibility of results.

Statistical Analysis

Given the non-normal distribution of the data, Spearman's rank correlation coefficient (ρ) was used to assess the relationship between the monthly number of samples with residual chlorine levels below 0.5 mg/L and the monthly incidence of gastroenteritis cases. Statistical significance was assessed at a threshold of $p < 0.05$.

To explore temporal relationships, water quality data and epidemiological data were compared on a monthly basis. Given the level of data collection available, formal time-lagged or regression analyses were not applied. Instead, descriptive and correlational analyses were used to identify patterns and trends between disinfection performance and disease incidence.

The distribution of variables was assessed using descriptive statistics and visual inspection, confirming non-normal distribution and supporting the use of non-parametric statistical methods.

3. RESULTS AND DISCUSSIONS

During January–December 2023, a total of 8,029 water samples were analyzed across the Vlora municipal distribution network. Of these, 18.7% showed residual chlorine ≤0.2 mg/L, while 4.5% had critically low levels (0–0.1 mg/L), indicating insufficient disinfection. On several summer dates, these low values were recorded simultaneously across all sampling points, suggesting systemic chlorination failure.

Despite these deficiencies, microbiological and physicochemical parameters, including Escherichia coli, ammonium (NH_4^+), nitrite (NO_2^-), nitrate (NO_3^-), turbidity, and pH, remained within national and WHO standards (WHO, 2017). However, epidemiological data revealed a pronounced seasonal increase in gastroenteritis, peaking in August (1,117 cases; 33.5%) and July (752 cases; 22.6%), together accounting for 56% of annual cases. This temporal overlap with reduced residual chlorine levels suggests a gap in microbial barrier protection not captured by routine indicators (WHO/UNICEF, 2021). As shown in Table 1, suboptimal residual chlorine levels (<0.5 mg/L) were consistently observed, with the most pronounced deficiencies in January, March, July, and August. In July, no samples reached ≥0.5 mg/L, while in August values were predominantly around 0.3 mg/L, indicating reduced disinfection during peak demand. This pattern is further supported by Table 2, which demonstrates that July (682 samples <0.5 mg/L) and August (640 samples) coincided with the highest number of gastroenteritis cases, together accounting for 17.6% of all low-chlorine samples but 56% of total annual cases.

Table 1. Monthly residual chlorine levels (mg/L) recorded in the municipal water distribution system of Vlora, January–December 2023 mg/L

Months	0 mg/l	0.1 mg/l	0.2 mg/l	0.3 mg/l	0.4 mg/l	0.5mg/l	0.6mg/l
January	88	121	212	139	88	34	0
February	8	30	216	272	73	17	0
March	22	30	81	352	179	18	0
April	0	0	27	162	344	126	0
May	0	4	11	336	303	28	0
June	0	22	41	308	274	15	0
July	0	2	421	19	240	0	0
August	2	0	86	456	96	26	16
September	2	1	31	395	231	0	0
October	2	0	7	395	185	60	33
November	23	0	15	266	311	45	0
December	0	0	0	187	373	122	0

Table 2. Monthly distribution of water samples with residual chlorine <0.5 mg/L and reported gastroenteritis cases during 2023

Month	Samples <0.5 mg/L	Gastroenteritis Cases
January	648	76
February	599	67
March	664	59
April	533	57
May	654	92
June	645	128
July	682	752
August	640	1117
September	660	443
October	589	308
November	615	112
December	560	118

These trends are visually confirmed in Figure 1, which shows the monthly distribution of samples with residual chlorine <0.5 mg/L, with a clear peak in July, and in Figure 2, which provides a detailed breakdown of chlorine levels during July–August, confirming insufficient disinfection during peak consumption periods.

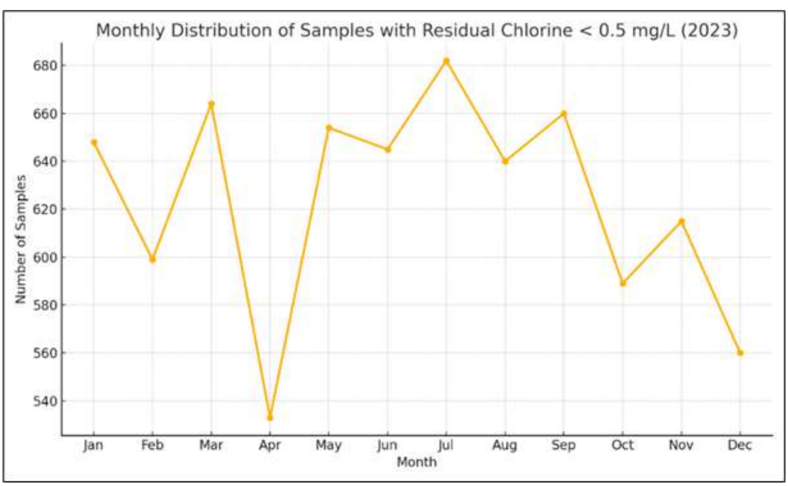

Fig.1: Monthly distribution of water samples with residual chlorine below <0.5 mg/L in Vlora, (January–December 2023).

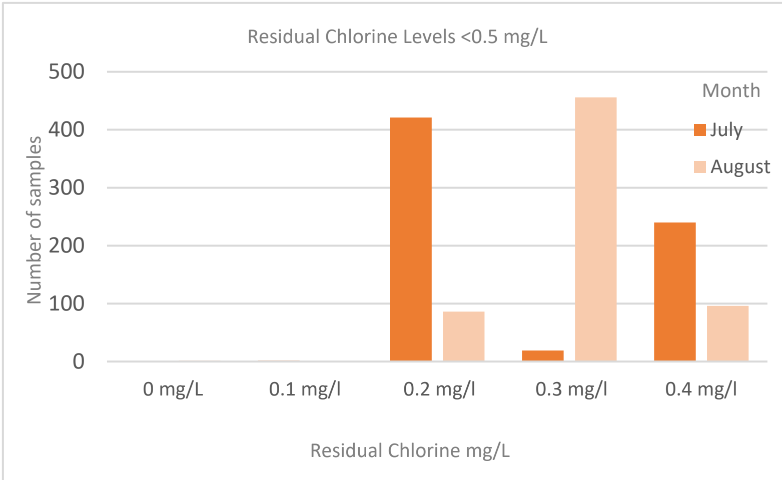

Fig. 2. Monthly distribution of drinking water samples with residual chlorine levels below 0.5 mg/L, July–August 2023.

Physicochemical parameters remained stable throughout the study and showed no temporal association with disease incidence. Correlation analysis (Table 3) revealed a weak, non-significant relationship between residual chlorine <0.5 mg/L and gastroenteritis incidence (Spearman $\rho = 0.252$, $p > 0.05$), indicating that chlorine deficiency alone does not fully explain disease patterns. Additional factors, including increased water demand, higher temperatures, hydraulic inefficiencies, and potential undetected pathogens, likely contributed to the observed seasonal increase in disease incidence.

Table 3. Spearman correlation between the number of samples with residual chlorine <0.5 mg/L and monthly gastroenteritis cases.

Variable	Spearman ρ	p-value	Interpretation
Samples <0.5 mg/L vs Gastroenteritis cases	0.252	>0.05	Weak positive, not statistically significant

These findings highlight important vulnerabilities in the Vlora water supply system. Similar discrepancies between water quality compliance and public health outcomes have been reported elsewhere (Egorov *et al.* 2003; O'Connor, 2002). Seasonal increases in water demand can accelerate chlorine decay and reduce disinfection efficiency within distribution systems (Fisher and Kastl, 2010; Le Chevallier and Au, 2004).

While maintaining adequate residual chlorine is essential for microbial control, excessive chlorination may produce harmful disinfection by-products (Richardson *et al.* 2007; Li and Mitch, 2018). Therefore, optimized dosing and improved operational control are required.

Overall, the results emphasize the need to shift from compliance-based monitoring to integrated, risk-based water quality management. This approach should combine continuous residual chlorine monitoring, advanced operational tools (e.g., real-time sensors, hydraulic modeling), and epidemiological surveillance to better identify and mitigate public health risks, particularly in systems affected by seasonal demand variability (WHO/UNICEF, 2021; WHO, 2017).

4. CONCLUSION

This study identifies critical vulnerabilities in the drinking water safety management of Vlora, particularly in relation to disinfection performance within the municipal distribution system. Although routine microbial and physicochemical analysis remained within acceptable limits, persistently low residual chlorine concentrations revealed important deficiencies in operational control and system monitoring. These findings suggest that conventional compliance alone may be insufficient to ensure effective protection of public health, especially during periods of increased seasonal water demand.

The discrepancy observed between standard laboratory indicators and the epidemiological pattern of gastroenteritis cases highlights the limitations of relying exclusively on routine testing to assess drinking water safety. In systems affected by ageing infrastructure, hydraulic instability, or fluctuating demand, traditional indicators may fail to detect short-term or localized failures in the disinfection barrier.

Accordingly, effective water safety management should move beyond static compliance-based monitoring toward a more integrated and adaptive framework that combines continuous technical surveillance—including real-time residual chlorine monitoring—with epidemiological oversight and operational risk assessment. Strengthening disinfection control, improving infrastructure resilience, and implementing responsive management strategies are essential for building a safer, more sustainable, and climate-resilient municipal water supply system capable of meeting future public health challenges.

Ethics. This study used aggregated routine surveillance data on water quality and reported gastroenteritis cases obtained from the Regional Health Directorate of Vlora and the Institute of Public Health, Albania. No individual or identifiable personal data were used. Therefore, ethical approval was not required under national regulations for public health surveillance studies. All data were analyzed in anonymized form in accordance with the Declaration of Helsinki and applicable data protection principles.

Data accessibility. https://www.ishp.gov.al

Declaration of AI use. There has been no use of AI when writing the actual paper.

Author Contributions. SHP- Conceptualization; writing of the original draft; structuring the manuscript; coordinating the study framework; Data collection; database development and data entry; data organization and preparation for analysis. EM- Methodology; epidemiological analysis of data; interpretation of results; writing - review and editing; technical editing; final manuscript review. AS- Statistical analysis; validation of analytical procedures; methodological support; interpretation of statistical findings.

All the authors have approved the final version of the manuscript

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SEASONAL DYNAMICS OF POTENTIALLY TOXIC PHYTOPLANKTON IN THE BUTRINTI LAGOON (SOUTHERN ALBANIA)

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Research
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ABSTRACT

Data on potentially toxic phytoplankton in the Butrinti Lagoon (Saranda) during 2024 are this paper reported. The dominant genus observed was *Pseudo-nitzschia* spp., a group of diatoms (microscopic algae) that constitutes an important component of marine phytoplankton communities. These microalgae commonly form chain-like colonies that are visible under microscopic investigation. Certain species within this genus are known to produce domoic acid, a neurotoxin that can accumulate through the food chain, affecting marine organisms and posing a risk to human health. Harmful algal blooms (HABs) associated with *Pseudo-nitzschia* represent a serious threat to food safety, biodiversity, and the fisheries. In Butrinti Lagoon, peak abudance of *Pseudo-nitzschia* spp. was recorded in February, reaching a maximum of 291,060 cells L^{-1}, while the lowest values were observed during the summer months. No other potentially toxic algae were detected, except for *Prorocentrum cordatum (P. minimum)*, which reached a maximum of 560 cells L^{-1} in March. Regular monitoring of potentially toxic phytoplankton is essential for evaluating ecological risks and preventing adverse impacts on aquatic ecosystem. Elevated concentrations of these microalgae can lead to substantial economic losses in fisheries and mytiliculture due to shellfish harvesting bans and seafood contamination. Moreover, their effects on marine organisms—from bivalves to marine mammals—may result in long-term ecological consequences. Therefore, systematic assessment of the distribution and abundance of harmful phytoplankton is crucial for ensuring food safety and mantaining environmental balance.

Keywords: Phytoplankton monitoring, Harmful Algal Blooms (HABs), Butrinti Lagoon, *Pseudo-nitzschia* spp., *Prorocentrum cordatum*

1. INTRODUCTION

Butrinti Lagoon, located in the southern part of Albania (Fig. 1) is a typical crypto-depression of tectonic origin, relatively deep (20 m deep), with its bottom lying below sea level (Pano, 2015). The Lagoon receives freshwater inputs from multiple sources: partially from the Bistrica River (since 1990s) and from the Monastery Pumping Station in the northern sector; from a small branch of the Pavlla River and several underwater springs in the eastern part; and from the Lake Rreza/Bufi and the Dajlani/Vrina Pumping Station in the southern sector (Bushati, 2013). Historically, Butrinti has been an important fishing area, supporting species such as mullets, sea bass, bream, and eel. In the 1980s, approximately 80 concrete mussel rafts were constructed for the cultivation of Mediterranean mussel (*Mytilus galloprovincialis*). Production peaked at approximately 4,500 tons prior to the 1990s (Miho, 1994; Bushati, 2013 Miho *et al.* 2013), followed by a significant decline; current production is estimated around 1,700 t (2025), of which approximately 70% is consumed on the domestic market. Monitoring the chemical, microbiological, and biological quality of Butrinti represents the primary objective of the Food Safety and Veterinary Institute (ISUV), Tirana, in order to ensure the safe production and commercialization of aquaculture products.

Phytoplankton generally plays a beneficial role as the base of the aquatic food webs. However, a limited number of species—approximately 90 worldwide—are capable of producing potent toxins (Hallegraeff, 1995; Hallegraeff *et al.* 2004). Rapid proliferation of these taxa at high cell densities can result in harmful algal blooms (HABs; Moestrup, 2004). Butrinti Lagoon is also for periodic anoxic events that disrupt ecological balance (Moisiu *et al.* 2016). Such events, often associated with blooms of certain microalgae, can have widespread impacts on marine ecosystems, fisheries, and public health. Among the most closely monitored genera in 2024 was *Pseudo-nitzschia*, a group of diatoms known for their potential to produce domoic acid, a neurotoxin responsible for amnesic shellfish poisoning (ASP) in humans and marine organisms. The collected data indicate a clear seasonal pattern, with peak cell abundances recorded during winter, particularly in February, and markedly concentrations during the summer.

In addition, *Prorocentrum cordatum* was detected at low abundance. This species is considered potentially toxic, capable of producing diarrhetic shellfish poisoning (DSP) and possibly contributing to neurotoxic events such as tetrodotoxin (TTX) accumulation in shellfish. Blooms of this species may cause fish mortality, pose a risk to human health through contaminated shellfish, and negatively affect ecosystems through oxygen depletion and related processes. Its toxicity also negatively impacts filter-feeding bivalves by altering physiological functions, including filtration rates and enzymatic activity (Koteska *et al.* 2022).

These findings underscore the importance of continuous phytoplankton monitoring in Butrinti Lagoon to improve understanding of bloom dynamics and to support the safe management of local aquaculture, and particularly for the sustainable survival of aquatic organisms and the healthy growth of the *M. galloprovincialis*.

2. MATERIALS AND METHODS

During 2024, a total of 273 water samples were collected and analyzed for the presence of potentially toxic phytoplankton. Sampling followed the *Sampling Plan for the Cultivation and Harvesting of Live Bivalve Mollusks,* BM1: Butrinti Lagoon, Saranda (Ref. No. 1587, dated 07.03.2014; Protocol No. 424, dated 16.01.2015).

Sampling was conducted at eight stations selected based on lagoon morphology and hydrological connectivity with the Ionian Sea: (stations 1- 8; Fig. 1). These sites were established during the sanitary survey (MA & IFSV, 2013), (Table1) in accordance with Regulation (EC) No. 854/2004, considering pollution source inventories, seasonal discharge patterns, and water circulation dynamics. A representative sampling program for live bivalve mollusks was developed, using pre-existing data and ensuring appropriate frequency and spatial coverage.

Table 1. Geographic coordinates of the designated stations in Butrinti Lagoon (Fig. 1).

POINTS	X	Y
1	20.01609	39.80614
2	20.02406	39.80576
3	20.04648	39.79116
4	20.01234	39.78816
5	20.02051	39.77206

6	20.02412	39.76419
7	20.03181	39.75483
8	20.04102	39.75516

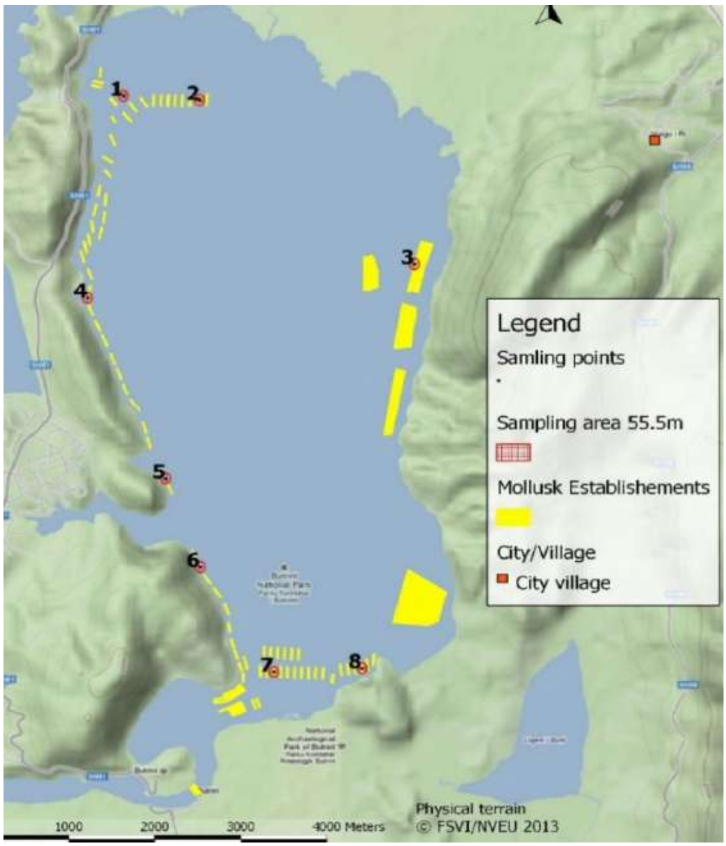

Fig. 1. Map of Butrinti Lagoon with the eight sampling stations (numbers 1-8).

Samples were collected two to four times per month, depending on weather conditions. Phytoplankton samples were collected at a depth of 1 m using dark glass bottles and immediately preserved with alkaline Lugol's iodine solution. Microscopic analysis and species identification were performed using an inverted Zeiss Axiovert 40 CFL microscope equipped with a digital imaging system. For diatom identification, samples were subjected to an acid-cleaning procedure (Utermöhl, 1958), followed by species determination using standard taxonomic references (Krammer, 1986–2001; Witkowski, 2000). Subsamples of 25 ml were allowed to settle for 24 hours prior to quantitative analysis ((Utermöhl, 1958; EN 15204, 2006). Cell counts were carried out using phase-contrast microscopy at 400x magnification, following the Utermöhl method (1958) and European standard EN 15204:2006.

Data on potentially toxic algae were analyzed using One-Way (Single Factor) Anova One Way, Microsoft Excel to assess differences among stations and months. Relationships between phytoplankton abundance and environmental parameters (temperature and rainfall) were evaluated using correlation and regression analyses, including calculation of Pearson correlation coefficients.

3. RESULTS AND DISCUSSIONS

In the present study, emphasis was placed on the most abundant potentially toxic taxa, *Pseudonitzschia* spp. (associated with amnestic shellfish poisoning), likely represented by *P. delicatissima* and *P. seriata* (Miho, 1994; Bushati, 2013). Previous monitoring programs initiated in 2005 in Butrinti Lagoon reported additional potentially toxic species, including *Gonyaulax spinifera, Dinophysis sacculus, D. acuminata* (impact DSP), *Alexandrium* spp. (impact PSP), *Karenia* spp. (impact NSP), *Scrippsiella* spp. (linked to anoxic events affecting fish and invertebrates) (Bushati, 2013; Bushati *et al*. 2010, 2018). However, none of these taxa were detected during 2024. In contrast, *Pseudo-nitzschia* spp. (Fig. 2(a)) was present in approximately 70% of the monitored months, while *P. cordatum* (Fig. 2(b)) was detected at low abundance.

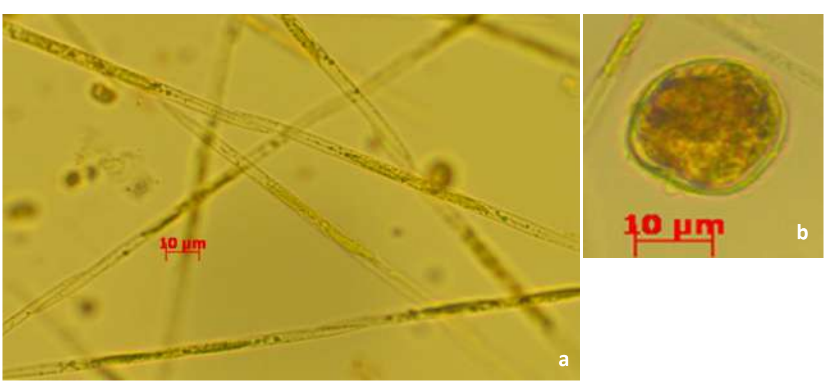

Fig. 2. *Pseudo-nitzschia* spp. (a; 600x), *Prorocentrum cordatum* (b; 1500x) from the phytoplankton of Butrinti.

Over ten months of monitoring in 2024, *Pseudo-nitzschia* spp. dominated the potentially toxic phytoplankton community, accounting for 99.84% of total cell abundance (Table 2). By comparison, *P. cordatum* represented only 0.16% of total abundance and occurred in approximately 20% of the sampled months (Table 2). This marked disparity reflects the strong ecological dominance and bloom-forming potential of *Pseudo-nitzschia* spp. under prevailing environmental conditions.

Two major events of *Pseudo-nitzschia* spp. were recorded: the first in February, reaching approximately 291,000 cells L^{-1} (notably at station BM4), and the second in October, with a maximum of approximately 208,000 cells L^{-1} (particularly at station BM5) (Figs. 3, 4; Tables 2, 3). The occurrence of these peaks suggests eutrophic conditions, likely driven by seasonal variability and anthropogenic nutrient inputs, favoring monospecific diatom blooms. These findings are consistent with previous studies identifying *Pseudo-nitzschia* as a characteristic bloom-forming taxon in nutrient-enriched environments (Bushati, 2013; Bushati *et al.* 2018; Sandoval-Belmar *et al*. 2023).

One-way ANOVA indicated no significant spatial differences in *Pseudo-nitzschia* abundance among the eight sampling stations ($F = 0.02456$, $p = 0.99998$; Table 4), suggesting a relatively homogeneous distribution across the lagoon. In contrast, temporal variability among months was highly significant ($F = 84.74$, $p < 0.001$; Figure 7; Table 4), demonstrating that seasonal dynamics play significant role in bloom development. February exhibited the highest monthly mean abundance, more than twice that observed in October, highlighting pronounced seasonal dynamics of species abundance.

The wide range between minimum and maximum values in February indicates substantial spatial heterogeneity among stations. Standard Deviation (SD) values were highest in February, confirming increased dispersion across sampling sites. Similarly, elevated coefficients of variation (CV) in February and October reflect inconsistent concentrations among stations. Linear trend analysis revealed a slight overall decline in mean abundance throughout the study period, despite pronounced peaks in February and October (Figure 3; Table 3).

Table 2. Monthly maximum concentrations (cell/L) of *Pseudo_nitzschia*_spp. and *Prorocentrum cordatum* in Butrinti phytoplankton during 2024 (AVG – average, MAX - maximum).

MAX (cell/L)	*Pseudo_nitzschia* spp.	*Prorocentrum cordatum*
January	720	0
February	291,060	0
March	0	560 (average 113)
April	600	0
May	600	0
June	0	0
July	0	0
August	440	0
September	5,600	0
October	163,170	200 (average 20)
AVG MAX	46,219	76
MAX MAX	291,060	560
Frequency	**99.84**	**0.16**

Table 3. Maximum values of the phytoplankton of *Pseudo-nitzschia* spp. (cell/L) in every station in Butrinti during 2024; average of maximum (Av_{max}), minimum of maximum (min), maximum of maximum (max), standard deviation (sd) and variation coefficient (cv)

Pseud.	**BM 1**	**BM 2**	**BM 3**	**BM4**	**BM 5**	**BM 6**	**BM 7**	**BM 8**	**AV**	**MIN**	**MAX**	**SD**	**CV**
Jan.	0	0	0	0	500	720	640	0	233	0	720	326	140
Feb.	282,240	262,836	276,066	291,060	208,152	221,382	259,749	278,271	259,970	208,152	291,060	29,854	11
March	0	0	0	0	0	0	0	0	0	0	0	0	0
Apr	0	0	0	0	0	0	0	0	0	0	0	0	0
May	320	600	240	0	160	0	0	0	165	0	600	216	131
June	0	0	0	0	0	0	0	0	0	0	0	0	0
July	0	0	0	0	0	0	0	0	0	0	0	0	0
Aug	200	160	200	160	0	0	160	440	165	0	440	138	83
Sept	4,560	5,600	3,920	2,960	5,040	2,080	4,680	400	3,655	400	5,600	1,740	48
Oct	94,374	102,312	163,170	101,430	208,152	97,020	154,350	120,393	130,150	94,374	208,152	41,114	32
Av_{max}	38,169	37,151	44,360	39561	42,200	32,120	41,958	39,950	39,434	32,120	44,360	3,758	10
Max	282,240	262,836	276,066	291,060	208,152	221,382	259749	278,271	259,970	208,152	291,060	29,854	11

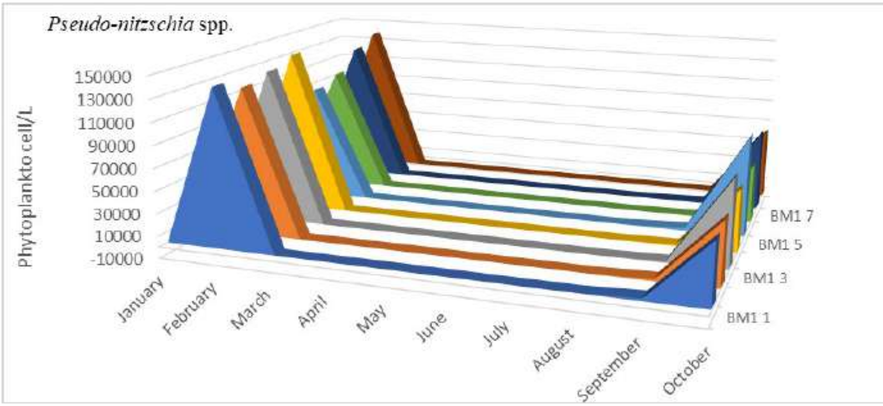

Fig. 3: Monthly average of *Pseudo-nitzschia* spp. in the phytoplankton (cell/L) for the 8 stations in Butrinti during 2024.

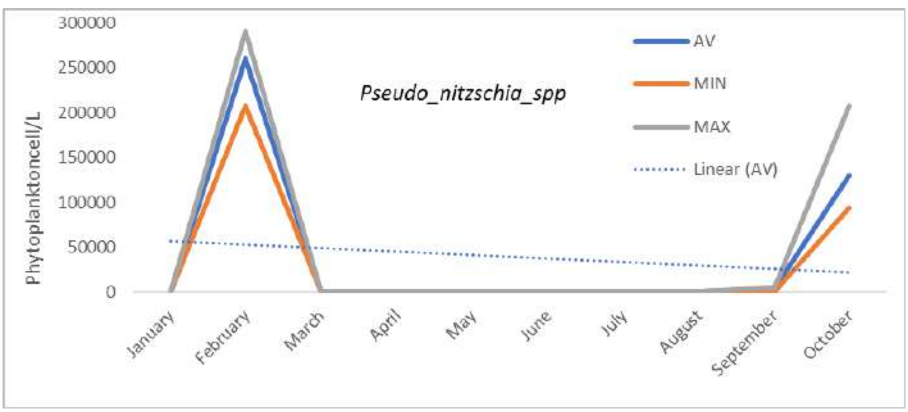

Fig. 4. Monthly maximum of 8 stations (maximum, minimum, average, and linear trend) of *Pseudo-nitzschia* spp. in phytoplankton (cells/L) in Butrinti during 2024.

Table 4. F and F_{crit} for the toxic species *Pseudo-nitzschia* spp. across months and stations

	F	***P-value***	F_{crit}
Months	84.74169	0.00000026	4.60011
Stations	0.024562	0.999984	2.115472

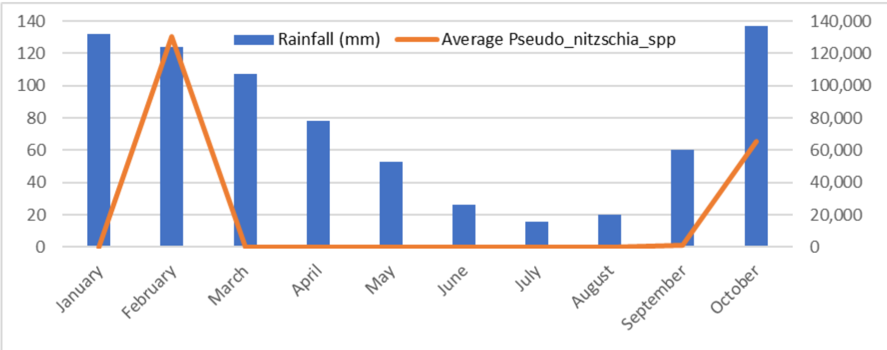

Fig. 5. Monthly average concentrations of *Pseudo-nitzschia* spp. in phytoplankton (cells/L) and monthly average rainfall (mm) in the Butrini area during 2024 (Monitor.al, 2024).

Environmental conditions during the two bloom peaks differed markedly. February, characterized by exhibited lower water temperatures (~11°C) (Monitor.*al*. 2024; SeaTemperature.info, 2024), reduced salinity (12.9–20‰), and elevated dissolved oxygen (~10.2 ml L^{-1}), creating stable conditions favorable for phytoplankton growth. In contrast, October coincided with the onset of the wetter season with warmer temperatures (~22–25°C), increased salinity (up to 33‰), lower dissolved oxygen (~7.2 ml/L), and higher pH values (up to 8.9) (Figures 4, 5; Tables 5, 6). Such autumnal conditions may induce physiological stress, potentially stimulating domoic acid production in *Pseudo-nitzschia* spp. Comparable large-scale anomalous oceanographic conditions have been linked to extensive toxic algal blooms in other marine systems (McCabe *et al*. 2016).

Table 5: The mean main parameters from Butrinti Lagoon, 2022, 2023 (Monitor *et al.* 2024).

Parameter	**Average Value / Range**	**Unit**
Water Temperature	21.9 – 24.3	°C
Dissolved Oxygen (*in situ*)	5.6 – 7	mg O_2/L
Water Transparency	1.6	m
Chemical Oxygen Demand (COD)	24	mg O_2/L
Nitrates (NO_3^-)	0.377	mg/L

Regression analysis revealed a moderate but statistically non-significant relationship between rainfall (Meteoblue, 2024) and *Pseudo-nitzschia* abundance ($R^2 = 0.31$, $p = 0.096$), suggesting that rainfall-mediated nutrient inputs, particularly via surface runoff, may partially contribute to the bloom initiation. Conversely, water temperature showed a weak and statistically non-significant relationship with cell abundance ($R^2 = 0.10$(Fig. 6; Tab. 6),), indicating that factors such as nutrient availability, salinity, and hydrodynamic circulation likely exert stronger control over population dynamics. Climate change and eutrophication have been widely identified as major drivers of the increasing frequency and intensity of *Pseudo-nitzschia* blooms in coastal waters (Trainer and Trick, 2020).

These findings further demonstrate the broad ecological versatility of *Pseudo-nitzschia* spp., which are capable of proliferating under diverse environmental conditions, ranging from cold, oxygen-rich winter waters to warm, saline autumn conditions. The observed bimodal bloom pattern suggests a complex interaction among nutrient loading, hydrodynamics, and climate-related drivers. Consequently, *Pseudo-nitzschia* spp. may serve as useful bioindicator of stress within coastal lagoon ecosystems.

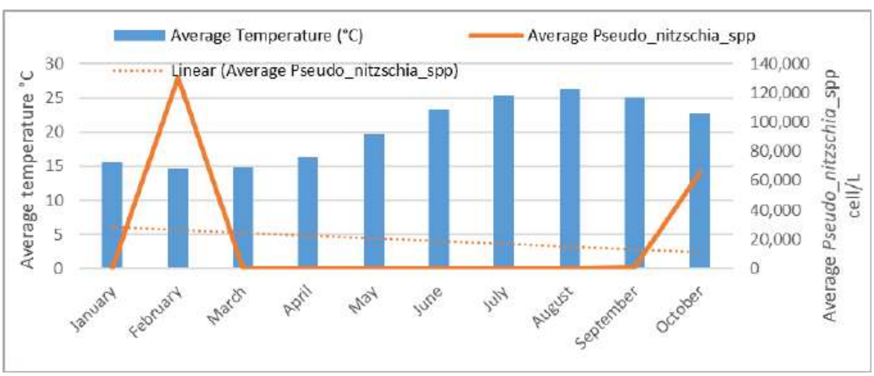

Fig.6. Monthly average concentrations of *Pseudo-nitzschia* spp. (cells/L) and water temperature in the Butrint region during 2024 (Monitor.al, 2024).

Although *Prorocentrum cordatum* was also detected, its low abundance, limited temporal occurrence, and ongoing concerning its toxicogenic potentialindicate a minimal ecological risk within the scope of this study. Accordingly, *Pseudo-nitzschia* spp. was considered the primary toxic taxon during the 2024 monitoring period.

Table 6. Monthly average of the physicochemical characteristics of Butrinti Lake based on previous studies (Bushati, 2013; Maçi *et al.* 2024)
(AV - average)

Average2007-2017	O2 mg/l	Temp	pH	Salinity	O2 %
January	8.18	9.43	8.29	19.00	135.45
February	8.36	10.72	8.26	18.21	149.41
March	8.11	13.96	8.27	19.20	120.06
April	7.99	16.81	8.30	20.78	107.22
May	8.19	19.86	8.30	21.88	114.99
June	7.72	22.69	8.32	23.07	104.94
July	6.98	26.70	8.47	26.76	73.23
August	6.92	26.48	8.46	26.52	83.11
September	6.96	24.52	8.40	25.61	84.62
October	7.83	20.28	8.32	22.37	77.93
November	8.28	18.33	8.29	20.12	133.51
December	8.26	13.95	8.28	18.63	74.30
Av	**7.81**	**18.64**	**8.33**	**21.85**	**104.90**
Max	**8.36**	**26.70**	**8.47**	**26.76**	**149.41**
Min	**6.92**	**9.43**	**8.26**	**18.21**	**73.23**

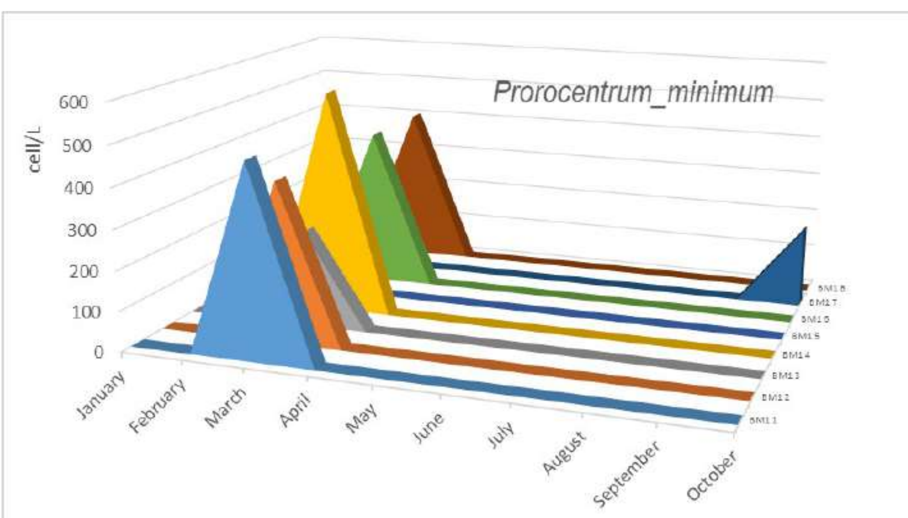

Fig. 7: Monthly maximum concentration (cell/L) of *Prorocentrum cordatum* in Butrinti phytoplankton for the 8 Stations during 2024.

Toxicological Status of *Prorocentrum minimum*

Prorocentrum minimum, currently regarded as a synonym of *Prorocentrum cordatum* (Ostenfeld) Dodge, 1975 (Guiry, 2024), has been historically associated with shellfish poisoning events, most notably Venerupin Shellfish Poisoning (VSP) reported in Japan during the 1940s Japan. These early accounts described hepatotoxic symptoms following consumption of contaminated shellfish (Mock *et al*. 2021). However, no comparable events have been confirmed in recent decades, even in regions where blooms are frequent, such as Chesapeake Bay.

Recent studies indicate that toxicity in *P. minimum* is highly strain-specific and strongly modulated by environmental conditions. While certain strains exhibit hemolytic and ichthyotoxic activity, the vast majority of blooms documented in Europe and North America have been classified as non-toxic or ecologically benign (Mock *et al*. 2021; Matus Hernández *et al*. 2021). Although some bloom events have coincided with symptoms resembling diarrhetic shellfish poisoning (DSP), there is limited and inconclusive evidence that *P. minimum* produces classical DSP toxins such as okadaic acid or dinophysistoxins (Heil *et al*. 2005). Instead, these toxins are more likely attributable to co-occurring toxic species rather than direct synthesis by *P. minimum* (Hattenrath-Lehmann *et al*. 2023). Owing to these uncertainties, *P. cordatum* remains classified as "potentially toxic." Its toxicological expression appears to be influenced by multiple ecological factors, including phosphate availability, light intensity, temperature, and microbial interactions.

4. CONCLUSIONS

The 2024 survey of Butrinti Lagoon demonstrated the clear predominance of *Pseudo-nitzschia* spp. as the principal potentially toxin-producing phytoplankton taxon, with pronounced bloom events observed in February and October. These seasonal maxima were associated with contrasting environmental conditions—lower temperatures and increased freshwater input during winter, and elevated salinity and pH during early autumn. The species exhibited marked ecological plasticity, thriving under both nutrient-enriched and stress-related environments, confirming its role as a dominant bloom-forming diatom in eutrophic systems.

Statistical analyses revealed significant temporal variability but no significant spatial differences in *Pseudo-nitzschia* abundance, indicating a relatively homogeneous distribution across sampling stations. This suggests that seasonality and hydrological dynamics exert a stronger influence on bloom formation than spatial heterogeneity within the lagoon.

Although *Prorocentrum cordatum* was detected, it occurred at low frequencies and concentrations, and its toxic potential remains uncertain. Further molecular and toxicological investigations are therefore required.

Regression analysis indicated a moderate positive relationship between *Pseudo-nitzschia* abundance and rainfall, consistent with nutrient enrichment from terrestrial runoff. No significant relationship was observed with temperature, suggesting that additional factors, including nutrient availability, salinity, and water circulation, play key roles in regulating bloom dynamics.

Overall, these findings highlight the importance of sustained long-term phytoplankton monitoring in semi-enclosed coastal lagoons such as Butrinti. Environmental drivers—particularly rainfall patterns and nutrient loading—should be prioritized in HAB risk assessments to safeguard public health, support sustainable aquaculture management, and maintain ecosystem stability.

Ethics. This study used routine environmental monitoring and publicly available data, without human or animal experimentation or personal data. Therefore, ethical approval was not required. The work was conducted in accordance with the Declaration of Helsinki and national research ethics guidelines.

Data Accessibility (websites, platforms). Data supporting the findings of this study are derived from field monitoring and laboratory analyses conducted during 2024 in Butrinti Lagoon. Supporting environmental and contextual data were obtained from publicly available platforms, including: i) Meteoblue (weather archive data), ii) SeaTemperature.info (water temperature data), iii) Monitor.al (environmental reports) and, iv) AlgaeBase (taxonomic reference database) All data sources are properly cited within the manuscript references.

Declaration of AI Use. There has been no use of AI in writing this paper.

Author contributions. M.B.: Conceptualization; study design; field and laboratory data interpretation; writing, original draft preparation; writing, review and editing; E.K.: DAta collection; laboratory analysis; methodology implementation.

All the authors have approved the final version of the manuscript.

Conflict of Interest Declaration. The authors declare that no conflict of interest exist.

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ASSESSMENT OF THE IMPACT OF ENVIRONMENTAL AND RISK FACTORS ON THE EPIDEMIOLOGY OF TUBERCULOSIS, 2015–2024

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Subject Category: Applied +Life Sciences area**:** Infectious disease, epidemiology

ABSTRACT

Tuberculosis (TB) remains a significant public health challenge in Albania, driven by a complex interplay of biological, environmental, and socio-economic determinants. This study examines the impact of selected environmental and risk factors—including air pollution, climate variability, migration, substandard housing, inadequate ventilation, and population density—on TB incidence and transmission in Albania from 2015 to 2024. Data were sourced from the Albanian National TB Program and the University Hospital, Shefqet Ndroqi, in Tirana. A structured questionnaire was administered to approximately 2,400 hospitalized TB patients. Statistical analysis was performed using SPSS to evaluate associations between identified risk factors and TB occurrence. Of the respondents, 68.7% were male and 31.3% female, with 62% residing in urban areas. More than half of the patients (51%) reported living in areas with high levels of air pollution. Additionally, 33% utilized wood for heating or cooking, primarily in rural settings. Suboptimal housing conditions were prevalent: 26% of participants reported dampness or mold, and 21% lacked adequate ventilation. Overcrowding (defined as sharing a room with three or more individuals) was reported in 20% of cases. Furthermore, 12% were migrants living in densely populated environments. Other significant comorbidities and behavioral factors included smoking (41%), malnutrition (32%), alcohol use (30%), and diabetes mellitus (5.7%). Notably, 25% of cases originated from regions with historically high TB incidence. These findings underscore the critical role of environmental and social determinants in TB transmission dynamics. Effective TB control in Albania requires a comprehensive, multisectoral strategy that integrates public health interventions with improvements in housing quality, environmental protection policies, and social services to reduce both infection rates and progression to active disease.

Keywords: environmental factors, risk factors, epidemiology of TB, public health

1. INTRODUCTION

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains a major global health challenge, particularly in low- and middle-income countries. It continues to rank among the leading causes of morbidity and mortality from a single infectious agent. Determinants such as poverty, overcrowding, malnutrition, air pollution, and climate change significantly increase the risk of infection and disease progression. Despite decades of coordinated global efforts, including the WHO's End TB Strategy, elimination targets remain distant (WHO, 2025).

The COVID-19 pandemic further disrupted TB prevention, diagnosis, and treatment services worldwide, leading to reduced case detection, treatment interruptions, and increased transmission. However, recent global data indicate a gradual stabilization of TB control efforts. In 2023, approximately 10.8 million individuals developed TB—a slight increase from the previous year, largely attributable to population growth. Encouragingly, TB-related deaths declined from 1.32 million in 2022 to 1.25 million in 2023, reflecting a partial recovery of TB services and improved clinical outcomes (Ministry of Health of Albania, 2020). Nevertheless, TB continues to disproportionately affect vulnerable and marginalized populations. The interaction of environmental and socio-economic determinants—including poor ventilation, indoor air pollution, and limited healthcare access—contributes to marked disparities in TB burden at global, regional, and national levels. In Albania, TB is classified as a low-incidence disease. Substantial progress has been achieved in surveillance, diagnosis, and primary care access. In 2024, a total of 232 TB cases were reported, of which 209 (90%) were new cases and 23 (10%) were retreatment cases. Key metrics include: i) incidence rate: 8.7 per 100,000 population, ii) mortality rate: 0.2 per 100,000 population, iii) drug resistance: 2.2% (remaining low), as did mortality (0.2 per 100,000 population) and, iv) treatment success rate: 89%.

Age-specific trends indicate that 25% of cases occurred in individuals aged over 65, while incidence among those aged 35–54 increased by an average of 4.7%. Geographically, the highest burden was recorded in urban centers: Tirana (34%), Durrës (10%), and Shkodër (9.5%). Conversely, declining trends were noted in districts such as Korça, Vlora, Lushnja, and Dibra.

Although Albania has achieved progress in TB control, persistent challenges remain regarding environmental exposures. Smoking, secondhand smoke, and indoor air pollution from solid fuels continue to increase susceptibility. Furthermore, inadequate infection control measures in healthcare settings may expose both patients and workers to increased risk, emphasizing the need for robust ventilation systems and consistent use of Personal Protective Equipment (PPE).

This study utilizes a case-only dataset, which limits causal inference. In the absence of a control group, observed exposures—such as overcrowding or air pollution—cannot be definitively identified as independent risk factors. Consequently, the findings are descriptive and pertain exclusively to the characteristics of confirmed cases. While providing valuable insight into the profile of affected individuals, the data do not allow for the estimation of relative risk (RR) or odds ratios (OR) necessary to establish causality (PLOS Global Public Health, 2024).

Sustainable prevention requires integrated approaches that address housing quality, indoor air pollution, and social protection. A comprehensive understanding of the interplay between biological and socio-economic determinants is essential for designing effective interventions in transitional settings (Anwar *et al*. 2022).

Objective

The primary objective of this study is to assess the impact of key environmental and socio-economic determinants specifically air pollution, climate change, migration, substandard housing, inadequate ventilation, and high population density on the incidence and transmission dynamics of tuberculosis (TB) in Albania from 2015 to 2024.

Specifically, the study aims to: i)evaluate climate-related vulnerabilities: Examine how rising temperatures, shifting precipitation patterns, and extreme weather events exacerbate risk factors such as poverty, malnutrition, degraded indoor air quality, and population displacement, ii) analyze vulnerable populations: focus on economically disadvantaged communities in rural and peri-urban areas to identify disparities in healthcare access and disease burden, iii) identify context-specific risks: assess the impact of localized risk factors, including indoor air pollution from biomass fuel combustion and the high prevalence of tobacco smoking, iv) make policy assessment: evaluate the extent to which current Albanian national TB control policies integrate environmental and climate-sensitive health considerations and, v) make strategic recommendations: provide evidence-based frameworks for strengthening

TB prevention through the integration of environmental health and climate-resilient public health strategies.

2. MATERIALS AND METHODS

This study employed a cross-sectional observational design to evaluate the influence of environmental and socio-economic risk factors on the epidemiology of tuberculosis (TB) in Albania. The investigation spanned a nine-year period from 2015 to 2024. Primary data were sourced from the Albanian National Tuberculosis Program (NTP) and the University Hospital, Shefqet Ndroqi, which serves as the national reference center for pulmonary diseases and TB care. The study cohort comprised approximately 2,400 patients with a confirmed diagnosis of active TB hospitalized at the University Hospital "Shefqet Ndroqi." TB cases were confirmed using a combination of sputum smear microscopy, mycobacterial culture, and the GeneXpert MTB/RIF rapid molecular assay. In cases where bacteriological confirmation was unavailable, diagnosis was established based on clinical and radiological criteria in strict accordance with National TB Guidelines. While the hospital-based nature of this study may limit generalizability to the broader community, the geographic distribution of participants—originating from all major urban and rural regions of Albania—ensures a representative sample of the country's diverse environmental and socio-economic contexts. Data were gathered via a structured, pre-tested questionnaire administered through face-to-face interviews conducted by trained healthcare professionals. This approach ensured high data reliability and consistency (Narasimhan *et al.* 2013). The instrument was divided into four primary domains: i) Sociodemographic Characteristics: Age, gender, and occupation. ii) Clinical Variables: HIV status, comorbidities (e.g., diabetes mellitus), and treatment outcomes, iii) Behavioral Risk Factors: Smoking status and alcohol consumption, iv) Environmental Exposures: Household overcrowding, ventilation quality, and indoor air pollution (e.g., biomass fuel use). Supplementary clinical data regarding treatment history and long-term outcomes were retrieved from the NTP centralized database.

Quantitative data were processed and analyzed using IBM SPSS Statistics (Version 25). Descriptive statistics (frequencies, percentages, means, and standard deviations) were utilized to summarize participant profiles and exposure distributions. Bivariate analyses were conducted to explore the associations between environmental risk factors and TB-related clinical characteristics. For all analyses, a p-value < 0.05 was defined as the threshold for statistical significance.

3. RESULTS AND DISCUSSIONS

Among the 2,400 tuberculosis (TB) cases analyzed, demographic, environmental, behavioral, and clinical characteristics revealed distinct patterns influencing disease distribution and presentation. The study population was predominantly male (68.7%), and the majority of patients resided in urban areas (62%), reflecting a significant concentration of TB cases in urban settings (Table 2). Environmental and Socio-economic Factors Environmental exposures were highly prevalent among participants. Over half of the cohort (51%) reported residing in areas with high ambient air pollution, while 33% utilized indoor biomass fuel. Additionally, suboptimal housing conditions were frequently reported: i) dampness or mold: 26%, ii) inadequate ventilation: 21% and, iii) overcrowding: 20% (defined as ≥3 persons per room). Migrants accounted for 12% of the study population, representing a vulnerable subgroup potentially facing systemic barriers to healthcare access and continuity of care. Behavioral and clinical risk factors known to impair immune response and worsen TB outcomes were widespread (Prasetya *et al*. 2023). Smoking was reported by 41% of patients, and 30% reported alcohol use. Nutritional and metabolic comorbidities were also significant, with malnutrition present in 32% of cases and diabetes mellitus in 5.7%. Furthermore, 25% of cases originated from regions with historically high TB endemicity, indicating persistent localized disease clusters. In terms of clinical manifestations, infiltrative pulmonary TB was the most frequent form (45.3%), followed by generalized pulmonary TB (28%) and pleural TB (17.8%). Extrapulmonary and complex manifestations, though less frequent, remained clinically significant: i) tuberculous lymphadenitis: 2.6%, ii) bone and joint TB: 2.3%, iii) TB/HIV Co-infection: 1.2% and, iv) silico-TB: 1.2%. Rare forms, including TB meningitis, accounted for less than 1% of cases and were observed primarily in highly vulnerable groups. Collectively, these findings underscore the high prevalence of environmental exposures, suboptimal living conditions, and behavioral comorbidities among confirmed TB cases in Albania. This distribution supports the necessity for integrated TB control strategies that address both biomedical factors and broader socio-environmental determinants.

Table 1. Distribution of TB Cases by Year, Gender, and Place of Residence

Year	**Frequency**	**Percentile**
2015	222	9.3
2016	181	7.5
2017	452	18.8
2018	217	9.0
2019	372	15.5
2020	192	8.0
2021	251	10.5
2022	53	2.2
2023	273	11.4
2024	187	7.8
Gender	**Frequency**	**Percent**
Male	1649	68.7
Female	751	31.3
Place of Residence	**Frequency**	**Percent**
Urban	1477	61.5
Rural	923	38.5

Among the 2,400 confirmed TB cases, a pronounced gender imbalance was observed, with 68.7% of patients being male. This finding aligns with international epidemiological data indicating higher TB notification rates among men, a phenomenon frequently attributed to increased occupational exposure, a higher prevalence of tobacco and alcohol consumption, and distinct healthcare-seeking behaviors.

The predominance of cases in urban settings (61.5%) likely reflects the synergy between high population density and specific environmental stressors. Notably, 51% of patients reported exposure to significant ambient air pollution and overcrowded living conditions, both of which are known to facilitate the transmission of *M. tuberculosis*. Conversely, rural patients (38.5%) exhibited higher vulnerability to structural determinants, including: i) energy poverty: reliance on biomass fuels (33%), ii) substandard housing: high prevalence of dampness (26%) and inadequate ventilation (21%) and, iii) healthcare barriers: geographically limited access to specialized respiratory services.

Overcrowding, reported by 20% of participants across both urban and rural contexts, remains a critical environmental factor associated with prolonged household exposure. These environmental risks interact with broader social determinants—most notably poverty and malnutrition (32%)—which significantly elevate the risk of progression from latent infection to active disease. Furthermore, the migrant population (12%) represents a high-risk subgroup necessitated by precarious living arrangements and systemic barriers to healthcare continuity. Collectively, these socio-epidemiological patterns underscore the necessity of a multisectoral TB control framework. Effective management must extend beyond biomedical interventions to include targeted policies for housing quality improvement, indoor air pollution mitigation, enhanced social protection, and the removal of barriers to equitable healthcare (Zabroski *et al*. 2025).

Table 2. Environmental Factors Influencing Tuberculosis Risk and Transmission

Risk Factor	**Frequency (%)**	**P-value**	**Interpretation**
Air pollution	1224 (51%)	0.046	Statistically significant; exposure to air pollution is associated with TB incidence.
Use of heating (biomass fuels, etc.)	792 (33%)	0.000	Highly significant; heating methods may contribute to indoor air pollution, increasing TB risk.
Dampness	647 (26%)	0.024	Statistically significant; damp living conditions may promote respiratory infections including TB.
Inadequate ventilation	504 (21%)	0.000	Highly significant; poor airflow can facilitate TB transmission indoors.
Sharing rooms	480 (20%)	0.004	Significant; overcrowding increases TB exposure risk.
Alcohol use	720 (30%)	0.000	Highly significant; alcohol impairs immunity and is a known TB risk factor.
Smoking	984 (41%)	0.000	Strong significance; smoking damages lung function, increasing TB susceptibility.
Malnutrition	786 (32%)	0.000	Highly significant; malnutrition weakens the immune system, raising TB risk.
Living in high-incidence areas	600 (51%)	0.000	Highly significant; living in TB-endemic areas increases exposure and transmission likelihood.
Diabetes	137 (5.7%)	0.000	Statistically significant; diabetes is a well-known comorbidity that increases TB risk.

Table 3. Assessment of Risk Associated with Alcohol and Smoking

Gender	Alcohol use		Total	P-value	Smoking		Total	P-value
	Yes	No			Yes	No		
Male	603	1046	1649	< 0.001	822	827	1649	< 0.001
Female	117	634	751		162	589	751	
Total	720	1680	2400		984	1416	2400	

Statistical analysis of the association between gender and alcohol consumption revealed a significant disparity. The Odds Ratio (OR) for male versus female patients was 3.124 (95% CI:2.504–3.897), indicating that male patients were more than three times as likely to report alcohol use compared to their female counterparts. Because the 95% Confidence Interval did not include the null value of 1.0, the association is confirmed as statistically significant ($p < 0.001$ These findings demonstrate that, within the study cohort, alcohol use is markedly more prevalent among males, necessitating gender-specific considerations in behavioral health interventions (Yang *et al*. 2024).

Analysis of the association between gender and tobacco use revealed a statistically significant disparity within the study cohort. The Odds Ratio (OR) for male versus female patients was 3.614 (95% CI: 2.962–4.409), indicating that male TB patients have more than 3.6 times higher odds of reporting tobacco use compared to female patients. As the 95% Confidence Interval (CI) does not include the null value of 1.0, the association is statistically significant ($p < 0.001$). These findings underscore the disproportionate prevalence of smoking among males in this population, a factor known to exacerbate TB pathology and complicate treatment adherence.

Table 4. Risk Factors for Tuberculosis Stratified by Age group

Age Group	Air Pollution (%)	Use of Heating (%)	Dampness (%)	Inadequate Ventilation (%)	Shared Room (%)	Alcohol Use (%)	Smoking (%)	Malnutrition (%)	Diabetes (%)
15–24	10	6	5,4	4	4	1,4	2,1	5	0
25–34	9,9	6	5,5	5	4	5,3	7,5	5,7	0
35–44	6,1	4	3,6	3	2	4	4,7	3,5	0

45–54	6,4	4	3,8	2,5	3	4,5	4,8	4,1	1,1
55–64	7,9	4	3,2	2,7	3	6,1	6,7	4,8	2,4
≥ 65	11	9	5,6	3,8	4	8,7	15	8,9	2,2
Total	51	33	27,1	21	20	30	40,8	32	5,7

Analysis of the 2,400 confirmed TB cases revealed significant age-dependent variations in environmental, behavioral, and metabolic factors ($p < 0.05$). Key findings include: i) Biomass Fuel Use: Most frequently reported among patients aged ≥65, likely reflecting generational domestic practices and a higher proportion of rural residency within this demographic (Li *et al*. 2022), ii) Substandard Ventilation**:** Predominantly observed in young adults (15–24) and the elderly (≥65), potentially due to overcrowded housing and aging residential infrastructure, respectively, iii) Behavioral Factors**:** Both alcohol consumption and tobacco use exhibited clear age-related increases, peaking among patients aged≥55. This suggests cumulative exposure to behavioral risks that may impair immune function and diminish treatment adherence and, iv) Comorbidities: The prevalence of diabetes mellitus was significantly higher among older patients. Conversely, malnutrition followed a U-shaped distribution, appearing most frequently in the youngest and oldest age groups, indicating heightened nutritional vulnerability at both life stages.

Overall, the highest TB burden was observed in individuals aged ≥65, followed by the 25–34 and 15–24 cohorts. This bimodal distribution likely reflects the convergence of biological susceptibility in older adults and increased social or household exposure among younger populations (Table 4).

The majority of TB cases were concentrated among the unemployed (32.5%), retirees (22.6%), and individuals categorized as "other" (29%), collectively accounting for approximately 84% of all cases (Table 5). While miners represented only 0.4% of the cohort, they remain a high-priority group due to documented occupational exposure to silica dust and adverse working conditions. Despite the contraction of the mining sector in Albania, persistent case reporting in this group underscores the necessity for sustained occupational surveillance. Conversely, the low incidence among students and professionals (e.g., engineers, teachers) suggests that lower social vulnerability and better healthcare access serve as protective factors. These findings indicate that TB control efforts must prioritize socially and occupationally vulnerable groups rather than focusing exclusively on the absolute volume of cases in any single category.

Table 5. Distribution According to Profession

Profession	Frequency	Percentage
Teacher	17	0.7%
Farmer	24	1.0%
Economist	19	0.8%
Emigrant	5	0.2%
Disabled	62	2.6%
Engineer	19	0.8%
Miner	9	0.4%
High School Student	92	3.8%
Unemployed	781	32.5%
Retired	543	22.6%
Others	697	29.0%
Healthcare Worker	29	1.2%
Student	88	3.7%
Military/Police Officer	15	0.6%
Total	**2400**	**100.0%**

Although relatively uncommon, TB/HIV co-infection (1.2%) and multidrug-resistant TB (MDR-TB) (0.3%) were observed more frequently among individuals characterized by a history of migration, limited healthcare access, and social instability. These conditions are prevalent among highly vulnerable subgroups, including migrants, the unemployed, and individuals with long-term disabilities. Such populations often face overlapping risk factors, such as substance abuse, malnutrition, and poorly managed comorbidities (Frontiers in Public Health, 2025). The notable occurrence of pleural TB and miliary TB (the latter characterized by hematogenous spread) suggests a pattern of delayed diagnosis, often leading to advanced or disseminated disease. These clinical presentations were more frequently recorded among: i) Older Adults: Due to age-related immune senescence and atypical symptoms, ii) Chronically Ill Patients: Where underlying conditions may mask early TB indicators and, iii) Socially Isolated Individuals: Such as retirees or those with permanent disabilities, who may face barriers to early screening. The prevalence of these advanced forms underscores the critical need for strengthened community-level awareness, active case-finding, and streamlined referral pathways to ensure early intervention (World Health Organization, 2025).

4. CONCLUSIONS

To our knowledge, this study represents one of the first comprehensive efforts in Albania to evaluate the role of environmental and socio-economic determinants in the epidemiology of tuberculosis (TB). While localized evidence has historically been limited, our findings align with the global consensus that TB is a multifactorial disease shaped by the dynamic interplay of biological, environmental, and socio-economic drivers (GBD 2021 Study Collaborators, 2024). Within the study cohort, a significant proportion of TB cases was associated with ambient air pollution, indoor biomass fuel smoke, inadequate ventilation, tobacco and alcohol use, diabetes mellitus, and malnutrition.

- Clinical Correlations: Pulmonary TB was predominantly observed in contexts characterized by airborne pollutants and indoor smoke exposure. Conversely, extrapulmonary manifestations were more prevalent among individuals with heightened biological vulnerability, particularly those with compromised immune systems.
- Demographic Trends: Age-specific patterns were evident; cases among the elderly (age $\geq$ 65 years) were primarily associated with metabolic and behavioral risk factors, whereas cases among younger adults (15–34 years) were characterized by exposure to substandard living conditions and environmental stressors.
- Climate Impact: The indirect effects of climate change—including exacerbated poverty, food insecurity, and population displacement—threaten to create conditions that facilitate TB transmission and complicate national control efforts.

These findings underscore the necessity of a multisectoral framework for TB prevention in Albania. To achieve sustainable reduction and move toward elimination targets, the following priority actions are recommended:

1. Surveillance & Early Detection: Strengthen active case-finding and diagnostic surveillance systems, with a specific focus on high-risk occupational and socially marginalized groups.

2. Environmental Mitigation: Implement public health interventions aimed at improving housing quality, optimizing household ventilation, and reducing indoor air pollution.
3. Structural Interventions: Address the distal determinants of health, including poverty, food insecurity, and social exclusion, through integrated social protection programs.
4. Intersectoral Collaboration: Foster formal partnerships between the Ministry of Health and sectors governing housing, labor, and the environment to align TB control with broader sustainable development goals (Huang *et al*. 2019).

Integrating environmental health and social protection into national TB strategies will provide a more equitable, resilient, and sustainable pathway toward TB elimination in Albania.

Ethics. The study was conducted in accordance with the Declaration of Helsinki. All participants were informed about the objectives of the study, and written informed consent was obtained from all hospitalized patients (or their legal guardians for participants under 18) prior to the administration of the questionnaire.

Privacy and Confidentiality. To ensure patient anonymity, all data were de-identified during collection and analysis. Access to the raw data was restricted to the primary research team, and information was stored in a secure, password-protected database in compliance with national data protection laws.

Data accessibility https://www.ishp.gov.al

Declaration of AI use: There has been no use of AI when writing the actual paper.

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URBAN-RELATED ENVIRONMENTAL RISK FACTORS AND RISK OF EARLY-ONSET DEMENTIA IN MODENA PROVINCE, NORTHERN ITALY

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ABSTRACT

Early-onset dementia (EOD) involves cognitive decline in individuals under 65, influenced by a complex interplay of genetic and environmental stressors. Applying a One Health framework, this study investigates the association between urban environmental factors—traffic-related air pollution, greenness, and artificial light at night (LAN)—and EOD risk. We conducted a population-based case-control study in Modena, Northern Italy (327 cases; 1949 age/sex-matched controls). Residential exposures were georeferenced using benzene as a traffic proxy, the Normalized Difference Vegetation Index (NDVI) for greenness, and VIIRS satellite data for LAN. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated via conditional logistic regression with mutual adjustment for all environmental variables. High benzene exposure (≥1 $\mu g/m^3$), was associated with increased EOD risk. NDVI exhibited a non-linear relationship, with peak risk observed at intermediate greenness levels. Conversely, LAN exposure showed an inverse, approximately linear association with EOD risk. Sex-stratified analyses revealed a more pronounced association between benzene and EOD in males, while NDVI showed a linear risk reduction primarily in females. No sex-specific differences were observed for LAN. Urban environmental factors—specifically motorized traffic emissions, vegetation density, and nocturnal light—significantly correlate with EOD risk. These associations are characterized by non-linearity and sex-specific susceptibility, highlighting the need for multi-sectoral public health strategies within urban planning.

Keywords: benzene; early-onset dementia; environmental epidemiology; greenness; light-at-night; one health

Dementia is a neurodegenerative disorder characterized by progressive severe cognitive impairment. Although, it predominantly affects older adults, it can also occur in individuals younger than 65 years, in which case it is defined as early-onset dementia (EOD) (Fadil *et al*. 2009). The prevalence of EOD among individuals aged 30-64 years has been estimated at approximately 119 cases per 100 000 population, although this figure varies geographically (Chiari *et al*. 2021; Hendriks *et al*. 2021). EOD encompasses multiple subtypes (Seo *et al*. 2018; Zamboni *et al*. 2024) and is associated with a range of risk factors, including genetic predisposition (Jarmolowicz *et al*. 2015; Cacace *et al*. 2016), as well as traumatic brain injury and lifestyle-related factors (Nordstrom and Nordstrom, 2018*;* Adani *et al.* 2020*;* Filippini *et al*. 2020; Giannone *et al*. 2022; Lin *et al*. 2025).

Environmental exposures have also been increasingly investigated in relation to EOD. Neurotoxic air pollutants associated with motorized traffic, such as benzene, have been implicated in its etiology (Rajendran *et al*. 2022). Green spaces (or "greenness") has been linked to dementia risk, with evidence suggesting both protective and adverse effects depending on context and exposure characteristics (Zaganas *et al*. 2013; Zagnoli *et al*. 2020; Besser, 2021). Additionally, exposure to artificial light-at-night (LAN) may influence brain health through mechanisms including circadian rhythm disruption, sleep disturbances, and endocrine dysregulation (Chen *et al.* 2022; Bożejko *et al*. 2023; Mazzoleni *et al*. 2023).

In this study, we aimed to investigate the possible association between selected urban-related environmental factors namely traffic-related air pollution, greenness, and light pollution — and the risk of EOD in a population from Northern Italy.

2. MATERIALS AND METHODS

Study population

We conducted a retrospective case-control study including patients diagnosed with early-onset dementia (EOD) while residing in the province of Modena, Italy, during the period 1999-2021. Cases were identified through the provincial network of dementia services, which covers the entire study area and includes two hospitals, and eight community-based Centres for Cognitive Disorders and Dementia (CDCDs). (CDCD).

All dementia diagnoses were established according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) (Mazzoli *et al*. 2024). We excluded individuals with developmental disorders, major psychiatric conditions, non-neurological cognitive impairments, age below 30, or residence outside the Modena province at the time of diagnosis.

For each EOD case, up to six controls were randomly selected from the Modena National Health Service (NHS) database, matched by sex, birth year, and calendar year. Due to Due to incomplete geolocation data, some controls could not be assigned exposure estimates; consequently, a small proportion of cases were matched to only 5 controls.

Exposure assessment

Residential addresses of all study participants at the time of diagnosis (or corresponding index date for controls) were geocoded within a Geographic Information System (GIS). At each geocoded location, we estimated annual average outdoor concentrations of benzene at a height of 2 meters above ground level, using California Line Source Dispersion Model version 4 (CALINE 4) (Vinceti *et al*. 2012)..

Exposure to green space exposure was assessed using Normalized Difference Vegetation Index (NDVI), derived from PROBA-V satellite. NDVI values were calculated within a a 100-meter buffer around each participant's residence over the period 1999-2021. For cases exposure assessment focused on the five years preceding diagnosis, while for controls, the same temporal window corresponding to their matched case was applied.

Exposure to artificial light at night LAN was estimated using satellite data from the Visible Infrared Imaging Radiometer Suite (VIIRS) (Elvidge *et al.* 2017). Due to differences in radiometric resolution compared with earlier datasets, LAN exposure was assigned based on 2014 measurements for all participants, assuming temporal stability of this variable within the study area.

Data analysis

Data were analyzed using multivariable conditional logistic regression models, accounting for the matched design (sex and age) and with mutual adjustment for all environmental exposures. Associations were estimated as odds ratios (ORs) and 95 % confidence intervals (CIs), modeled both per 1-unit in exposure and across predefined exposure categories. For benzene, exposure categories were defined using cut-points --0.60 µg/m^3 and 1.20 µg/m^3, based on distribution observed in the control population. For greenness, the 25th and the 75th percentiles of the overall population distribution were used to define categories, rounded to NDVI values of 0.30 and 0.45. For light at night (LAN), three exposure categories were defined based on thresholds reported in previous studies, with cut-points at 10 and 30 nW/sr/cm^2.

To explore potential non-linear associations, we fitted restricted cubic spline models with three knots placed at fixed percentiles (10th, 50 th and 90th) of the exposure distributions. Reference values were set at 1.20 µg/m^3 for benzene, 0.36 (median) for NDVI, and 26 nW/sr/cm^2 (median) for LAN. All analyses were performed using Stata software (version StataNow 18.5, Stata Corp., College Station, TX, 2023), employing the *mkspline* and *clogit* commands. Analyses were conducted for the overall study population and stratified by potential effect modifiers, including sex and age groups.

3. RESULTS AND DISCUSSIONS

The table 1 reports the study population including 327 EOD patients (153 males and 174 females) and 1949 controls (913 males and 1036 females). The median age was 60 years (IQR 57-64), with a range of 39 = 65 years.

Table 1. Characteristics of the study population and distribution of environmental exposures

	Controls (N=1949)	**Cases (N=327)**
	N (%)	**N (%)**
Sex		
Females	1036 (53.2)	174 (53.2)
Males	913 (46.8)	153 (46.8)
Age		
Median (IQR)	60 (57-64)	60 (57-64)
<55 years	310 (15.9)	52 (15.9)
≥55 years	1639 (84.1)	275 (84.1)
Green spaces (NDVI)		
Median (IQR)	0.36 (0.29-0.47)	0.34 (0.29-0.42)

<0.30	557 (28.6)	90 (27.5)
≥0.30; <0.45	858 (44.0)	180 (55.1)
≥0.45	534 (27.4)	57 (17.4)
Benzene ($\mu g/m^3$)		
Median (IQR)	0.39 (0.23-0.79)	0.36 (0.18-0.84)
<0.60	1322 (67.9)	222 (68.1)
≥0.60; <1.20	373 (19.2)	59 (18.1)
≥1.20	252 (12.9)	45 (13.8)
LAN ($nW/sr/cm^2$)		
Median (IQR)	25.7 (10.3-36.5)	23.1 (9.4-35.7)
<10	475 (24.4)	88 (26.9)
≥10; <30	681 (34.9)	113 (34.6)
≥30	793 (40.7)	126 (38.5)

In conditional logistic regression analyses, using the lowest exposure category as the reference, greenness (NDVI) showed a non-linear association with EOD risk. Specifically, a modest increase in risk was observed in the intermediate exposure category (0.30-<0.45 NDVI; OR=1.15, 95%; CI 0.86-1.55), while a strong inverse association was found in the highest exposure category (≥0.45 NDVI; OR of 0.43,95%; CI:0.28-0.67). This inverse association appeared more pronounced among females (Table 2). For exposure benzene, we observed an increased EOD risk in the highest exposure category (≥1.20 $\mu g/m^3$; OR=1.19, 95%, CI: 0.80-1.78), with slightly stronger association among males compared to females. Exposure to light at night (LAN) was associated with a progressive decrease in the risk of early-onset dementia (EOD). Compared with the lowest exposure category (<10 $nW/sr/cm^2$), the odds ratios were 0.63 (95% CI: 0.45–0.89) for 10–<30 $nW/sr/cm^2$ and 0.52 (95% CI: 0.35–0.77) for ≥30 $nW/sr/cm^2$, indicating lower risk at higher exposure levels. This inverse association was consistent across males, females, and individuals aged ≥55 years. However, among younger individuals, the relationship was non-linear, with risk increasing at intermediate exposure levels and decreasing again at higher levels, forming an inverted U-shaped pattern.

Table 2. Odds ratio (OR) and 95% confidence intervals (CIs) for early-onset-dementia (EOD) associated with greenness, benzene, and light at night exposure in the overall population and stratified by sex and age groups.

		Total		Males		Females
Exposure	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Green spaces (NDVI)						
<0.30	1.00	-	1.00	-	1.00	-
≥ 0.30; <0.45	1.15	0.86-1.55	1.56	1.01-2.41	0.87	0.58-1.30
≥0.45	0.43	0.28-0.67	0.47	0.23.0.93	0.38	0.21-0.68
Benzene (μg/m³)						
<0.60	1.00	-	1.00	-	1.00	-
≥0.60; <1.20	0.97	0.70-1.36	1.18	0.73-1.90	0.81	0.50-1.30
≥1.20	1.19	0.80-1.78	1.28	0.70-2.32	1.13	0.66-1.95
LAN (nW/sr/cm²)						
<10	1.00	-	1.00	-	1.00	-
≥10; <30	0.63	0.45-0.89	0.60	0.36-1.00	0.66	0.42-1.03
≥30	0.52	0.35-0.77	0.64	0.36-1.13	0.43	0.25-0.73
				Age <55 years		**Age ≥55 years**
			OR	**95% CI**	**OR**	**95% CI**
Green spaces (NDVI)						
<0.30			1.00	-	1.00	-
≥ 0.30; <0.45			1.11	0.51-2.42	1.17	0.85-1.61
≥0.45			0.72	0.24-2.16	0.39	0.24-0.63
Benzene (μg/m³)						
<0.60			1.00	-	1.00	-
≥0.60; <1.20			1.58	0.72-3.50	0.89	0.61-1.28
≥1.20			1.18	0.46-3.05	1.19	0.76-1.86
LAN (nW/sr/cm²)						
<10			1.00	-	1.00	-
≥10; <30			1.33	0.55-3.20	0.55	0.38-0.80
≥30			0.97	0.34-2.76	0.47	0.31-0.71

*Estimates were obtained from conditional logistic regression mode matched by sex and age, with mutual adjustment for all environmental factors.

In dose-response analyses (Figure 1), greenness exhibited a non- linear association with EOD risk. Specifically, little variation in risk was observed across low to average NDVI levels, whereas risk decreased approximately linearly at higher levels of greenness. Benzene exposure showed a positive association with EOD risk, with an approximately linear increase in risk at concentrations above 1.5 µg/m^3. In contrast, exposure to light at night (LAN) was inversely associated with EOD risk, with a steady decrease in risk observed across the entire exposure range.

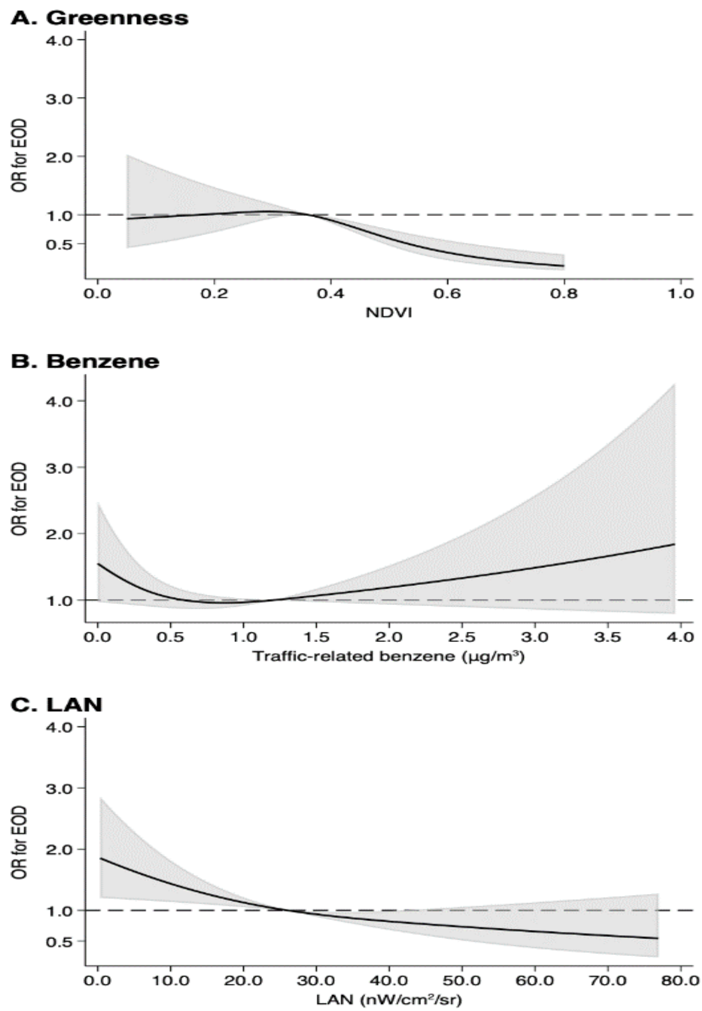

Fig. 1. Odds ratio (OR - solid line) with 95% confidence interval (grey area) for early-onset-dementia (EOD) associated with mean greenness (A), benzene (B), and light at night (LAN) (C) exposure. Conditional logistic model matched by sex and age and with mutual adjustment of all environmental factors.

4. DISCUSSIONS

In this study, we observed evidence suggesting a protective association between exposure to green spaces and light-at-nigh (LAN) and the risk of early onset-dementia (EOD), whereas traffic-related benzene exposure showed indications of a detrimental effect.

With regard to greenness, we found little evidence of an association with OED risk at low to intermediate levels of exposure. However, at higher levels of greenness, a clear protective effect emerged. Several mechanisms may underlie this association. Green spaces are known to promote physical activity and outdoor engagement (Blondell *et al*. 2014; James *et al*. 2015; McMorris *et al*. 2015), as well as reduce oxidative stress (De Petris *et al*. 2021), which has been implicated in neurodegeneration.

In addition, greenness may contribute to improved air quality (James *et al*. 2015). Notably, our findings suggest that the observed association between greenness and EOD is independent of air pollution levels.

These results are consistent with studies reporting a reduced risk of neurodegenerative diseases associated with higher greenness exposure (Rodriguez-Loureiro *et al*. 2022; Hu *et al*. 2023; Zhu *et al*. 2023). However, they contrast with previous evidence suggesting a U-shaped relationship between greenness and dementia risk (Zagnoli *et al*. 2020). Importantly, most prior studies have not specifically examined EOD, a relatively under-investigated condition in terms of etiology (Bosi *et al.* 2022).

Regarding air pollution, our findings indicate that benzene, as a marker of motorized traffic emissions, may represent an independent risk factor for EOD. The body of evidence linking air pollution to dementia risk is steadily increasing (Huang *et al*. 2025; Jones *et al*. 2025; Yuan *et al.* 2025), although data specifically addressing benzene remain limited (Trentalange *et al*. 2025). A direct neurotoxic effect of benzene cannot be excluded, as it can cross the blood–brain barrier and interfere with protein expression and enzymatic activity (Sun *et al.* 1992; Zheng *et al*. 2024). At the same time, benzene exposure may act as a proxy for broader traffic-related air pollution (Filippini *et al.* 2019), suggesting a more general adverse role of urban air pollution in both late- and early-onset dementia.

With respect to LAN exposure, we observed an inverse association with EOD risk, with decreasing risk at higher exposure levels. One possible explanation is that LAN may be correlated with increased social interaction and outdoor activity, factors known to protect against cognitive decline (Hennig *et al*. 2025; Li *et al.* 2025a). Indeed, higher LAN exposure has been associated with extended working hours and increased participation in evening social activities (Mahalingam *et al*. 2023). However, the relationship between LAN and dementia remains complex and warrants further investigation, as some studies have reported detrimental effects of light pollution on cognitive function and neuropsychiatric outcomes (Li *et al*. 2025b; Tondelli *et al*. 2026). Notably, previous studies have not specifically addressed EOD, and our findings may suggest that early- and late-onset dementia (LOD) differ in their environmental risk profiles. This hypothesis is supported by emerging evidence indicating distinct etiological pathways for EOD and LOD (Klompmaker *et al*. 2022; Li *et al.* 2023; Mazzoleni *et al*. 2023; Park *et al*. 2025).

Several limitations should be considered. First, greenness was assessed solely using NDVI, which may not fully capture qualitative aspects of green space. However, long-term analyses of vegetation trends in Europe (1981–2018) indicate relatively modest changes in NDVI over time (Eisfelder *et al*. 2023), suggesting limited potential for exposure misclassification. Second, the relatively low prevalence of high benzene exposure in the study population restricted the ability to characterize risks at higher exposure levels. Third, benzene exposure estimates were based on a single reference year (2006), which may not fully reflect long-term exposure patterns. Nevertheless, given the stability of population characteristics, traffic density, and benzene concentrations in the study area over time (Modena Municipality, 2025), these estimates are likely representative of the broader study period. Similarly, for LAN exposure, the use of 2014 data for all participants may have introduced some degree of measurement error. However, evidence suggests that LAN levels are relatively stable over time (Bennie *et al*. 2014; Yılmaz, 2025), reducing the likelihood of substantial exposure misclassification. Additionally, we were unable to distinguish between indoor and outdoor LAN exposure, although these have been shown to be positively correlated (Cleary-Gaffney *et al*. 2022). More broadly, exposure assessment was limited to residential addresses, without accounting for time–activity patterns or occupational exposures. Finally, residual confounding cannot be excluded, particularly due to the lack of data on education, socioeconomic status, and comorbidities, which may be associated with both environmental exposures and dementia risk.

Despite these limitations, the study has several strengths. It represents one of the largest population-based investigations of EOD to date, a relatively rare condition. The use of routinely collected healthcare data minimized selection and recall biases, as data collection did not rely on direct participant involvement. Furthermore, case ascertainment was based on comprehensive neurological evaluation using standardized and validated diagnostic criteria, enhancing the validity of the findings.

5. CONCLUSIONS

This population-based case–control study provides evidence that environmental exposures may influence the risk of early-onset dementia (EOD). Specifically, residential proximity to green spaces and exposure to light at night (LAN) were associated with a reduced risk of EOD, whereas outdoor air pollution from motorized traffic showed a potential detrimental association. Taken together, these findings suggest that certain modifiable environmental factors may contribute to the etiology of EOD. Further research is warranted to elucidate the underlying mechanisms and to support the development of effective public health and prevention strategies.

Data accessibility. www.geo.edu.al, EMSC-CSEM.org

Declaration of AI use. There has been no use of AI when writing the actual paper.

Authors' contributions A.C., M.V., T.F.: conceptualization**;** C.S., A.C., N.M., S.C., F.D., T.F.: data curation; C.S., and T.F.: formal analysis; T.F.: funding acquisition; C.S., T.F.: investigation; S.T., T.F., M.V.: methodology; A.C., N.M., S.C., F.D., M.T., G.Z.: resources; M.V., T.F.: project administration; A.C., M.V., T.F.: supervision; C.S., M.V., T.F.: writing – original draft, all the authors: writing – review and editing

All the authors have approved the final version of the manuscript

Conflict of interest declaration. The authors declare that they have no conflict of interest related to this work.

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A REVIEW ON THE IMPACT OF AIR POLLUTION AND VIRAL DISEASES ON HUMAN HEALTH

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ABSTRACT

Infectious diseases continue to represent a major global public health burden, particularly in low- and middle-income countries, where they contribute substantially to morbidity, mortality, and socio-economic instability. Their high mutation rates and adaptive capacity complicate prevention and control efforts, thereby sustaining pressure on healthcare systems. Before the COVID-19 pandemic, several Balkan countries had achieved measurable progress in poverty reduction and household income growth; however, these gains were partially reversed following the pandemic, highlighting the vulnerability of socio-economic development to large-scale infectious disease outbreaks. Beyond the socio-economic consequences of the COVID-19 crisis, this study examines the relationship between long-term exposure to ambient air pollution and increased susceptibility to viral infections. Epidemiological evidence increasingly supports an association between chronic exposure to air pollutants, including particulate matter and nitrogen oxides, and the prevalence of chronic respiratory and cardiovascular diseases. These comorbidities act as important risk modifiers, increasing both susceptibility to infection and the likelihood of severe clinical outcomes, including hospitalization and mortality. The central hypothesis of this study is that air pollution acts as an effect modifier and potential co-factor in the progression and severity of viral diseases through mechanisms involving systemic inflammation, oxidative stress, and impaired immune response. Prolonged exposure to pollutants may compromise pulmonary defense mechanisms and alter immune competence, thereby facilitating viral entry and pathogenesis. Two major epidemiological implications arise from this interaction: (i) an increased risk of infection in populations exposed to high pollution levels, and (ii) a greater probability of severe disease progression among infected individuals. Recognizing the interaction between environmental exposure and infectious disease dynamics is essential for risk assessment, targeted interventions, and the development of integrated public health strategies. Incorporating environmental risk factors into infectious disease models may improve causal interpretation, predictive accuracy, and health system preparedness.

Keywords: air pollution; COVID-19; viral infections; environmental exposure; susceptibility; comorbidity; public health

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clinical manifestations range from asymptomatic infection to mild and moderate disease, with the majority of cases resolving without the need for specialized medical intervention. However, a significant proportion of individuals—particularly those with advanced age or underlying comorbidities—develop severe disease requiring hospitalization and intensive care support.

The earliest confirmed cases of COVID-19 were reported in China in December 2019, although subsequent epidemiological investigations suggest that viral circulation may have occurred prior to this period. On January 20, 2020, the National Health Commission of China confirmed human-to-human transmission, indicating efficient viral spread through respiratory pathways. Shortly thereafter, on January 22, 2020, the European Centre for Disease Prevention and Control (ECDC), based on available surveillance data, assessed the outbreak as having a high potential impact, a substantial likelihood of further global dissemination, and a moderate probability of case importation into European Union (EU) countries.

The first laboratory-confirmed case of COVID-19 in Europe was reported in France on January 24, 2020, followed by rapid geographic spread across neighboring countries, consistent with patterns of international mobility and community transmission. The World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern (PHEIC) on January 30, 2020, and subsequently characterized COVID-19 as a global pandemic on March 11, 2020. By early March 2020, Europe had emerged as the epicenter of the pandemic, before North America assumed this role in April 2020 based on reported incidence and case counts. Transmission of SARS-CoV-2 occurs predominantly via respiratory droplets and aerosols, with additional contribution from indirect contact through contaminated surfaces (fomites), particularly in high-density settings. Epidemiological data indicate that disease severity is strongly associated with age and the presence of pre-existing conditions, including cardiovascular and respiratory diseases, which act as key risk modifiers influencing clinical outcomes. The initial phase of the pandemic was characterized by substantial uncertainty regarding transmission dynamics, clinical progression, and effective mitigation strategies, posing significant challenges for public health authorities worldwide. In response, the WHO called upon all countries to implement comprehensive pandemic preparedness and response plans, emphasizing national responsibility for health system capacity, financing, and service delivery. Core non-pharmaceutical interventions (NPIs) were widely adopted to reduce transmission, including physical distancing, mandatory face mask use, large-scale testing, contact tracing, and the rapid expansion of healthcare infrastructure, such as the establishment of temporary or field hospitals to manage surges in patient volume (Figure 1). In Albania, the first confirmed case of COVID-19 was reported in Tirana on March 8, 2020. As case numbers increased, the Albanian government declared a state of natural disaster on March 24, 2020, reflecting the significant public health and systemic pressures associated with the pandemic (Supreme Audit Institution of Albania, 2021).

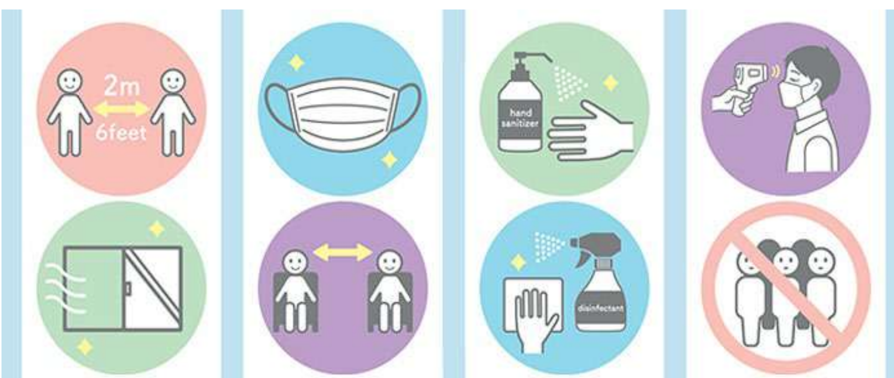

Fig. 1: Typical public health measures taken in response to COVID-19 (Source: The EU's initial contribution to the public health response to COVID-19.

Beyond its direct health impacts, coronavirus disease 2019 (COVID-19) has generated profound economic and social disruptions. The pandemic represents one of the most significant systemic shocks in the history of the European Union, affecting health systems, labor markets, and macroeconomic stability. These impacts are particularly pronounced in small, open economies such as Albania, where structural vulnerabilities—including economic volatility, limited industrial diversification, and high dependence on services—amplify the effects of external shocks. In the Albanian context, the pandemic was associated with substantial labor market contraction, including increased unemployment—particularly among temporary and informal workers—alongside a decline in household purchasing power. Additional macroeconomic consequences included business closures and suspensions (notably among small and family-owned enterprises), reduced domestic production and trade flows, disruptions in financial stability reflected in decreased loan repayment capacity, and a marked contraction in tourism-related activities. Given the service-oriented structure of the Albanian economy, non-pharmaceutical interventions (NPIs), particularly mobility restrictions and business closures, exerted disproportionate sectoral impacts. While agriculture remained relatively resilient, sectors such as tourism experienced severe declines, whereas more adaptable sectors—including pharmaceuticals and information technology—demonstrated relative stability due to their capacity for remote operation and digital service delivery. Furthermore, the pandemic accelerated digital transformation processes, prompting firms to adopt online platforms, restructure investment strategies toward technological innovation, and strengthen risk management frameworks (Supreme Audit Institution of Albania, 2021).

Concurrently, the global spread of COVID-19 has intensified research into environmental determinants of infectious disease dynamics. A growing body of epidemiological and toxicological evidence, including studies conducted by the United States Environmental Protection Agency (EPA), has established robust associations between fine particulate matter ($PM_{2.5}$) exposure and adverse health outcomes, including increased all-cause and cause-specific mortality[1]. Current hypotheses posit that chronic exposure to $PM_{2.5}$ contributes to underlying respiratory and cardiovascular pathophysiology, thereby acting as a susceptibility-enhancing factor and potential effect modifier in the context of COVID-19. Specifically, long-term pollutant exposure may exacerbate disease severity through mechanisms involving systemic inflammation, oxidative stress, and impaired host immune response. Epidemiological investigations assessing the association between long-term air pollution exposure and COVID-19-related hospitalization, severity, and mortality have expanded rapidly and constitute a critical area of ongoing research. However, these studies face

[1] Wu X, Nethery RC, Sabath MB, Braun D, Dominici F. 2020. Air pollution and COVID-19 mortality in the United States: Strengths and limitations of an ecological regression analysis, pg 1.

substantial methodological challenges, including limited access to individual-level health data, potential residual confounding, exposure misclassification, and heterogeneity in testing and reporting practices across populations. As noted by Wu *et al.* (2020), the lack of large-scale, high-resolution, individual-level datasets constrains causal inference and limits the generalizability of findings.

Air pollution remains a major global environmental health risk, with increasing emissions and ambient concentrations observed in many regions. Although exposure affects the entire population, vulnerability is unevenly distributed, with heightened risk observed among children, older adults, pregnant women, and individuals with pre-existing health conditions. Socio-economic disparities further exacerbate exposure differentials: lower-income populations are more likely to reside in proximity to high-traffic corridors or industrial zones, resulting in elevated pollutant exposure. According to the European Environment Agency (2019), energy poverty—particularly prevalent in Southern and Central-Eastern Europe—drives reliance on low-quality solid fuels (e.g., coal and wood) for residential heating, leading to increased indoor and outdoor exposure to particulate matter (PM) and polycyclic aromatic hydrocarbons (PAHs). Compounded by reduced access to high-quality healthcare and a higher baseline prevalence of chronic conditions, these factors collectively increase susceptibility to the adverse health effects of air pollution.

The primary objective of this study is to systematically collect, synthesize, and critically evaluate international evidence to assess the relationship between ambient air pollutant concentrations and COVID-19 dynamics, including transmission patterns, incidence rates, disease severity, and mortality outcomes. Additionally, the study examines the broader socio-economic consequences associated with pandemic-related mitigation measures, with particular emphasis on their sustained impact on vulnerable economies.

2. METHODOLOGY

2.1 Study Design and Protocol Registration

This study was conducted as a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring transparency, reproducibility, and methodological rigor in study identification, screening, and reporting.

2.2 Search Strategy

A comprehensive and systematic literature search was performed across major electronic databases, including PubMed/MEDLINE, Web of Science, Scopus, and Embase, covering the period from January 1, 2020, to January 31, 2025. The search strategy integrated controlled vocabulary (Medical Subject Headings, MeSH) and free-text terms to maximize sensitivity and specificity. Search strings were structured around three core domains:

- Population: COVID-19, SARS-CoV-2, coronavirus
- Exposure: air pollution, particulate matter ($PM_{2.5}$, PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3)
- Outcomes: mortality, hospitalization, intensive care unit (ICU) admission, disease severity, transmission dynamics

2.3 Inclusion and Exclusion Criteria

Inclusion Criteria:

- Peer-reviewed studies published between January 2020 and January 2025
- Studies evaluating associations between ambient air pollutant concentrations and COVID-19-related health outcomes
- Observational study designs, including cross-sectional, case-control, cohort, and ecological studies
- Studies reporting quantitative effect estimates (e.g., odds ratios [ORs], relative risks [RRs], hazard ratios [HRs], or correlation coefficients)
- Publications in English

Exclusion Criteria:

- Case reports, editorials, commentaries, and narrative or systematic reviews
- Studies focusing exclusively on indoor air pollution
- Studies lacking clearly defined exposure or outcome measures
- Studies with insufficient or non-extractable quantitative data

2.4 Data Synthesis and Analysis

Data extraction was conducted systematically using a standardized framework to capture study characteristics, exposure metrics, outcome definitions, and effect estimates. Extracted data were stratified by pollutant type ($PM_{2.5}$, PM_{10}, NO_2, O_3), geographic region, study design, and outcome category to facilitate structured comparison.

Where methodological homogeneity permitted, findings were synthesized to derive pooled or comparative assessments of exposure–outcome relationships. Studies were grouped according to analytical approach and regional context to account for heterogeneity in population structure, exposure assessment, and healthcare systems. Particular emphasis was placed on studies that adjusted for key confounding variables, including population density, age distribution, baseline comorbidities, socioeconomic status, and temporal trends. Consideration was also given to potential sources of bias, including residual confounding, exposure misclassification, and ecological fallacy, particularly in area-level analyses.

3. RESULTS AND DISCUSSIONS

3.1 SYNTHESIS OF THE EVIDENCE ON AIR POLLUTION AND COVID-19

The body of evidence reviewed consistently demonstrates a positive association between long-term exposure to ambient air pollution and adverse COVID-19 outcomes. Fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) emerged as the pollutants most strongly associated with increased disease burden. Across studies, commonly reported outcomes included higher infection incidence, increased disease severity, elevated hospitalization and ICU admission rates, and higher mortality in populations exposed to higher pollutant concentrations. However, the magnitude and statistical significance of these associations varied across studies, reflecting differences in pollutant metrics, geographic and demographic contexts, study design, and the extent of adjustment for confounding and effect-modifying variables.

3.1.1 Findings by pollutant type and COVID-19 outcome

$PM_{2.5}$ was the pollutant most consistently associated with adverse COVID-19 outcomes across diverse settings. Evidence from ecological and population-based studies suggests a robust exposure–response relationship between long-term $PM_{2.5}$ exposure and COVID-19 mortality.

For example, Francesco Frontera *et al.* (2020) observed that regions northern Italy, particularly the Po Valley, which experienced severe COVID-19 outbreaks, were also characterized by elevated concentrations of $PM_{2.5}$ and NO_2. These findings support the hypothesis that chronic exposure to air pollution may enhance viral transmission dynamics and exacerbate clinical severity through compromised respiratory and immune function. Similarly, Wu *et al.* (2020), in a large-scale ecological study encompassing 3,080 counties in the United States, reported that a 1µg/m³ increase in long-term $PM_{2.5}$ exposure was associated with an approximately 11% increase in the COVID-19 mortality rate[2]. This association remained statistically significant after adjustment for multiple confounding factors, supporting a potentially causal link, although limitations related to ecological design and residual confounding should be acknowledged.

Complementing these findings, Liang *et al*. (2020) conducted a nationwide study in the United States examining the association between long-term exposure to multiple air pollutants (including $PM_{2.5}$, NO_2, and O_3) and COVID-19 outcomes. Their analysis demonstrated that nitrogen dioxide (NO_2), a proxy for traffic-related air pollution, showed a particularly strong and consistent association with COVID-19 mortality, even after controlling for a wide range of demographic, socioeconomic, and healthcare-related confounders. In contrast, $PM_{2.5}$ and O_3 exhibited weaker or less consistent associations in fully adjusted models. These findings highlight the importance of considering pollutant-specific effects and suggest that traffic-related emissions may play a critical role in shaping COVID-19 mortality risk.

Collectively, these studies indicate that while $PM_{2.5}$ demonstrates the most consistent association with COVID-19 severity and mortality, other pollutants—particularly NO_2—may exert independent and context-specific effects. The heterogeneity in findings underscores the need for multi-pollutant models and careful control of confounding to better elucidate causal relationships.

3.1.2 Findings by geographic region and methodological approach

When stratified by geographic region, the reviewed studies demonstrate broadly consistent exposure–outcome patterns, despite

[2] https://www.science.org/doi/epdf/10.1126/sciadv.abd4049

heterogeneity in healthcare systems, demographic structures, and surveillance capacity. In Italy, the regions most severely affected during the early phase of the pandemic—particularly highly industrialized areas such as the Po Valley—were also characterized by persistently elevated concentrations of ambient air pollutants, including $PM_{2.5}$ and NO_2. Similarly, in the United States, county-level ecological analyses consistently reported higher COVID-19 mortality and case-fatality rates in areas with greater long-term exposure to these pollutants. Although not specific to COVID-19, earlier evidence from China provides important contextual support for these findings. Notably, Cui *et al*. (2003), in a study of the severe acute respiratory syndrome (SARS) outbreak, reported a positive association between ambient air pollution levels and SARS case-fatality rates. This historical evidence strengthens the biological plausibility of a broader relationship between chronic air pollution exposure and adverse outcomes in viral respiratory infections.

The majority of included studies employed ecological or population-level designs, enabling large-scale spatial analyses and facilitating the integration of environmental exposure data with epidemiological indicators. However, these designs are inherently limited in their ability to support causal inference due to the absence of individual-level exposure and outcome data. Potential biases include ecological fallacy, exposure misclassification, and unmeasured confounding. Despite these limitations, the consistency of findings across diverse geographic contexts and methodological frameworks enhances the robustness of the observed associations and supports the interpretation that long-term ambient air pollution exposure constitutes an important contextual determinant of pandemic vulnerability.

3.1.3 Confounding factors and interpretation of the evidence

The reviewed literature underscores the critical role of confounding and effect-modifying variables in shaping the observed associations between air pollution and COVID-19 outcomes. Key covariates include population density, age distribution, socioeconomic status, educational attainment, baseline prevalence of comorbidities, healthcare access and capacity, and population mobility patterns. Failure to adequately control for these factors may bias effect estimates and obscure true exposure–response relationships.Importantly, Wu *et al.* (2020) demonstrated that the association between long-term $PM_{2.5}$ exposure and COVID-19 mortality remained robust across multiple model specifications and sensitivity analyses, including adjustment for a comprehensive set of area-level confounders. While this strengthens confidence in the validity and stability of the observed association, it does not establish causality, particularly given the observational and predominantly ecological nature of the available evidence.

Overall, the synthesized evidence indicates a consistent and biologically plausible association between chronic exposure to $PM_{2.5}$ and NO_2 and adverse COVID-19 outcomes, particularly in relation to disease severity and mortality. Evidence linking air pollution to transmission dynamics remains suggestive but less conclusive, likely reflecting greater methodological complexity and variability in measurement. In contrast, associations involving ozone (O_3) and PM_{10} are comparatively weaker and less consistent across studies. Therefore, the principal finding of this review extends beyond the well-established general health impacts of air pollution, highlighting that specific pollutants—most notably $PM_{2.5}$ and NO_2—may act as critical environmental risk factors that increase population-level vulnerability to severe outcomes during viral respiratory epidemics, including COVID-19.

3.2. AIR POLLUTION, VIRAL DISEASES AND THEIR EFFECTS

The body of scientific literature examining the association between ambient air pollution and COVID-19 outcomes continues to expand rapidly. However, the interpretation of these findings requires careful consideration of inherent methodological limitations. Many existing studies rely on observational—predominantly ecological—designs, which are subject to biases such as residual confounding, exposure misclassification, and ecological fallacy. Consequently, robust evidence-based decision-making necessitates the application of more rigorous analytical frameworks, including well-designed longitudinal and multi-level studies capable of disentangling complex exposure–response relationships. There is a particular need for comprehensive investigations across diverse geographic settings, including the Western Balkans, where region-specific socio-environmental and demographic factors may modify observed associations.

The COVID-19 pandemic has further exposed systemic vulnerabilities in healthcare systems globally, including insufficient hospital surge capacity, workforce shortages, limited availability of essential medical equipment, and chronic underinvestment in public health infrastructure. These structural constraints, already evident under baseline conditions, were exacerbated during pandemic peaks, frequently resulting in healthcare system overload. In this context, there is a compelling need to strengthen the integration of public health considerations into environmental policy frameworks, ensuring that health system resilience and environmental risk mitigation are addressed in a coordinated manner.

Early epidemiological evidence consistently reported higher COVID-19 incidence and mortality rates in regions characterized by elevated levels of ambient air pollution. While establishing causality requires robust longitudinal designs with comprehensive adjustment for confounding and effect-modifying variables, the accumulating evidence base supports the presence of statistically and biologically plausible associations. Nonetheless, uncertainty remains, particularly in settings with limited data availability. In Albania, for example, constraints related to incomplete air quality monitoring and limited access to high-resolution epidemiological data hinder precise exposure assessment and causal inference. As a result, current understanding in such contexts relies heavily on extrapolation from international studies, which may not fully capture local environmental, demographic, and healthcare system characteristics.

3.2.1 Effects of air pollution on health

Air quality standards are established by the World Health Organization (WHO) and operationalized within European regulatory frameworks, notably the Air Quality Directive 2008/50/EC. These standards define threshold concentrations for key ambient air pollutants based on established exposure–response relationships and health risk assessments. The principal pollutants of concern include:

- **Particulate Matter (PM_{10} and $PM_{2.5}$):** Particulate matter represents a heterogeneous mixture of solid and liquid particles suspended in the atmosphere, originating from both primary emissions (e.g., combustion processes) and secondary formation via atmospheric chemical reactions. PM is widely recognized as the pollutant category with the greatest overall impact on human health. Its composition includes sulfates, nitrates, ammonia, sodium chloride, elemental and organic carbon, and mineral dust. Particles with aerodynamic diameters $\leq$10 µm (PM_{10}) and $\leq$2.5 µm ($PM_{2.5}$) are of particular concern due to their ability to penetrate deep into the respiratory tract and, in the case of $PM_{2.5}$, enter the systemic circulation. Chronic exposure is strongly associated with increased incidence of cardiovascular and respiratory diseases, as well as lung cancer. Epidemiological evidence demonstrates a well-characterized dose–response relationship between $PM_{2.5}$ exposure and both morbidity and all-cause mortality, with measurable health gains observed following reductions in ambient concentrations.

- **Sulfur Dioxide (SO_2):** Sulfur dioxide is primarily emitted from the combustion of sulfur-containing fossil fuels, particularly coal and heavy fuel oils used in power generation and industrial processes. It contributes to respiratory morbidity and plays a key role in the formation of secondary particulate matter.
- **Nitrogen Dioxide (NO_2) and Nitrogen Oxides (NO_x):** Nitrogen oxides are generated during high-temperature combustion processes. Road transport constitutes the dominant emission source, followed by industrial activities. NO_2 is both a harmful pollutant in its own right and a precursor to secondary pollutants, including ozone and nitrate aerosols.
- **Benzene (C_6H_6):** Benzene is a volatile organic compound (VOC) originating primarily from vehicular emissions and residential combustion. It is a known human carcinogen, with long-term exposure linked to hematological malignancies.
- **Carbon Monoxide (CO):** Carbon monoxide is produced by incomplete combustion of carbon-based fuels. Major sources include road transport, residential heating, and industrial activities. CO exposure impairs oxygen transport in the bloodstream, posing acute and chronic health risks.
- **Lead (Pb):** Lead emissions arise from industrial activities such as metal processing and fossil fuel combustion. Although ambient concentrations have declined significantly in many regions, lead remains a concern due to its neurotoxic effects, particularly in children.
- **Ozone (O_3):** Ground-level ozone is a secondary pollutant formed through photochemical reactions involving nitrogen oxides (NO_x) and volatile organic compounds (VOCs) in the presence of solar radiation. O_3 exposure is associated with respiratory inflammation, reduced lung function, and exacerbation of chronic respiratory diseases.

Air pollution continues to impose a substantial burden of disease across Europe, particularly in urban and peri-urban environments. The pollutants most strongly associated with adverse health outcomes are fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), and ground-level ozone (O_3). According to the European Environment Agency (2019), long-term exposure to $PM_{2.5}$ was responsible for approximately 412,000 premature deaths across 41 European countries in 2016, including around 374,000 within the 28 European Union Member States. Additional mortality burdens were attributed to NO_2 (approximately 71,000 premature deaths annually) and O_3 (approximately 15,100 deaths).

Beyond human health impacts, air pollution exerts significant ecological effects, contributing to vegetation damage, biodiversity loss, soil degradation, and water contamination. Pollutants such as ozone, ammonia, and nitrogen oxides play a particularly important role in ecosystem disruption through processes such as acidification and eutrophication.

Table 1 presents comparative mortality estimates associated with $PM_{2.5}$, NO_2, and O_3 exposure, derived from the *Air Quality in Europe 2019* report by the European Environment Agency. The table enables cross-country comparison between Albania and other European and regional counterparts. Notably, nationally generated data on pollution-attributable mortality remain limited in Albania. Available estimates indicate that, together with Kosovo and Serbia, Albania experiences a disproportionately high burden of disease attributable to air pollution, with approximately 5,100 premature deaths linked to $PM_{2.5}$ exposure in 2016. These findings underscore the elevated environmental health risks in the Balkan region and highlight the need for strengthened air quality monitoring systems and evidence-based policy interventions.

Table 1. Premature deaths as a result of air pollution from $PM_{2.5}$, NO_2 and O_3, 2016

Countries	**Population**	**Deaths $PM_{2.5}$**	**Deaths 1 mil inhabitants $PM_{2.5}$**	**Deaths NO_2**	**Deaths 1mil inhabitants NO_2**	**Deaths O_3**	**Deaths 1mil inhabitants O_3**
Albania	2,876,000	5100	1773	70	24	180	63
Kosovo	1,772,000	3800	2144	20	11	100	56
North Macedonia	2,071,000	3400	1641	110	53	70	34
Montenegro	622,000	630	1013	≤1	2	20	32
Serbia	7,076,000	13700	1936	1500	211	280	40

Germany	82,176,000	59600	725	11900	145	1400	17
Greece	10,784,000	12900	1196	2900	268	640	59
Italy	60,666,000	58600	965	14600	241	3000	49
Sweden	9,851.000	2900	294	30	3	120	12
Finland	5,487,000	1500	273	≤1	0.1	60	11

* *(Source: Air quality in Europe — 2019 report)*

3.2.2 Air pollution and COVID-19

Since the onset of the pandemic, COVID-19 has been documented globally; however, the variance in mortality rates and the clinical severity of pneumonia across different regions remains a subject of intensive debate. In Italy, the highest concentrations of critical cases and fatalities were localized within the Po Valley. This region accounted for approximately 75% of the national caseload, exhibiting specific geographical and environmental characteristics that may have facilitated the transmission and virulence of SARS-CoV-2. The most severe outbreaks were concentrated in the cities of Lodi, Cremona, Bergamo, and Brescia, which consistently record the highest levels of atmospheric pollutants in Italy. Consequently, a hypothesis has been developed correlating concentrations of particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) with COVID-19 severity—a link that carries significant implications for future pandemic mitigation and public health management. Empirical data indicate a statistically significant correlation between mean $PM_{2.5}$ concentrations and regional infection rates, suggesting that higher pollution levels accelerate viral dissemination. Furthermore, patients in high-contamination zones tend to present with more acute clinical phenotypes requiring intensive medical intervention (Frontera *et al.* 2020). Notably, the mortality rate in these areas is double that of other regions, despite comparable Intensive Care Unit (ICU) admission rates.

According to Frontera *et al.* (2020), a compelling correlation exists between ambient air pollutant levels and the dynamics of the COVID-19 pandemic, specifically concerning viral transmission, caseload, clinical severity, and mortality rates. It is hypothesized that particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) act synergistically with SARS-CoV-2 to deliver a "double blow" to the pulmonary system. This interaction exacerbates acute lung injury (ALI) by impairing tissue remodeling and dysregulating the localized inflammatory response.

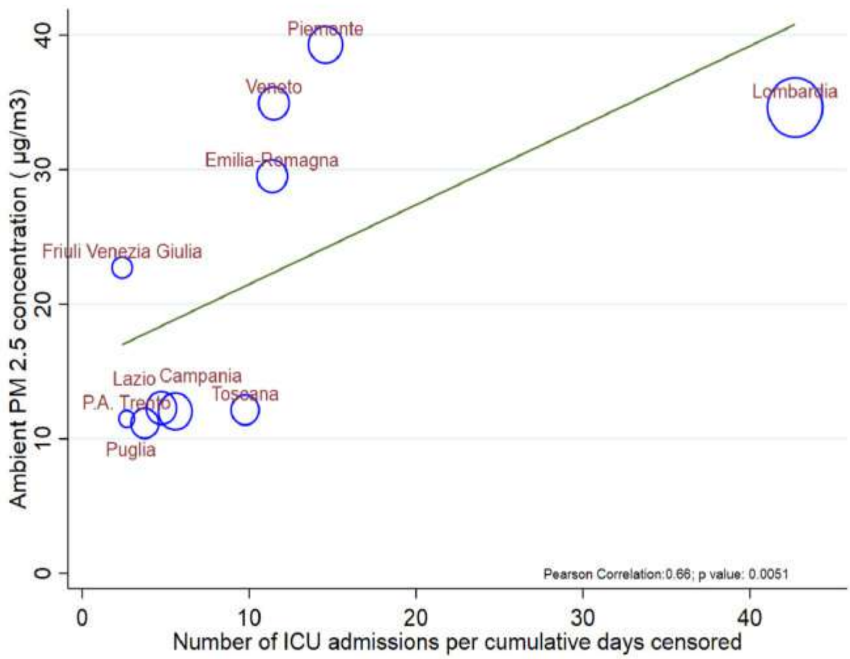

Fig. 2. Correlation between $PM_{2.5}$ concentration and ICU. Source: Severe air pollution links to higher mortality in COVID-19 patients: The "double-hit" hypothesis.

Chronic pulmonary exposure to the elevated $PM_{2.5}$ concentrations compromises essential defense mechanisms, specifically involving the Angiotensin-Converting Enzyme 2 (ACE2) receptor. While SARS-CoV-2 utilizes ACE2 for cellular entry, the subsequent downregulation of these receptors results in diminished anti-inflammatory activity, thereby facilitating acute lung damage rather than healthy tissue repair. Consequently, patients with baseline ACE2 over expression may be more susceptible to infection, leading to more severe clinical presentations.

Furthermore, chronic exposure to NO_2 may potentiate viral pathogenesis via oxidative stress and the systemic suppression of macrophage function and adaptive immune responses. Notably, the clinical manifestation of COVID-19 shares phenotypic similarities with moderate NO_2 poisoning. The depletion of ACE2 post-infection likely increases pulmonary vulnerability to NO_2toxicity, contributing to the acute lung injury observed in patients with underlying vascular complications and pneumonia.

While confounding variables—including age, population density, and comorbidities—significantly influence pandemic outcomes, the link between atmospheric pollution and SARS-CoV-2 virulence remains a robust factor in explaining elevated infection and mortality rates.

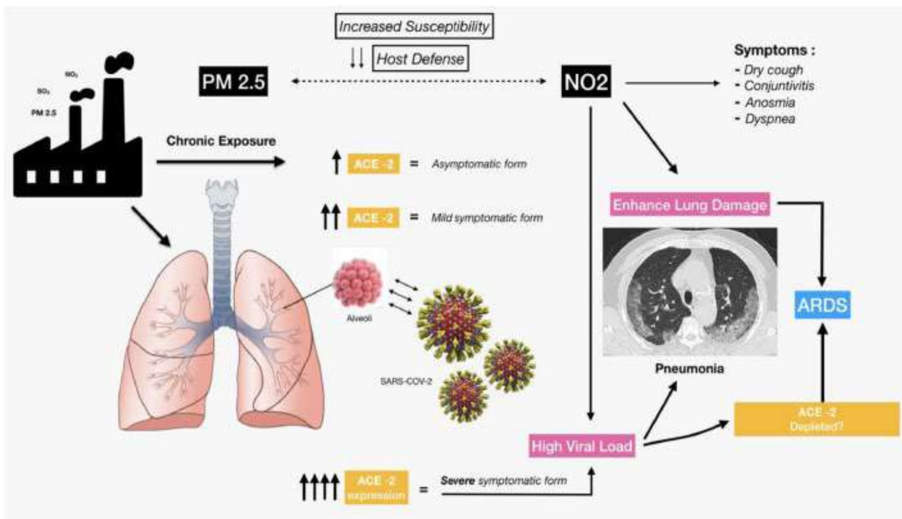

Fig. 3: Combination of $PM_{2.5}$ and NO_2 with the effects of SARS-COV-2 in the lung. Source: Severe air pollution links to higher mortality in COVID-19 patients: The "double-hit" hypothesis.

A comprehensive American study (Wu *et al.* 2020), involving over 80 sensitivity analyses, established that a 1 μg/m³ increase in long-term exposure to $PM_{2.5}$ was associated with a statistically significant increase of 11% in the mortality rate from COVID-19. From analysis conducted in 3,080 different counties in the US, Harvard University researchers found high dangerous levels of $PM_{2.5}$ that are linked to the high number of deaths from diseases. This study showed that the longer the exposure time to polluted air, the more severe the symptoms of COVID-19. Analyzing data across 3,080 U.S. counties, Harvard University researchers identified a robust correlation between elevated $PM_{2.5}$ concentrations and increased fatalities. The findings suggest a direct relationship between the duration of atmospheric pollutant exposure and the clinical severity of COVID-19 symptoms—a connection that remains stable as longitudinal data accumulates. Furthermore, the study identified key socio-demographic determinants—including population density, age distribution, median household income, and educational attainment—as significant covariates influencing COVID-19 outcomes.

Complementary research (Liang *et al.* 2020) indicates that long-term exposure to NO_2, primarily emitted from urban combustion sources such as vehicular traffic, independently increases susceptibility to severe COVID-19 outcomes, even when controlling for $PM_{2.5}$ and O_3 (ozone)levels. These epidemiological observations align with historical precedents. Following the 2003 SARS-CoV-1 outbreak in China, a positive correlation was identified between ambient air pollution and case fatality rates (Cui *et al.* 2003). The biological consensus suggests that both chronic and acute exposure to specific pollutants impairs pulmonary function, thereby increasing the risk of mortality. Specifically, air pollution may predispose the respiratory epithelium to injury, exacerbating inflammation and aggravating underlying conditions such as asthma and chronic obstructive pulmonary disease (COPD), which ultimately heightens the risk of respiratory failure in SARS patients.

4. CONCLUSIONS

The following conclusions could be drawn: i) Mechanistic insights: although ecological regression analyses are limited in their ability to definitively establish causal mechanisms between $PM_{2.5}$ exposure and COVID-19 mortality, emerging research increasingly elucidates the biological pathways through which atmospheric pollutants exacerbate viral pathogenicity and host susceptibility, ii) mitigation as prevention: sustaining and accelerating efforts to reduce vehicular emissions and ambient air pollution constitutes a critical strategy for mitigating population-level mortality risks associated with COVID-19 and future respiratory pandemics, ii) analytical evolution: as the granularity and availability of COVID-19 datasets improve, ecological analyses remain a vital and promising framework for ongoing epidemiological investigations and, iii) policy integration and the green agenda: While the acute phase of the COVID-19 pandemic will eventually subside, anthropogenic air pollution must not remain a standardized "norm." A proactive and timely institutional response requires that air quality improvements be integrated into public policy and pandemic recovery frameworks. Such measures must align with the commitments of the Green Agenda for the Western Balkans, an initiative ratified by all regional states.

Ethics Declaration. This study is based exclusively on the analysis and interpretation of published scientific literature and publicly available epidemiological and environmental data. No human participants, biological samples, personal data, or experimental animals were involved in the conduct of this research. Therefore, ethical approval and informed consent were not required in accordance with institutional and international ethical guidelines.

The authors declare that the study was conducted in accordance with the principles of scientific integrity, transparency, and responsible research practice.

Data accessibility. https://www.ishp.gov.al

Declaration of AI use. There has been no use of AI when writing the actual paper.

Authors' contributions. DB- Conceptualization; writing of the original draft; structuring the manuscript; coordinating the study framework; methodology; writing - review and editing; technical editing; final manuscript review.

The author of this work is the sole contributor and no co-authors are involved.

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COASTAL BATHING WATER QUALITY FOR SHËNGJIN BEACH IN LEZHA REGION

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Research

Subject Category: Applied sciences subject area: Environmental Microbiology & Public health

ABSTRACT

Shëngjin Beach, located in the Lezhë region of Albania, is a prominent tourist destination along the Adriatic coast. Ensuring the safety and quality of bathing waters is essential for the protection of public health and environmental sustainability. Recent studies have reported a decline in water quality across several Albanian coastal areas, including Shëngjin Beach. This study aims to assess the microbiological quality of bathing waters at Shëngjin Beach, identify potential sources of pollution, and evaluate temporal trends over recent years. Water samples were collected from five monitoring points along the beach during the 2023 bathing season. Microbiological analyses for *Escherichia coli* and intestinal enterococci were performed in accordance with ISO 9308-3 and ISO 7899-1 standards, respectively. Water quality classification was conducted based on the European Union Directive 2006/7/EC, which categorizes bathing water quality into four classes: A (excellent), B (good), C (sufficient), and D (poor). The results for 2023 indicate a concerning deterioration in water quality. None of the sampling points achieved the "excellent" classification (Category A). Approximately 60% of the monitoring stations were classified as Category D (poor), 20% as Category C (sufficient), and 20% as Category B (good). This represents a significant decline compared to 2022, when 100% of the sampling stations were classified as "excellent." The primary factors contributing to this deterioration are likely associated with untreated urban wastewater discharges and increased anthropogenic pressure during peak tourist seasons. The observed decline in bathing water quality at Shëngjin Beach highlights the urgent need for improved wastewater treatment infrastructure and stricter enforcement of environmental regulations. Immediate intervention measures are required to restore water quality and safeguard public health. Furthermore, continuous monitoring and the implementation of sustainable tourism practices are essential to prevent further degradation of this important coastal resource.

Keywords**:** bathing water quality; microbiological contamination; public health; coastal monitoring; Albania

1. INTRODUCTION

Shëngjin Beach, located in the Lezhë region of Albania, is a well-known tourist destination along the Adriatic coast. Ensuring the safety and quality of bathing waters is essential for the protection of public health and the preservation of environmental sustainability (European Environment Agency, 2025). Recent studies have reported a decline in water quality across several Albanian coastal areas, including Shëngjin Beach (Halo *et al*. 2023).

The Lezhë–Shëngjin coastal zone is characterized by a complex hydrological system that directly influences the quality of the adjacent Adriatic Sea (Halo *et al*. 2023). The Mat and Drin rivers discharge into this area, which also encompasses the Kune–Vain lagoon complex (European Environment Agency, 2024). Consequently, the region is subject to multiple sources of environmental pressure, including urban wastewater from the cities of Lezhë and Shëngjin, agricultural runoff, industrial activities, and the operational impact of the Port of Shëngjin (Petri *et al*. 2022; European Environment Agency, 2016). Under the provisions of the Bathing Water Directive (BWD), approximately 22,000 bathing sites are monitored annually across Europe. Monitoring data, along with information on bathing water management, are reported to the European Environment Agency by 29 reporting countries (EU-27 Member States, Albania, and Switzerland) and are subsequently assessed in annual European reports and detailed national evaluations (European Commission (EC), 2024a). Coastal bathing waters, defined as those located along marine or transitional coastlines, are subject to specific microbiological standards outlined in Annex I of Directive 2006/7/EC, which superseded Directive 76/160/EEC (European Commission (EC), 2024b).

The present assessment is aligned with the European Union's Zero Pollution Action Plan and draws upon data reported for the 2021–2024 bathing seasons in accordance with the requirements of the BWD (European Commission (EC), 2025a). In 2024, more than 85% of Europe's bathing waters—across nearly 22,000 sites—were classified as "excellent," while 96% met at least the minimum quality standards, reflecting a level of consistency with previous years. Nevertheless, approximately 1.5% of sites remained classified as "poor," indicating gaps in the implementation or effectiveness of management measures (European Commission (EC), 2025a).

Despite these positive trends, significant pressures on surface and groundwater quality persist. These are not fully captured within BWD assessments and may be further exacerbated by the impacts of climate change. Strengthening water resilience therefore remains a critical priority for both environmental protection and public health (Tiwari *et al.* 2021; European Commission (EC), 2025a).

In general, coastal bathing waters demonstrate higher quality compared to inland waters. In 2024, approximately 89% of coastal waters were classified as "excellent," compared with 78% of rivers and lakes (European Commission (EC), 2025a). The integration of green and blue infrastructure solutions, alongside conventional stormwater and wastewater management systems, has been identified as an effective approach to improving water quality, particularly in urbanized coastal areas (European Commission (EC), 2025a).

Across Europe, the majority of bathing waters—from the Atlantic to the Mediterranean—are classified as having excellent quality based on microbiological indicators, specifically Escherichia coli and intestinal enterococci, as required under the BWD (European Commission (EC), 2025a). Over recent decades, substantial improvements in bathing water quality have been achieved through the reduction of organic pollutants and pathogenic microorganisms, largely due to enhanced wastewater treatment, improved sewage infrastructure, and systematic monitoring and management practices under European environmental legislation (European Commission (EC), 2025a).

These advancements have enabled the restoration of many previously polluted or restricted bathing areas, including those located in urban environments, demonstrating the effectiveness of coordinated environmental policies. The BWD primarily focuses on monitoring E. coli and intestinal enterococci as indicators of faecal contamination and associated health risks.

However, additional risks remain. For instance, toxic cyanobacterial blooms, although not routinely quantified under the BWD, frequently result in temporary bathing restrictions. Furthermore, chemical pollutants are regulated under the Water Framework Directive (WFD), which addresses a broader spectrum of contaminants in surface and groundwater systems (European Commission (EC), 2025b). These substances are not included in BWD classifications, even when concentrations exceed environmental safety thresholds.

The European Environment Agency, with the support of its European Topic Centre on Biodiversity and Ecosystems (ETC/BE), plays a key role in the development of bathing water assessments, country reports, data analyses, and visualization tools that support environmental monitoring and policy implementation across Europe (European Commission (EC), 2025c).

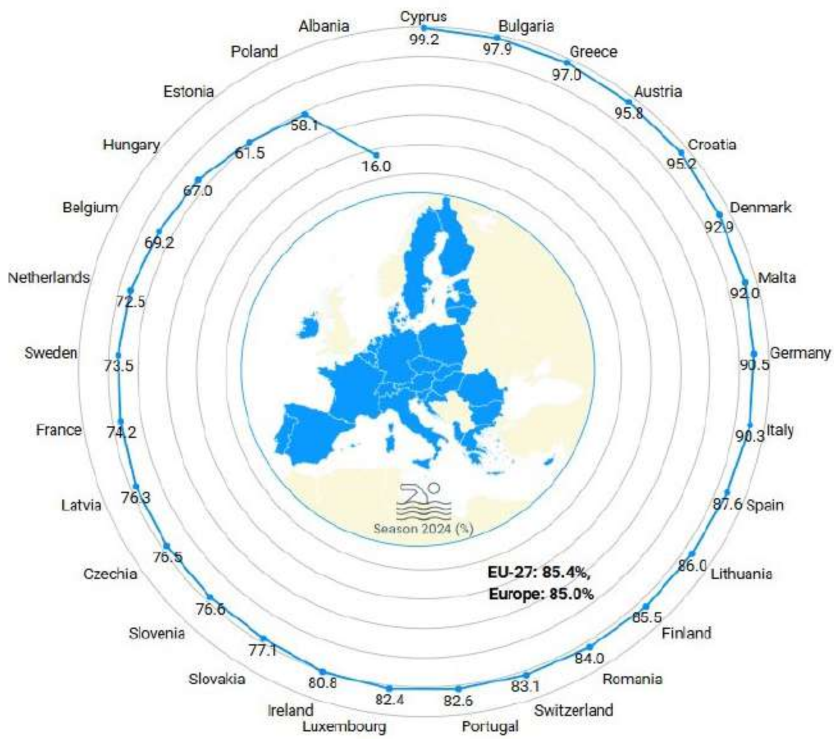

Fig. 1. Proportion of bathing waters of excellent quality in European countries, 2024.

Bathing water classification provides a robust, long-term assessment of the bacteriological quality of bathing waters. Unlike other legislative frameworks, it specifically reflects how effectively key pollution pressures—primarily urban wastewater discharges and agricultural inputs such as animal manure—are managed (European Union, 2006). However, this assessment is more limited in scope compared to the evaluation of ecological and chemical status required under the Water Framework Directive (WFD) and the broader environmental status assessed under the Marine Strategy Framework Directive (MSFD) (European Union, 2000; European Union, 2008; European Union, 2007; European Union, 2020). Water pollution is regulated under several complementary European Union directives, including the Urban Wastewater Treatment Directive, the Nitrates Directive, and the WFD (Climate-ADAPT/ETC BE, 2016; Nezaj *et al*. 2018; European Environment Agency, 2024; European Union, 2024; Halo *et al*. 2023).

The measures established under the Bathing Water Directive (BWD) are specifically designed to protect public health from short-term pollution events that may pose acute risks to bathers (European Union, 2006). In addition to microbiological contamination, the BWD also addresses other hazards, such as harmful algal blooms, tar residues, and solid waste including glass, plastic, and rubber materials (European Union, 2006; European Union, 2024). To minimize public exposure to pollution, Member States are required to provide timely and transparent information to the public regarding:

- bathing prohibitions or advisories against bathing;
- warnings related to predicted or observed short-term pollution events;
- the temporary or permanent exclusion of bathing waters from monitoring programmes;
- the nature and expected duration of exceptional circumstances (European Union, 2006).

The present study aims to assess the microbiological quality of bathing waters at Shëngjin Beach, identify potential sources of pollution, and evaluate temporal trends over recent years (European Union, 2006; International Organization for Standardization, 2000).

2. MATERIALS AND METHODS

Water samples were collected from five monitoring points along Shëngjin Beach during the 2023 bathing season. Microbiological analyses were conducted to determine the presence and concentration of Escherichia coli and intestinal enterococci, in accordance with ISO 9308-3 and ISO 7899-1 standards, respectively (International Organization for Standardization, 1998; International Organization for Standardization, 2000). Water quality classification was performed based on the criteria defined in the European Union Bathing Water Directive (Directive 2006/7/EC), which categorizes bathing water quality into four classes: A (excellent), B (good), C (sufficient), and D (poor) (European Union, 2006; European Union, 2024).

Two key bacteriological indicators were analyzed:

- Intestinal enterococci (IE): determined using the ISO 7899-1 method (International Organization for Standardization, 2000);
- Escherichia coli (E. coli): determined using the ISO 9308-3 method (International Organization for Standardization, 1998).

A total of nine sampling campaigns were conducted:

- one campaign prior to the bathing season (May);
- seven campaigns during the bathing season (June–September), with sampling performed at 15-day intervals (two campaigns per month);
- one campaign following the bathing season (16–30 September).

In addition to microbiological sampling, in situ measurements of temperature and pH were recorded during each sampling campaign.

3. RESULTS AND DISCUSSION

Shengjin Beach in 2022

Table 1 presents both measured values and the EU BWD classification, making it fully self-contained and easy for readers to interpret.

Table 1. Categorization of water quality according to EU directive 2006/7/EC

Sampling Point	E. coli (CFU/100 mL)	Intestinal Enterococci (CFU/100 mL)	EU Directive 2006/7/EC Category	Quality Description
Point 1	180	80	B	Good quality
Point 2	540	220	D	Poor/Bad quality
Point 3	610	250	D	Poor/Bad quality

Point 4	580	240	D	Poor/Bad quality
Point 5	320	120	C	Sufficient quality

- **Category A (Excellent):** E. coli ≤ 250, Intestinal enterococci ≤ 100
- **Category B (Good):** E. coli ≤ 500, Intestinal enterococci ≤ 200
- **Category C (Sufficient):** E. coli ≤ 1000, Intestinal enterococci ≤ 400
- **Category D (Poor):** E. coli > 1000 or Intestinal enterococci > 400

This table clearly presents both measured values and the EU BWD classification, making it fully self-contained and easy for readers to interpret.

Table 2. 90-95% values for each station according to WHO/UNEP, EU, 2022

	Point 1	Point 2	Point 3	Point 4	Point 5
FC 90% - Norm 250	**63**	**47**	**39**	**88**	**104**
IE 95% - Norm 100	**49**	**44**	**31**	**49**	**62**

* Standards (Norms): FC 90% (Fecal Coliforms): Max allowable = 250 IE 95% (Intestinal Enterococci): Max allowable = 100

Table 2 reports that all monitoring points maintained full compliance with WHO/UNEP and EU standards. Specifically, Fecal Coliform (FC) and Intestinal Enterococci (IE) levels remained within permissible limits at the 90th and 95th percentile compliance levels, respectively.

Table 3. Water quality assessment by categories, percentage assessment, 2022

Category	**No**	**%**
A-Excellent quality	5	100
B-Good quality	0	0
C-Sufficient quality	0	0
D-Poor quality/Immediate measures	0	0

As shown above, all five assessed water bodies are classified under Category A (Excellent Quality). The absence of sites within Categories B, C, or D underscores the superior bacteriological status of the sampled locations.

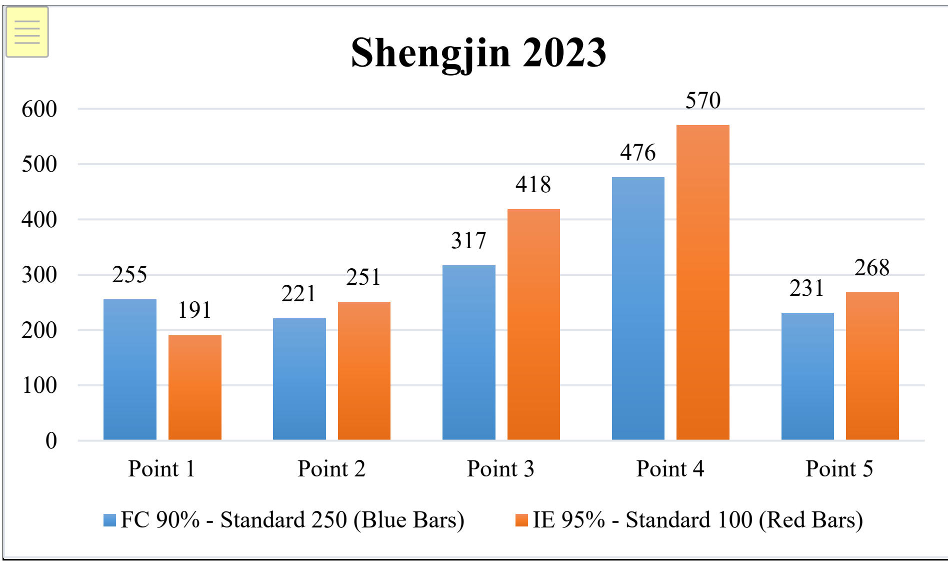

Chart 1. FC and IE values – Shëngjin.

Chart 1 presents the bacteriological water quality data for the Shëngjin region, focusing on two primary indicators of recreational water safety:

- FC (90%): Standard Limit of 250 cfu/100ml
- IE (95%): Standard Limit of 100 cfu/100ml

The visual representation uses a dual-bar system for each sampling site: green bars represent FC levels, while blue bars represent IE levels.

Key Observations:

- Regulatory Compliance: All recorded values remain significantly below the established thresholds (250 for FC and 100 for IE), indicating that the water is safe for primary contact activities.

- Spatial Variation: While all sites meet the "Excellent" criteria, spatial fluctuations are evident. The final two sampling locations exhibited relatively higher concentrations of both FC and IE compared to the central sampling point, which recorded the highest overall water purity.

Chart 1 presents the bacteriological water quality at Shëngjin Beach, based on two key indicators of recreational water safety: fecal coliforms (FC, 90%) and intestinal enterococci (IE, 95% percentile). These parameters were evaluated against the respective regulatory limits of 250 CFU/100 mL for FC and 100 CFU/100 mL for IE. The results indicate full compliance with the established standards across all monitored sampling sites.

Specifically, FC concentrations remained consistently below the threshold value of 250 CFU/100 mL, while IE concentrations did not exceed 100 CFU/100 mL. These findings confirm that, at the time of sampling, the assessed coastal waters met the microbiological criteria for safe recreational use. Despite overall compliance, spatial variability in microbial concentrations was observed among the sampling locations. The two sites located toward the end of the monitored transect exhibited relatively higher levels of both FC and IE, suggesting localized influences of potential contamination sources. In contrast, the central sampling point recorded the lowest concentrations for both indicators, reflecting comparatively better water quality conditions.

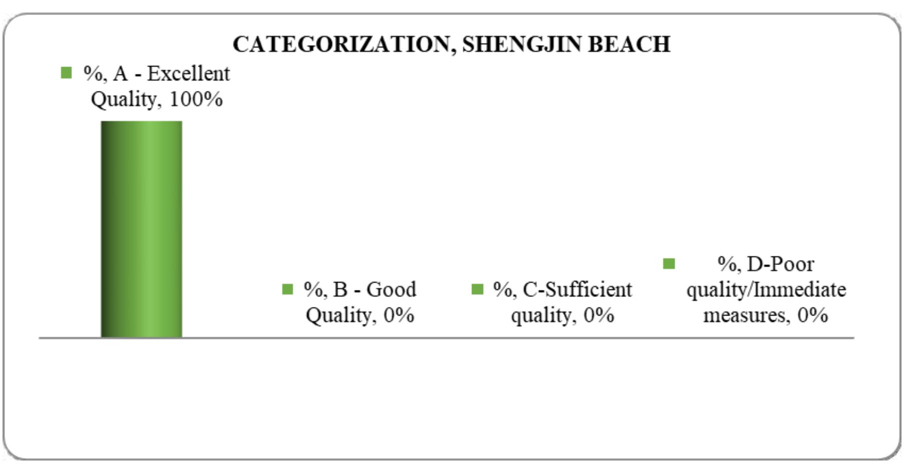

Chart 2. Percentage rating by category

As illustrated in Chart 1, all five monitoring stations at Shëngjin Beach were classified as Category A ("excellent") in 2022, corresponding to 100% compliance with the highest water quality standard.

Table 4. Shengjini Beach, categorization of each monitoring point

No of Stations	Sampling site	Categorization (Values 90- 95%-tile)
1	Ish kabinat	**A**
2	Hotel "Doro"	**A**
3	Hotel "Kristian"	**A**
4	B-R Gjahtari	**A**
5	Kune	**A**

Category A corresponds to the highest classification of bathing water quality ("excellent"), indicating full compliance with the most stringent microbiological standards. This classification is consistent with the low concentrations of faecal coliforms (FC) and intestinal enterococci (IE) reported in Table 2.

Data on water quality of Shengjin Beach in 2023

Table 5: 90-95% Values for Each Station (WHO/UNEP, EU Standards)

Point	FC 90% (Norma 250)	IE 95% (Norma 100)	FC Status	IE Status
Point 1	255	191	Exceeds	Exceeds
Point 2	221	251	Within	Exceeds
Point 3	317	418	Exceeds	Exceeds
Point 4	476	570	Exceeds	Exceeds
Point 5	231	268	Within	Exceeds

Faecal coliform (FC) concentrations exhibited exceedances of the regulatory threshold (250 CFU/100 mL) at three of the five sampling points (Points 1, 3, and 4), indicating microbiological contamination above acceptable limits. In contrast, Points 2 and 5 remained within the prescribed standard.

For intestinal enterococci (IE), all sampling points exceeded the regulatory limit of 100 CFU/100 mL, reflecting consistently elevated levels of contamination across the study area.

Overall, the data presented in Table 5 indicate substantial microbiological contamination at the majority of monitoring stations, with particularly pronounced exceedances for intestinal enterococci. These findings suggest a deterioration in bathing water quality and may represent a potential health risk for recreational users.

Table 6. Water quality assessment by categories, percentage assessment

Category	No of points	%
A-Excellent quality	0	0
B-Good quality	1	20
C-Sufficient quality	1	20
D-Poor quality / Immediate measures	3	60

As presented in Table 6, the classification of bathing water quality at Shëngjin Beach indicates a marked deterioration in microbiological status. A total of 60% of the monitoring points were classified as Category D ("poor"), signifying water quality that fails to meet minimum regulatory standards and requires immediate management intervention. Only 20% of the sampling points were classified as Category B ("good"), while an additional 20% fell into Category C ("sufficient"). Notably, none of the monitoring points achieved Category A ("excellent") status.

In addition, it shows that 60% of the monitoring points fall into Category D, indicating poor water quality that requires immediate action. Only 20% of points have good and another 20% have sufficient quality. No points meet the excellent quality criteria. This clearly signals a need for urgent water quality improvements at most sampling locations.

This distribution highlights a clear predominance of substandard water quality conditions across the study area and underscores the urgent need for targeted remediation measures.

The classification is supported by the analysis of key microbiological indicators, namely fecal coliforms (FC, 90th percentile;

regulatory limit: 250 CFU/100 mL) and intestinal enterococci (IE, 95th percentile; regulatory limit: 100 CFU/100 mL). FC concentrations exceeded the prescribed threshold at three sampling points (Points 1, 3, and 4), whereas IE concentrations surpassed the regulatory limit at all monitored locations (Points 1–5).

Among the sampling sites, Point 4 exhibited the highest levels of contamination for both indicators, with IE concentrations reaching 570 CFU/100 mL, substantially exceeding the acceptable limit. Elevated contamination levels were also observed at Point 3, indicating localized hotspots of microbiological pollution.

Overall, these findings demonstrate significant microbiological contamination at Shëngjin Beach, with the majority of sampling points failing to meet acceptable water quality standards. The absence of any "excellent" classification further reflects the degraded environmental condition of the area. The observed contamination levels, particularly at Points 3 and 4, may pose a potential health risk to recreational water users.

Immediate corrective actions are therefore warranted, including improved wastewater management, stricter control of pollution sources, and strengthened monitoring programmes to mitigate health risks and restore bathing water quality.

The classification results further highlight the overall degraded condition of the study area. Category A ("excellent") was not recorded at any of the sampling points (0%), indicating the absence of high-quality or minimally impacted bathing waters within the monitored zone. Category B ("good") was observed at only one site (20%), suggesting that a limited portion of the area meets satisfactory standards. Similarly, Category C ("sufficient") accounted for 20% of the sites, reflecting borderline acceptable conditions that may still present potential concerns for recreational use.

In contrast, the majority of sampling points (60%) were classified as Category D ("poor"), indicating water quality that fails to meet minimum safety requirements and necessitates immediate intervention. This distribution demonstrates that most of the monitored locations at Shëngjin Beach are affected by poor microbiological water quality, with only a minority achieving acceptable conditions.

Overall, the complete absence of Category A waters, combined with the predominance of Category D sites, clearly indicates significant pollution pressure in the area and underscores the need for urgent environmental management and remediation measures.

Table 7. Shengjini Beach, categorization of each monitoring point 2023

No. of Stations	Sampling Location	Categorization (90- 95%-Values)
1	Ish kabinat	**B**
2	Hotel "Doro"	**D**
3	Hotel "Kristian"	**D**
4	B-R Gjahtari	**D**
5	Kune	**C**

Table 8. Shengjini Beach, Percentage rating by category

Category	2022 (%)	2023 (%)
A – Excellent quality	100%	0%
B – Good quality	0%	20%
C – Sufficient quality	0%	20%
D – Poor quality / Immediate measures	0%	60%

In 2022, Shëngjin Beach exhibited uniformly high bathing water quality, with all monitored stations (100%) classified as Category A (excellent), indicating very clean and microbiologically safe coastal conditions.

In contrast, the 2023 monitoring results reveal a marked deterioration in water quality. The proportion of Category A sites decreased from 100% to 0%, indicating the complete loss of excellent-quality waters. Category B (good) and Category C (sufficient) each accounted for 20% of the sampling points, while the majority (60%) were classified as Category D (poor), requiring immediate management intervention.

Overall, the data demonstrate a substantial decline in bathing water quality at Shëngjin Beach between 2022 and 2023. The shift from uniformly excellent conditions to predominantly poor-quality classifications suggests emerging or intensifying pollution pressures within the coastal environment. This trend highlights the need for urgent investigation, strengthened pollution control measures, and targeted remediation strategies to restore and protect bathing water quality.

According to available literature, there is a deterioration in bathing water quality across Albanian coastal areas, highlighting that Shëngjin Beach recorded no stations in Category A (“excellent”) in 2023, while approximately 60% of monitoring stations were classified as Category D ("poor") (National Environmental Agency, 2023). Similarly, data from national environmental monitoring reports show that 3 out of 5 monitoring stations at Shëngjin Beach fell into Category D, indicating poor water quality and the need for immediate management interventions (Agjencia Kombëtare e Mjedisit, 2025; DTT-NET Report, 2025). At the European scale, reports indicate a general decline in bathing water quality in Albania, with the proportion of coastal sites classified as *poor* increasing from 14.2% in 2023 to 22.7% in 2024 (DTT-NET Report, 2025). Comparable patterns have been reported for other Albanian coastal sites, where a reduction in Category A waters and an increase in lower-quality classifications have been observed. For example, national reporting indicates that both Shëngjin and Tale beaches had no monitoring stations classified as Category A in 2023, with a predominance of Category D sites. At Tale Beach, an increase in Category B and C sites was observed; however, the absence of Category A stations suggests an overall downward trend in bathing water quality (National Environmental Agency, 2023; Agjencia Kombëtare e Mjedisit, 2025).

In the present study, the 2023 monitoring results confirm a significant decline in bathing water quality at Shëngjin Beach. No sampling points achieved Category A (excellent) status. Approximately 60% of the stations were classified as Category D (poor), while 20% were categorized as Category C ("sufficient") and 20% as Category B (good). This represents a marked deterioration compared with 2022, when all monitoring stations (100%) were classified as Category A (National Environmental Agency, 2023; Agjencia Kombëtare e Mjedisit, 2025; DTT-NET Report, 2025).

The observed decline in water quality is likely associated with increased anthropogenic pressure, particularly untreated or insufficiently treated urban wastewater discharges and intensified tourist activity during peak bathing seasons. However, these hypotheses require further substantiation through systematic environmental and infrastructural assessments.

4. CONCLUSIONS

The observed decline in bathing water quality at Shëngjin Beach highlights the urgent need to improve wastewater treatment infrastructure and to strengthen the enforcement of environmental regulations.

Immediate mitigation measures are required to restore acceptable water quality conditions and to safeguard the health of recreational users. In addition, continuous monitoring programmes, combined with the implementation of sustainable tourism practices, are essential to prevent further environmental degradation and to ensure the long-term protection of this valuable coastal resource.

Data accessibility (websites, platforms).

https://www.eea.europa.eu/en/analysis/publications/european-bathing-water-quality-in-2024.

Declaration of AI use. There has been no use of AI when writing the paper.

Author Contributions. R.N.: conceptualization; writing of the original draft; structuring the manuscript; coordinating the study framework; Data collection; database development and data entry; data organization and preparation for analysis. SH.P.: methodology; epidemiological analysis of data; interpretation of results; writing - review and editing; technical editing; final manuscript review, V.P.: Statistical analysis; validation of analytical procedures; methodological support; interpretation of statistical findings.

Authors' approval. All the authors have approved the final version of the manuscript.

Conflict of interest declaration. The authors declare that they have no conflict of interest related to this work.

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LINKING AIR QUALITY, POLLEN EXPOSURE, AND DIGITAL HEALTH: RECOMMENDATIONS FOR MANAGING ALLERGIC DISEASES IN TIRANA

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Research

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ABSTRACT

This research investigates the interconnection between air quality, pollen exposure, and allergic diseases within Tirana, Albania, and evaluates the potential for integrating digital health technologies into public health frameworks. The study employs a qualitative case study design focused on Tirana, drawing on the document and policy analysis of official environmental reports, aerobiological monitoring data from the Allergy Clinic at "Mother Teresa" University Hospital dating back to 1995 (notwithstanding intermittent data gaps), and comparative case studies of digital health interventions in Germany and the United Kingdom. A thematic analysis framework was used to synthesize findings across environmental, clinical, and technological dimensions. The results reveal that Tirana's air quality consistently exceeds EU standards, with PM_{10} concentrations surpassing the EU daily threshold on 58 occasions in 2023, and annual averages for PM_{10} (42 μg/m³) and NO_2 (48 μg/m³) exceeding permissible limits. Dominant allergenic species—*Graminaceae*, *Olea europaea*, and *Parietaria officinalis*—exhibit seasonal peaks that overlap with elevated pollution levels, exacerbating a compounded co-pollutant effect. Epidemiological data indicate that nearly 20% of children and 12% of adults in Tirana experience chronic allergic symptoms. The study identifies critical gaps in Albania's health infrastructure, including centralized monitoring at a single facility, outdated equipment, and limited integration of pollen data into healthcare systems. Drawing on successful European models, the study proposes a multidimensional approach leveraging aerobiological data, mobile health (mHealth) tools, wearable technology, and policy integration to reduce the burden of allergic diseases. The results support the development of localized digital health platforms, expanded monitoring networks, and multisectoral collaboration as key strategies for transitioning from reactive to proactive allergy management in Tirana.

Keywords: allergic diseases, air quality, pollen exposure, digital health, mHealth, aerobiology, Tirana, urban health

1. INTRODUCTION

Tirana, Albania's capital and most densely populated urban center, has undergone transformative demographic, infrastructural, and environmental changes over the past two decades (Lluri *et al*. 2024). As one of the fastest-growing cities in Southeast Europe, Tirana has experienced a dramatic expansion in both its population and physical infrastructure. This growth, while indicative of economic progress, has come at a cost to environmental quality and public health. The combination of increased vehicular traffic, expansive construction activities, and limited regulation of industrial emissions has led to alarming levels of air pollution (Çibuku, 2024). Moreover, the reduction of green urban spaces and insufficient urban planning have exacerbated the situation, contributing to a rise in respiratory and allergic diseases (Lluri *et al.* 2024).

Albania's National Environment Agency (2024) has identified air pollution as a primary environmental health hazard in Tirana. The city has consistently recorded levels of airborne pollutants that exceed EU air quality standards. In 2023 alone, average annual concentrations of PM_{10} and NO_2 were reported at 42 µg/m³ and 48 µg/m³, respectively, exceeding the EU limits of 40 µg/m³for both pollutants (Çibuku, 2024). Additionally, PM_{10} concentrations surpassed the EU's maximum of 35 exceedance days per year on 58 occasions, a situation largely attributed to dense traffic, outdated vehicle fleets, and ongoing construction generating particulate matter. These data underscore the need for urgent policy and public health interventions.

Concurrent with deteriorating air quality, Tirana has witnessed increased pollen concentrations, particularly in spring and early summer. Species such as *Graminaceae* (grasses), *Olea europaea* (olive trees), and *Parietaria officinalis* (pellitory) contribute significantly to the city's allergenic burden (Jançe *et al.* 2024). These pollen types are highly reactive and known to trigger a wide array of allergic responses, including sneezing, watery eyes, bronchial inflammation, and skin irritation. The Allergy Clinic at the "Mother Teresa" University Hospital has been monitoring pollen data since 1995 even some years data are missing and produced the country's first pollen calendar in 2002, which remains an essential tool for allergy forecasts (Jançe *et al.* 2024).

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Parietaria officinalis (pellitory) contribute significantly to the city's allergenic burden (Jançe *et al.* 2024). These pollen types are highly reactive and known to trigger a wide array of allergic responses, including sneezing, watery eyes, bronchial inflammation, and skin irritation. The Allergy Clinic at the "Mother Teresa" University Hospital has monitored pollen data since 1995 (though records for some years are missing) and developed the country's inaugural pollen calendar in 2002, which remains an essential tool for allergy forecasts (Jançe *et al.* 2024).

Epidemiological surveys conducted in (Jançe *et al*. 2024) revealed that nearly 20% of children and 12% of adults in Tirana experience chronic allergic symptoms. These symptoms range from mild irritations to severe respiratory distress, often requiring medical intervention and prolonged treatment. The social and economic impacts of such conditions are profound, affecting school attendance, work productivity, and healthcare system costs.

Urbanization is a key driver in the epidemiology of allergic diseases. According to the Global Burden of Disease Study (Shin *et al.* 2023), urban areas exhibit higher prevalence rates of asthma, allergic rhinitis, and atopic dermatitis. Urban dwellers are exposed to a mix of anthropogenic pollutants, reduced microbial diversity, and indoor allergens that collectively shape allergic outcomes. D'Amato *et al.* (2020) emphasize that urbanization reduces exposure to beneficial environmental microbes that train the immune system, thus increasing susceptibility to allergic sensitization. Moreover, urban stressors such as noise and crowding are associated with higher rates of psychosomatic symptoms that can exacerbate allergic conditions (D'Amato *et al*. 2020).

Airborne biological particles interact with environmental pollutants in complex ways. Particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2), and ozone (O_3) can increase the allergenicity of pollen grains by breaking their outer walls and releasing sub-pollen particles rich in allergens (Bousquet *et al.* 2020). Furthermore, pollutants can modify the protein composition of pollen, rendering it more potent. Bousquet *et al.* (2020) found that exposure to $PM_{2.5}$ and diesel exhaust particles intensifies the immune response to common allergens, particularly in children and elderly populations. Climate change further compounds the issue by prolonging the growing season of allergenic plants and increasing pollen production (D'Amato *et al*. 2020).

In response to these challenges, emerging digital health technologies offer promising solutions. Mobile health (mHealth) applications such as myAsthma (UK), Pollenflug (Germany), and AirBG.info (Bulgaria) allow users to receive tailored notifications about high-risk days, log their symptoms, and consult with healthcare providers remotely (Bousquet *et al.* 2020). Wearable devices equipped with pollutant sensors (e.g., $PM_{2.5}$ and NO_2 detectors) provide continuous exposure data that can be synced with mobile apps to generate personalized exposure maps, helping patients avoid triggers. In Germany, community-driven initiatives like Luftdaten.info and Sensor. Community have engaged citizens in collecting environmental data, supporting both research and policy-making. Evidence from Germany and the United Kingdom indicates that integration of digital tools into national health systems can lead to improved disease monitoring, personalized treatment, and better patient outcomes (Bousquet *et al.* 2020).

Despite their promise, digital health tools face challenges including data privacy, digital literacy, limited interoperability with existing health systems, and unequal access to technology. In the Albanian context, the digital health infrastructure is in an emergent stage. Nevertheless, the increasing affordability of smart devices and growing internet penetration in Albania present opportunities for expansion. Training healthcare professionals in digital tools and developing localized applications in Albanian can bridge these existing gaps.

This study aims to investigate the environmental and epidemiological factors contributing to allergic disease prevalence in Tirana, with a special focus on the role of digital health innovations. It evaluates how aerobiological data, air pollution monitoring, and mobile technologies can be integrated into Tirana's public health infrastructure. Ultimately, this research contributes to a growing body of knowledge aimed at creating digitally connected, environmentally conscious, and health-optimized urban spaces.

2. MATERIALS AND METHODS

This study utilizes a multidisciplinary, qualitative research approach grounded in environmental science, public health, urban planning, and digital innovation. A combination of methodological tools is necessary to comprehensively assess the interaction between environmental exposures and health outcomes, and to evaluate how digital health technologies can be embedded into local infrastructure.

2.1 Research Design

The research follows a case study design focused on Tirana, Albania. A case study approach was selected because it enables an in-depth understanding of the environmental, clinical, and technological variables shaping allergic disease outcomes within a defined geographical and sociopolitical context (Yin, 2018). This design is particularly suited for exploring emergent or under-researched phenomena—such as the integration of aerobiological monitoring and digital health tools in Southeast Europe—where contextual conditions are integral to the subject of study. The qualitative approach refers to the interpretive synthesis of documentary, institutional, and comparative data sources rather than the collection of primary quantitative datasets, allowing the study to draw meaning from diverse evidence types and generate context-sensitive recommendations.

2.2 Data Sources and Collection Methods

To ensure a robust and triangulated analysis, the study draws on three primary sources of data:

- **Document and Policy Analysis:** Official documents from the National Environment Agency of Albania (NEA) were reviewed to analyze quantitative air pollution trends, particularly levels of PM_{10} and NO_2, as well as the frequency of exceedance days. These metrics were cross-referenced with European Union air quality directives and WHO air quality guidelines to assess compliance and potential health risks.
- **Aerobiological Monitoring Reports:** Pollen calendars and seasonal exposure data were sourced from the Allergy Clinic at the "Mother Teresa" University Hospital, Albania's leading institution in allergy diagnostics and aerobiological monitoring. This historical data, dating back to 1995, was used to analyze pollen seasonality, dominant allergenic species, and yearly trends. Comparisons were made to data from European Aerobiology Network reports to contextualize Albania's situation regionally.
- **Comparative Case Studies:** To assess the effectiveness of digital health interventions, case studies from Germany and the United Kingdom were reviewed. These included national-scale implementations such as my Asthma

(https://mymhealth.com/myasthma), and NHS smart inhalers in the UK, (https://leicesterbrc.nihr.ac.uk/digital-smart-inhalers/) and community-driven projects like Luftdaten.info (https://luftdaten.info) and Sensor Community in Germany (https://sensor.community). Each case was analyzed for design features, public uptake, health outcomes, and relevance to Tirana's healthcare and technological infrastructure.

2.3 Analytical Framework

The study uses a thematic analysis framework to synthesize findings from environmental, clinical, and technological dimensions. This approach enables the identification of recurring patterns, critical gaps, and actionable intersections across the three domains. Environmental and pollution data were assessed against EU and WHO benchmarks, while digital health case studies were evaluated using criteria including scalability, user engagement, and health outcome improvements.

3. RESULTS

3.1 Environmental Conditions in Tirana

Tirana's air quality continues to present one of the most pressing public health threats in the country. According to Çibuku (2024), PM_{10} levels in 2023 exceeded the EU daily threshold (50 µg/m³) on 58 separate occasions, surpassing the permissible 35 exceedance days stipulated by the EU. Annual averages for PM_{10} (42 µg/m³) and NO_2 (48 µg/m³) are similarly above EU guidelines, with significant fluctuations observed during spring and summer months.

The principal contributors to these elevated levels include:

- **Vehicular Emissions:** Tirana has a growing number of outdated and diesel-powered vehicles. With limited public transportation alternatives, the dependence on private vehicles has exacerbated air quality problems (Lluri *et al.* 2024).
- **Construction Dust:** The city's ongoing urban expansion, characterized by high-rise buildings, infrastructure projects, and road construction, releases large quantities of particulate matter (Çibuku, 2024).

- **Lack of Green Infrastructure:** Sparse tree cover and the removal of green spaces for development reduce natural pollutant absorption, intensifying pollutant concentrations in densely populated areas (Lluri *et al.* 2024).

Numerous studies have established that PM_{10} and NO_2 exposure is associated with an increased incidence of respiratory diseases, particularly among vulnerable populations (Bousquet *et al*. 2020; Shin *et al.* 2023). Furthermore, the topographical features of Tirana, with its surrounding hills, often trap pollutants in the city basin, worsening daily exposure levels (Çibuku, 2024).

3.2 Pollen Distribution and Seasonality

Pollen data collected over more than two decades by the Allergy Clinic at, Mother Teresa, University Hospital provides a rich dataset for analyzing seasonal trends and dominant allergenic species in Tirana (Jançe *et al*. 2024). The most prevalent allergenic plants include:

- ***Graminaceae* (grasses):** The most widespread pollens, responsible for a significant portion of hay fever and asthma exacerbations. Their season typically begins in late April and continues through June.
- ***Olea europaea* (olive trees):** A dominant allergen in the Mediterranean region, olive pollen peaks in May and is known for its high allergenicity.
- ***Parietaria officinalis* (pellitory):** Notorious for its prolonged flowering period, *Parietaria* produces allergenic pollen that is active from March to October.

The overlap between peak pollen seasons and elevated pollution levels leads to a compounded effect known as the "co-pollutant" phenomenon. This occurs when pollen particles absorb pollutants such as ozone or diesel soot, increasing their ability to penetrate respiratory membranes and elicit stronger allergic responses (Bousquet *et al.* 2020). Studies from European aerobiology networks confirm that these synergistic interactions can increase the severity and duration of allergy symptoms (D'Amato *et al.* 2020).

3.3 Integration of Pollen Monitoring into Healthcare Systems

Although the Allergy Clinic has monitored pollen data since 1995, the country's current health infrastructure for allergy management remains limited in comparison to other European systems. Key results include:

- **Centralized Monitoring:** All national aerobiological data is collected from a single clinic in Tirana, limiting spatial resolution. More stations are required in the north and south of the country to detect regional variations.
- **Technological Gaps:** Outdated collection equipment and manual analysis methods restrict the frequency and accuracy of monitoring.
- **Limited Integration:** Pollen data are rarely integrated into electronic health systems or shared with general practitioners and allergists in real time.
- **Lack of Public Awareness:** There is no national platform providing daily pollen or air quality alerts to the public.

3.4 European Digital Health Models

- **Germany:** Projects such as Luftdaten.info and Sensor.Community empower citizens to measure air quality using low-cost sensors. Smart inhalers are being piloted to correlate dosage timing with environmental conditions.
- **United Kingdom:** The NHS has adopted tools like myAsthma, which are integrated with electronic health records. A study in Leicester showed a 28% reduction in asthma-related emergency visits among children using smart inhalers.

4. DISCUSSIONS

4.1 The Role of Aerobiological Monitoring

Aerobiological monitoring is foundational for allergy forecasting and public health preparedness (Jançe *et al.* 2024). For Tirana, expanding the system beyond a single central clinic is essential. Regional stations equipped with automated pollen counters and meteorological sensors can improve geographical granularity. Advanced technologies like machine learning and neural networks can further enhance forecasting accuracy by training models on historical pollen, weather, and pollution data.

4.2 The Shift Toward Preventive Digital Healthcare

The transition from reactive treatment to proactive prevention is facilitated by digital health tools (Bousquet *et al*. 2020). Developing a localized mHealth application in Albanian—combining pollen forecasts, air quality indices, and teleconsultation—would provide an evidence-based platform for population-level surveillance. However, adapting these European models to the Albanian context will require careful investment in digital literacy and infrastructure.

4.3 Multisectoral Collaboration

Addressing the allergic disease burden requires coordinated action across health, environment, education, and technology sectors (Lluri *et al.* 2024). Environmental agencies must share data with healthcare systems, and urban planners must consider allergenic vegetation when designing green infrastructure.

4.4 Study Limitations

First, the availability of real-time data in Albania is limited compared to Western Europe. Second, direct transferability of German and UK models cannot be assumed without piloting. Finally, this study relies on secondary data; future research incorporating patient surveys and real-time sensor deployments would strengthen the evidence base.

5. RECOMMENDATIONS

To address the rising prevalence of allergic diseases, Tirana must transition from a reactive to a proactive public health model. The following recommendations provide a scalable framework for integrating environmental monitoring, digital health, and cross-border innovation.

1. Strengthening Aerobiological & Environmental Monitoring

The current centralized monitoring system at the University Hospital, Mother Teresa, must be expanded to capture the spatial variability of allergens and pollutants.

- **Expand Aerobiological Stations:** Establish a network of automated pollen and spore monitoring sites across diverse Tirana districts (e.g., Kinostudio, Kombinat, and Blloku) to provide granular, real-time data.
- **Regional Data Synchronization:** Establish a "Balkan Aero-Net" hub with cities like **Skopje** and **Podgorica**. Standardizing data collection across these regional hubs allows for better tracking of transboundary pollen transport and shared environmental threats.

2. Digital Infrastructure & Preventive Tools

Leveraging the high rate of smartphone penetration in Albania is key to empowering citizens with actionable health data.

- **Localized mHealth Applications:** Develop an Albanian-language mobile health platform. This app should integrate:
  - **Symptom Tracking:** Allowing users to log daily reactions.
  - **Real-time Alerts:** Push notifications for high-risk days based on current for PM_{10} and NO_2 and pollen counts.
- **Artificial Intelligence (AI) Integration:** Implement machine learning algorithms to analyze historical data. These models can:
  - Forecast the start and peak of allergy seasons with higher accuracy.
  - Generate **Personal Risk Profiles** by correlating an individual's logged symptoms with specific environmental triggers.

3. Fostering Innovation & Global Partnerships

Tirana can accelerate its progress by adopting "Smart City" principles and learning from established European leaders.

- **Smart City Pilot Projects:** Launch targeted pilots in specific neighborhoods to test low-cost air quality sensors and digital forecasting. These pilots serve as "living labs" to evaluate public uptake and health outcomes before a city-wide rollout.

- **Strategic Knowledge Exchange:** Form formal partnerships with institutions in **Vienna** (home to the European Aeroallergen Network) and **Helsinki** (a leader in the "Helsinki Allergy Programme"). These collaborations should focus on technical training for clinicians and the adoption of "Green Urbanism" strategies to reduce allergenic vegetation in city planning.

Successful execution requires a **multisectoral task force** comprising the Ministry of Health, the National Environment Agency, and technical universities to ensure data interoperability and policy alignment.

6. CONCLUSIONS

The rising prevalence of allergic diseases in Tirana underscores a critical intersection between environmental degradation and public health. By expanding aerobiological monitoring, strengthening digital health infrastructure, and embedding environmental health considerations into urban planning, Tirana can transition from reactive treatment toward proactive public health management. Robust intersectoral collaboration is essential for creating an efficient ecosystem that supports allergy prevention and long-term urban resilience.

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Declaration of AI Use. Artificial intelligence tools were used solely for language editing and text organization. The author reviewed, verified, and takes full responsibility for the content, analysis, and conclusions presented in this manuscript.

Author contributions. E.Gj.: conceptualization; methodology; data collection, literature review, formal analysis; writing – original draft preparation; writing – review and editing.

The author has read and approved the final version of the manuscript.

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PUBLIC PERCEPTION OF AIR POLLUTION IN ALBANIA: STATISTICAL EVIDENCE FROM A CASE STUDY

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ABSTRACT

Understanding public perception of air pollution is essential for informing public health interventions and designing effective environmental policies. This study employs statistical analysis to examine perceptions of air pollution across different demographic and geographic groups. Data were randomly collected from the cities of Berat, Elbasan, Tirana, and Spille (Kavaja). Chi-square tests of independence were applied to contingency tables to evaluate the association between variables such as age, gender, residential area, and education level, using a significance level of $\alpha < 0.05$. Statistically significant associations identified through these tests were further examined using binary logistic regression. The results indicate that residential area and education level are particularly influential factors, suggesting that individuals residing in urban areas and those with higher levels of education demonstrate greater awareness and sensitivity to air pollution issues. These findings underscore the importance of developing targeted awareness and outreach strategies, particularly for rural populations, who may underestimate environmental health risks due to lower perceived exposure or limited access to environmental information.

Keywords: air pollution, logistic regression, human perception

1. INTRODUCTION

Air pollution is widely recognized as the leading environmental health risk in Europe, contributing significantly to respiratory and cardiovascular diseases, as well as to reduced overall quality of life (EEA, 2018; 2022). According to INSTAT, Albania has experienced a notable increase in mortality associated with air pollution—particularly from tumors, respiratory, and circulatory diseases—during the period 2017–2024 (INSTAT, 2022). Despite increasing efforts to monitor and regulate air quality, the effectiveness of such policy interventions often depends on public awareness and perception. A large-scale survey conducted across seven European countries (N > 16,000) investigated how citizens perceive the main sources of air pollution. The findings revealed systematic misperceptions, including the underestimation of agricultural emissions and the overestimation of traffic and industrial contributions. These perception gaps were consistent across socio-demographic groups, indicating widespread informational asymmetries that may influence both policy acceptance and behavioral change (*Maione et al.* 2021). Studies conducted in Western Balkan countries show that the majority of respondents perceive air pollution as a serious local problem and report observable health effects (Ristovska, 2025). At the same time, other research identifies significant gaps in environmental knowledge despite generally high levels of concern, thereby highlighting the importance of early environmental education in shaping long-term awareness and behavioral responses in regions facing persistent air quality challenges (Shabani *et al*. 2024). Furthermore, recent findings underscore the urgent need for stronger air quality policies in the Western Balkans, including stricter emission regulations, a transition to cleaner energy sources, and increased investment in pollution control measures (Belis *et al*. 2022). However, without informed and engaged citizens, even well-designed policies may fail to achieve their intended impact.

Understanding how individuals perceive air pollution is therefore crucial for designing effective public health and environmental strategies, as perception directly influences behavior, policy acceptance, and willingness to adopt environmentally responsible practices. Previous studies indicate that higher risk perception is associated with increased engagement in pro-environmental behaviors (Peng *et al.* 2025; Rajapaksa *et al*. 2018). Moreover, Slovic, (1987) demonstrated that perceptions of environmental risks are shaped by social and contextual factors. The inclusion of socio-demographic variables—such as age, gender, area of residence, and educational level—is well supported by both theoretical and empirical literature on environmental risk perception. These perceptions are influenced by a combination of personal experience, demographic characteristics, and geographic context (Stern, 2000). Socio-demographic factors have consistently been identified as key determinants of how individuals perceive environmental risks and related health threats (Zylfo and Pojani, 2021). In the Albanian context, empirical research conducted in Tirana using multinomial logistic regression has incorporated variables such as age, gender, and education to examine exposure to air pollution and concerns about its health impacts (Kacorri *et al*. 2023). Despite its growing importance, empirical evidence from Albania remains limited. This highlights the need to further investigate how factors such as education, urban versus rural residence, gender, and age group shape public perceptions of air quality and its associated health risks. Bridging the gap between scientific assessments and public understanding is essential to ensure both the effectiveness and the societal legitimacy of environmental policies. Notably, although efforts to monitor and regulate air quality have intensified, the success of such initiatives continues to depend heavily on public awareness and perception.

This study aims to examine how perceptions of air pollution vary across different demographic and geographic groups in Albania. Statistical methods are employed to analyze public perception and to generate insights into how air pollution is understood across communities, thereby supporting more effective communication strategies and targeted policy interventions.

2. MATERIALS AND METHODS

This study adopts a quantitative research approach to investigate public perceptions of air pollution. Data were collected through a randomly administered survey conducted between November and December 2024 across four locations in Albania: Lapardha (Berat), Elbasan, Tirana, and Spille (Kavaja). Respondents were asked to provide socio-demographic information, including age, gender, area of residence, and educational level, and to indicate their level of concern about air pollution using a categorical scale.

The analysis focuses on assessing whether age, gender, residential area, and educational level influence the likelihood of individuals perceiving air pollution as a concern. Survey data were collected randomly from four locations: Lapardha (Berat), Elbasan, Tirana, and Spille (Kavaja).

To examine the association between these variables and air pollution perception, Pearson's chi-square test of independence was applied to the corresponding contingency tables, using a significance level of $\alpha < 0.05$ (Harrell, 2015).

$$\chi^2 = \sum_{i=1}^{s} \sum_{j=1}^{k} \frac{(O_{ij}-E_{ij})^2}{E_{ij}} \qquad (1)$$

where O_{ij} represents the observed frequencies and E_{ij} the expected frequencies under the assumption of independence. This statistic follows a Chi-square distribution with degrees of freedom calculated as $(k-1) \times (s-1)$, where s and k are the numbers of rows and columns in the contingency table, respectively. A significance level of $\alpha = 0.05$ was used to determine statistical significance. A p-value less than 0.05 indicated a statistically significant association between the variables.

In contrast to previous studies (Kacorri *et al.* 2023; Prifti and Shehu, 2014; Prifti and Salillari, 2019), which have applied regression analysis to evaluate environmental perception and health-related data, this study employs a binary logistic regression model to examine the factors influencing public perception of air pollution. The dependent variable represents the perception of air pollution, coded as "Good" or "Bad." The independent variables include binary indicators for area of residence (urban = 1, rural = 0) and educational level (high diploma—defined as secondary or university education = 1; lower educational attainment, such as 8–9 years of schooling = 0). To assess the goodness of fit of the logistic regression model, McFadden's pseudo-R^2 was used (Agresti, 2018). This measure is based on the improvement in log-likelihood relative to a null (intercept-only) model and quantifies the extent to which the fitted model provides a better explanation of the observed data compared to a model without predictors. McFadden's pseudo- R^2 is defined as follows:

$$R^2_{\mathrm{McF}} = 1 - \frac{\ln L_{\mathrm{model}}}{\ln L_{\mathrm{null}}} \qquad (2)$$

where L_{model} is the likelihood of the fitted model (with predictors) and L_{null} is the likelihood of the null (intercept-only) model. Values in the range of 0.2–0.4 are generally considered indicative of a moderate model fit, while values exceeding 0.4 suggest a strong fit, particularly in social and behavioural sciences where explained variance is typically limited (Agresti, 2018).

Microsoft Excel was used for data organization, coding, and basic visualization, whereas all inferential statistical analyses—including chi-square tests and binary logistic regression—were conducted using the R statistical computing environment.

3. RESULTS AND DISCUSSIONS

The survey sample comprised 79 participants from Lapardha (Berat), Elbasan, Tirana, and Spille (Kavaja), selected through random sampling. Although a larger sample size would be required to ensure greater statistical robustness and generalizability, this study represents an important initial step in identifying trends in public perception and awareness of air pollution risks. Notably, it includes rural areas that are commonly perceived as having relatively clean air. The selection of study locations was aligned with air quality monitoring stations (within the framework of a related research project), encompassing both urban and rural settings where air pollution may also arise from localized sources such as open waste burning.

Figure 1 illustrates the distribution of respondents by gender, educational attainment, area of residence, and employment status. Females accounted for 54.4% of the sample, indicating a relatively balanced gender distribution. In terms of education, 31 participants held a university degree, 27 had completed secondary education, and 21 had completed 8–9 years of formal schooling. Analysis by area of residence revealed notable differences in educational attainment: respondents from rural areas were more likely to have completed only 8–9 years of education (56%), whereas those from urban areas predominantly held secondary or university qualifications (94%). Regarding employment status, 47 participants were employed, 18 were unemployed, and 14 were retired. The mean age of respondents was 30 years. Importantly, this study includes, for the first time, data from Lapardha and Spille—areas generally considered to have relatively good air quality. Overall, the sample demonstrates substantial diversity in gender, educational background, area of residence, and employment status, making it suitable for exploring variations in public perception of air pollution and its associated health impacts.

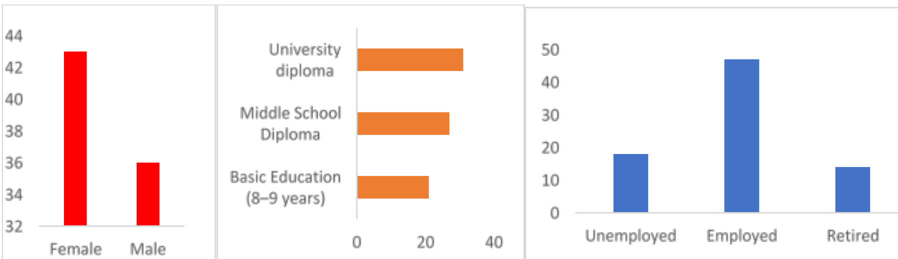

Fig. 1: The distribution of the survey data.

A Chi-Square (χ^2) test was conducted to examine whether perception of air quality (Good/Bad) is associated with area type (Rural/Urban), gender (Female/Male), age group, and education level. The results of these analyses are summarized in Table 1.

Table 1: Results of Chi-Square (χ^2) test for the variables in study

Variable	**χ^2 − value**	***DF***	***p*-value**
Education	16.446	1	$5.006e-05^*$
Gender	0.16854	1	0.6814
Age Group	0.21659	2	0.8974
Area Type	30.078	1	$4.15e-08^*$

Chi-square tests of independence indicated statistically significant associations between the perception of air quality and both area of residence and educational level ($p - values^* < 0.05$), suggesting that peoples' perceptions differ across rural and urban settings as well as educational backgrounds.

A binary logistic regression model was then estimated, with perception of air pollution as the response variable, coded as *Bad* = 1 (indicating that air pollution is perceived as a problem) and *Good* = 0. The predictor variables included area of residence (Urban = 1, Rural = 0) and educational level (High Diploma = 1; 8–9 years of schooling = 0). The model estimates the log-odds of perceiving air quality as "bad" based on these predictors.

$$log\left(\frac{p}{1-p}\right) = -2.4790 + 2.6231\ AreaUrban + 1.4211 EduHigh \quad (3)$$

where p denotes the probability that a respondent perceives air pollution as a serious problem (categorized as *Bad*).

In Model (3), the intercept is statistically significant (p-value = 0.000829), as is the variable *AreaUrban* (p-value = 5.78×10^{-5}). The variable *EduHigh*, however, is not statistically significant at the conventional $\alpha = 0.05$ level (p-value = 0.078279). This lack of statistical significance does not necessarily imply that *EduHigh* is irrelevant to the model (Agresti, 2018). It may instead reflect factors such as limited sample size, potential multicollinearity, or a relatively weaker effect in the presence of other predictors. Importantly, despite the non-significance of one predictor, the logistic regression model demonstrates strong overall performance. The McFadden's pseudo-R^2 value of approximately 0.57 indicates a very good model fit, suggesting that the combination of *AreaUrban* and *EduHigh* explains a substantial portion of the variation in public perceptions of air pollution. This finding highlights that predictors may contribute meaningfully to a model collectively, even when their individual coefficients are not statistically significant.

To further evaluate the practical relevance of these predictors, predicted probabilities derived from Model (3) are presented in Table 2 for different combinations of *AreaUrban* and *EduHigh*. This allows for assessment of whether the marginal differences between groups are substantively meaningful in context.

Table 2: Probability of perceiving air pollution as a problem

Area	Education	Probability of perceiving air pollution as a problem
Rural	8–9 years diploma	7.7%
Rural	High diploma	25.8%
Urban	8–9 years diploma	53.6%
Urban	High diploma	82.7%

Education alone increases the probability of perceiving air pollution as a problem by approximately 18–29 percentage points, depending on the area of residence. In contrast, residing in an urban area increases this probability by approximately 46–57 percentage points, depending on educational level—an effect that is both substantial and practically significant. These marginal effects are large and meaningful in applied terms, even though the p-value for *EduHigh* slightly exceeds the conventional 0.05 threshold. Thus, while *EduHigh* is not individually significant at the 5% level, its combined effect with *AreaUrban* yields clear and actionable insights.

As shown in Table 2, the predicted probabilities indicate that education enhances environmental awareness, while urban residence exerts a stronger baseline effect. The highest level of concern is observed among urban respondents with a high diploma, with a predicted probability of 82.7%. The corresponding 95% profile likelihood confidence interval ranges from 68.8% to 91.2%. This group exhibits the greatest likelihood of perceiving air pollution as a problem, suggesting that both exposure and awareness play a significant role. In contrast, the lowest level of concern is observed among rural respondents with 8–9 years of education, with a predicted probability of 7.7%, indicating a markedly lower perceived risk.

These findings are consistent with previous research indicating that socio-demographic variables such as age, gender, and education are not always consistently significant predictors of environmental perception, whereas place-based experience often plays a more decisive role. This underscores the importance of contextual and experiential factors in shaping environmental risk perception (Pinakidou *et al*. 2026).

Despite these important findings, the present study has several limitations. First, the relatively small sample size limits the statistical power of the analysis and may reduce the precision of the estimated effects. Accordingly, the results should be interpreted as indicative of general patterns and key associations rather than as definitive causal relationships. Future research should incorporate larger and more diverse samples to enhance statistical robustness, improve generalizability, and strengthen the external validity of the findings.

Notwithstanding these limitations, this study provides novel insights into public perceptions of air pollution in Albania. The results demonstrate that educational attainment and urban residence are key determinants of whether individuals perceive air pollution as a significant environmental issue. By estimating predicted probabilities across combinations of educational level and area of residence, the analysis shows that highly educated urban residents have the highest likelihood of perceiving air pollution as problematic, whereas rural residents with lower educational attainment exhibit the lowest probability.

4. CONCLUSIONS AND RECOMMENDATIONS

The logistic regression analysis indicates that area of residence is a statistically significant determinant of public perceptions of air pollution. Specifically, individuals residing in urban areas exhibit substantially higher odds of perceiving air pollution as a concern, with estimated odds approximately 13.8 times greater than those of individuals living in rural areas. Although respondents with a secondary (high school) diploma are approximately 4.1 times more likely to perceive air pollution as problematic compared to those with lower educational attainment, the independent effect of education diminishes once residential context is controlled for in the model. The overall model demonstrates strong goodness of fit, as reflected by a McFadden's pseudo-R^2 value of approximately 0.57, indicating that the included predictors explain a substantial proportion of the observed variation in environmental risk perception. Collectively, these findings suggest that geographic context exerts a more pronounced influence than educational attainment in shaping public concern about air pollution.

From a policy perspective, these results underscore the importance of designing targeted awareness and outreach interventions, particularly for rural populations, who may underestimate environmental health risks due to lower perceived exposure or limited access to environmental information.

Future research should aim to increase sample size in order to enhance statistical power and reduce estimation uncertainty. In addition, incorporating further explanatory variables—such as income level, occupational category, and media exposure—would enable a more comprehensive modelling of environmental perceptions. Complementary qualitative approaches are also recommended to explore the underlying reasons why rural populations report lower levels of concern despite potential exposure to environmental pollutants.

Overall, these findings contribute to the identification of priority target groups for environmental awareness campaigns and public education strategies. Furthermore, the study demonstrates the practical utility of logistic regression modelling and marginal effects analysis in examining perceptual and attitudinal data, thereby offering a robust methodological framework for future empirical research on environmental awareness and risk perception.

Ethics. Ethical approval was not required for this study, as it is based on aggregated, and anonymized data from public sources. No individual-level data or personal identifiers were accessed or analyzed.

Data accessibility: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of AI use. There has been no use of AI when writing the actual paper.

Author Contributions. L. P: Conceptualization, methodology, data analysis, writing – original draft and writing – review & editing; E.B.: Conceptualization, methodology, questionnaire design, data collection, and writing – review & editing; E.T.: Questionnaire design and data collection. All authors contributed to the interpretation and discussion of the results.

All the authors have approved the final version of the manuscript.

Conflict of interest declaration. The authors declare that they have no conflict of interest related to this work.

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FOOD ADDITIVES IN STREET AND PROCESSED FOODS: HEALTH IMPLICATIONS AND REGULATORY CHALLENGES WITH A FOCUS ON ALBANIA

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Research

Subject Category: Natural Sciences - Life Sciences subject category: Food Toxicology / Nutrition Science

Abstract

Food additives are widely used in street and processed foods to improve organoleptic properties, technological functionality, and shelf life. Although most additives are approved within established safety limits, growing evidence suggests that frequent consumption of additive-rich foods may be associated with adverse health effects, particularly in settings with limited regulatory oversight and low consumer awareness. This narrative review examined international and Albanian literature on food additives in street and processed foods using sources from PubMed, Scopus, Web of Science, Google Scholar, and selected institutional reports. The review focused on major additive categories, associated health effects, and regulatory challenges, with particular emphasis on Albania. The findings indicate that these foods commonly contain preservatives, colorants, sweeteners, emulsifiers, and flavor enhancers. Epidemiological and experimental studies associate frequent exposure to such additives with metabolic disorders, allergic and gastrointestinal manifestations, neurobehavioral effects in children, and other long-term health risks. The literature also highlights gaps between international food safety regulations and their implementation at the national level, particularly regarding monitoring and enforcement capacity. Food additives in street and processed foods represent an important public health concern, especially in populations with frequent exposure and unhealthy dietary patterns. In Albania, strengthening food monitoring systems, improving labeling practices, and increasing public awareness may help reduce potential health risks.

***Keywords*:** Food additives; street food; processed food; narrative review; health effects; food safety; Albania

1. INTRODUCTION

In recent decades, the globalization of the food system, rapid urbanization, and shifts in dietary patterns have contributed to increased consumption of processed, ready-to-eat, and street foods. To optimize shelf life, product stability, visual appeal, and sensory attributes, the food industry has increasingly relied on food additives, which are now ubiquitous in modern food products (Winter, 2013; WHO, 2023). Food additives encompass a broad spectrum of substances, including preservatives, colorants, sweeteners, emulsifiers, stabilizers, and flavor enhancers.

Within the European Union, the use of food additives is strictly regulated under Regulation (EC) No 1333/2008, which stipulates that additives must be authorized, technologically justified, safe at the proposed level of use, and non-misleading to consumers. At the international level, Codex Alimentarius standards provide a key reference framework governing the conditions of additive use in foods (Regulation (EC) No 1333/2008; WHO, 2019).

Available evidence indicates that consumers are routinely exposed to multiple food additives through the cumulative intake of processed foods and beverages. In a large-scale assessment of 126,000 food products available on the French market, Chazelas *et al*. (2020) reported that 53.8% of products contained at least one additive, while 11.3% contained five or more, underscoring the prevalence of additive co-occurrence and the complexity of real-world exposure scenarios.

This issue is particularly pertinent among children and adolescents, who may experience higher exposure relative to body weight and whose dietary patterns often include elevated consumption of sugar-sweetened beverages, packaged snacks, confectionery, and other ultra-processed foods. Recent review studies indicate that, in pediatric populations, concerns are most consistently associated with artificial colorants, non-nutritive sweeteners, preservatives, and patterns of frequent exposure, although limitations in study design and causal inference should be acknowledged (Kraemer *et al.* 2022).

Beyond acute intolerance and hypersensitivity reactions, emerging research has explored broader biological mechanisms through which food additives may influence health, including modulation of inflammatory pathways, disruption of metabolic homeostasis, and interactions with dietary patterns characterized by high intake of ultra-processed foods.

However, the strength of evidence varies across outcomes, with mechanistic data often exceeding the robustness of epidemiological confirmation. Careful interpretation is therefore required to avoid overstatement of causal relationships (Albani *et al*. 2018; Heindel and Blumberg, 2019).

At the population level, the health implications of additive exposure should be considered within the broader framework of ultra-processed food consumption. A 2024 umbrella review of epidemiological meta-analyses reported that higher intake of ultra-processed foods is associated with an increased risk of multiple adverse health outcomes, although the magnitude and certainty of associations vary across endpoints (Lane *et al.* 2024).

In Albania, evolving dietary behaviors—particularly among younger populations—have raised concerns regarding increasing consumption of ultra-processed foods and out-of-home meals. Evidence from Albanian youth suggests that the frequency of eating out may significantly influence the association between ultra-processed food intake and body mass index, highlighting the relevance of this issue in the national context (Vincze *et al.* 2023).

Concurrently, broader evaluations of the food safety system in Albania indicate persistent challenges related to regulatory implementation, market surveillance, and institutional capacity. These factors are directly relevant when assessing population exposure to food additives and the effectiveness of consumer protection mechanisms (Troka and Kapaj, 2025).

Against this background, a comprehensive synthesis of the available evidence is warranted to elucidate the potential health implications of food additives in street and processed foods, as well as the regulatory and monitoring challenges influencing exposure in Albania. The objective of this narrative review is to integrate international and national literature, with particular emphasis on reported health effects and the regulatory context governing additive use.

2. MATERIALS AND METHODS

This study was conducted as a narrative and integrative literature review examining the occurrence of food additives in street and processed foods, their reported health effects, and the associated regulatory context, with particular emphasis on Albania. The review relied exclusively on secondary data derived from peer-reviewed scientific literature, institutional reports, and regulatory documents. The study was not designed as a systematic review and did not follow a formal PRISMA-based protocol; however, the reporting approach was informed by established principles for transparent and structured review reporting (Page *et al.* 2021; Baethge *et al.* 2019).

2.1. Study design

The review was designed to provide a comprehensive, context-oriented synthesis of current evidence on food additives in commonly consumed street and processed foods. The analysis focused on three principal domains: (1) the main categories of food additives and their occurrence in food products; (2) reported health effects associated with additive exposure; and (3) regulatory and monitoring frameworks at the international level, with comparison to the Albanian context. Given the objective of integrating toxicological, epidemiological, public health, and regulatory perspectives, a narrative review approach was considered more appropriate than a formal systematic review methodology (Baethge *et al.* 2019).

2.2. Literature sources and search strategy

The literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar. Publications issued between 2000 and 2025 were considered. The search strategy incorporated combinations of the following keywords: *food additives*, *preservatives*, *artificial sweeteners*, *food colorants*, *processed food*, *street food*, *health effects*, *food safety*, *Albania*, *European Food Safety Authority*, *World Health Organization*, and *Codex Alimentarius*. In addition to peer-reviewed scientific articles, selected institutional reports and regulatory documents were included to provide contextual information on public health and policy aspects, particularly regarding additive authorization, monitoring practices, and conditions of use in foods (Regulation (EC) No 1333/2008; WHO, 2019). For the Albanian context, the review also incorporated available national reports, institutional publications, and locally produced studies addressing food safety, processed food consumption, and related public health issues. These sources were included to facilitate comparison between international regulatory frameworks and the national context, in line with the objectives of the review.

2.3. Selection criteria and screening process

The identification and selection of sources were based on screening of titles, abstracts, and full texts, where available. References were included if they addressed at least one of the following criteria: i) categories and occurrence of food additives in street or processed foods; ii) reported health effects associated with additive exposure; iii) food safety regulations, monitoring systems, or official standards; and iv) evidence specifically relevant to Albania. Priority was given to peer-reviewed publications, official regulatory documents, and reports issued by recognized public health or regulatory institutions. Sources were excluded if they were not directly related to food additives, did not address processed or street foods, lacked relevance to health or regulatory aspects, or duplicated information already covered by more comprehensive or recent references. Additional consideration was given to methodological clarity, relevance to the review objectives, and applicability to both international and Albanian contexts. No formal risk-of-bias assessment tool or critical appraisal framework was applied to the included studies. This approach is consistent with the narrative design but constitutes a methodological limitation that should be acknowledged (Baethge *et al.* 2019; Page *et al*. 2021).

2.4. Data synthesis and comparative approach

The selected literature was synthesized using a thematic approach. Evidence was organized into key categories, including types of food additives, representative food sources, reported health outcomes, and regulatory considerations. A comparative analytical framework was applied to examine differences between international standards and the Albanian context, with particular attention to authorization criteria, monitoring capacity, labeling practices, and consumer protection mechanisms. The interpretation of international regulatory frameworks was primarily based on European Union legislation governing food additives and Codex Alimentarius standards, which serve as central reference systems for permitted substances and conditions of use in foods (Regulation (EC) No 1333/2008; WHO, 2019).

2.5. Methodological limitations

This review has several limitations. First, it is based entirely on secondary sources and does not include primary data collection or laboratory-based assessment of additive concentrations in food products available on the Albanian market. Second, the study was not conducted as a systematic review and did not incorporate a formal quality assessment or risk-of-bias evaluation of the included studies. Consequently, the findings should be interpreted as a qualitative synthesis intended to summarize current evidence and highlight key public health and regulatory issues, rather than to provide quantitative estimates or establish causal relationships (Baethge *et al*. 2019; Page *et al*. 2021).

3. Findings from the Literature and Discussion

This section presents a thematic synthesis of findings derived from the reviewed literature, rather than original analytical results based on primary laboratory measurements. The discussion is structured according to the principal categories of food additives, their common food sources, reported health effects, and relevant regulatory considerations, with particular emphasis on the Albanian context.

3.1. Main Categories of Food Additives

Food additives comprise a diverse group of substances incorporated into food products to enhance preservation, sensory attributes (taste, color, and texture), physicochemical stability, and overall consumer acceptability. Based on their technological function, the principal categories include preservatives, colorants, sweeteners, flavor enhancers, emulsifiers, stabilizers, gelling agents, and thickeners (WHO, 2023; EFSA, 2020).

These substances are widely present in industrially processed foods and are also frequently encountered in ready-to-eat and convenience food products. Evidence from large-scale market analyses indicates that consumer exposure typically involves multiple additives rather than single compounds. In a comprehensive assessment of 126,000 food products, Chazelas *et al*. (2020) reported that 53.8% contained at least one additive, while 11.3% contained five or more, underscoring the high prevalence of additive co-occurrence and the complexity of cumulative exposure scenarios.

Preservatives, including sodium nitrite, benzoic acid, and sulfites, are primarily used to extend shelf life and inhibit microbial growth. Colorants, such as tartrazine, sunset yellow, and allura red, are added to enhance the visual appeal of foods and beverages. Sweeteners, including aspartame, saccharin, and sucralose, are commonly used in low-calorie or sugar-free products. Monosodium glutamate is widely employed as a flavor enhancer in savory, ready-to-eat foods. Emulsifiers and stabilizers are frequently present in sauces, desserts, dairy products, and bakery items, where they contribute to texture, consistency, and product stability (WHO, 2019; EFSA, 2020; WHO, 2023).

Given these patterns of use, the potential health implications of food additives should not be considered solely at the level of individual compounds but rather within the broader framework of cumulative and combined dietary exposure. This perspective is particularly relevant in the context of diets characterized by high consumption of ultra-processed foods. For clarity and synthesis, the main categories of food additives and their representative food sources are summarized in Table 1.

Table 1. Main categories of food additives and representative food sources reported in the literature

Category	**Representative additives (E-numbers)**	**Representative food sources**
Preservatives	Sodium nitrite (E250), Benzoic acid (E210), Sulfites (E220–E228)	Processed meats, sausages, canned foods, soft drinks, bakery products
Colorants	Tartrazine (E102), Sunset Yellow (E110), Allura Red (E129)	Sweets, confectionery products, chips, beverages, desserts
Sweeteners	Aspartame (E951), Saccharin (E954), Sucralose (E955)	Diet soft drinks, sugar-free beverages, chewing gum, low-calorie products
Flavor enhancers	Monosodium glutamate (E621)	Street foods, fast foods, instant noodles, savory snacks, ready-to-eat meals
Emulsifiers/Stabilizers	Lecithins (E322), Carrageenan (E407), Mono- and diglycerides of fatty acids (E471)	Ice cream, sauces, processed dairy products, desserts, bakery items

Street foods and fast foods constitute significant sources of dietary exposure to food additives, particularly among children, adolescents, and young adults. Their widespread availability, affordability, and frequent consumption in urban environments make them highly relevant in the context of cumulative additive exposure, especially when consumed in combination with sugar-sweetened beverages, packaged snacks, condiments, and processed meat components (Vincze *et al*. 2023).

The reviewed literature indicates that the additive profile of these foods varies according to product type, formulation, and mode of preparation. Flavor enhancers are most commonly associated with savory ready-to-eat products, whereas preservatives, colorants, and stabilizing agents are more frequently identified in sauces, processed meat ingredients, industrial bakery-based fast foods, and sweetened beverages commonly consumed alongside such meals. These patterns illustrate the complexity of real-world exposure scenarios, in which multiple additives may be ingested within a single meal or eating occasion (Chazelas *et al*. 2020).

In contrast to pre-packaged industrial foods, additive exposure from street foods may be more difficult to assess and monitor consistently. This is particularly relevant in settings where food labeling practices, vendor standardization, and routine inspection systems are less developed or inconsistently enforced. Accordingly, the primary concern is not necessarily that street foods contain higher levels of additives compared with industrial products, but rather that their composition is less transparent, limiting consumer awareness and informed dietary choices. From a public health perspective, this lack of transparency represents a critical challenge, especially in countries with developing or transitional food control systems (EFSA, 2020; WHO, 2023).

In Albania, ongoing shifts in dietary behavior—particularly among younger populations—have increased reliance on out-of-home eating, thereby amplifying the relevance of additive exposure from street and convenience foods. Empirical evidence from Albanian youth suggests that the frequency of eating out is a significant factor in the association between ultra-processed food consumption and body mass index, further supporting the importance of this issue in the national context (Vincze *et al*. 2023).

A comparative overview of additives commonly reported in street foods and processed foods is presented in Table 2.

Table 2. Comparative overview of food additives commonly reported in street foods and processed foods

Additive	Street foods / fast foods	Processed foods
Sodium nitrite	Less commonly reported directly in freshly prepared foods; may be present through processed meat ingredients	Commonly reported in sausages, cured meats, and processed meat products
Tartrazine	Commonly reported in sweetened drinks, desserts, and confectionery items	Commonly reported in candies, packaged snacks, and beverages
Monosodium glutamate	Frequently reported in savory fast foods, sauces, and ready-to-eat meals	Reported in instant foods, packaged savory snacks, and processed meals
Benzoates	May be present in sauces and beverages sold with meals	Commonly reported in soft drinks, bakery products, and sauces
Artificial sweeteners	Less commonly emphasized in freshly prepared foods	Frequently reported in diet beverages and sugar-free products

3.3. Additives in Processed Foods

Processed foods represent one of the most consistent and significant dietary sources of exposure to food additives, as their formulation is specifically designed to enhance shelf life, physicochemical stability, texture, color, and sensory acceptability. In contrast to freshly prepared foods, industrially processed products are more likely to contain multiple additives within a single formulation, including preservatives, colorants, sweeteners, emulsifiers, stabilizers, and flavor enhancers (Chazelas *et al.* 2020; WHO, 2023).

The reviewed literature indicates that exposure to additives through processed foods is typically repetitive and cumulative, reflecting the frequent and habitual consumption of these products across multiple food categories. Common sources of multi-additive exposure include confectionery products, packaged snacks, sugar-sweetened beverages, processed meats, industrial bakery items, and ready-to-eat meals (Chazelas *et al.* 2020).

Processed meat products warrant particular attention due to their frequent content of nitrites and nitrates, which are used for preservation and color stabilization. These compounds have been extensively evaluated in relation to the endogenous formation of N-nitroso compounds and their potential contribution to long-term carcinogenic risk, particularly in the context of sustained high consumption of processed meats (WHO, 2019; EFSA, 2020). However, this association should be interpreted within the broader dietary context, as risk is modulated by overall intake patterns, co-exposures, and general dietary quality.

Other processed food categories—including soft drinks, sugar-free products, packaged desserts, and industrial bakery items—often contain combinations of colorants, benzoates, non-nutritive sweeteners, emulsifiers, and acidity regulators. Emerging evidence suggests that repeated consumption of such products may be associated with metabolic disturbances and gastrointestinal effects, although the strength and consistency of evidence vary depending on the specific additive group and study design (Albani *et al.* 2018; Heindel and Blumberg, 2019).

In Albania, this issue is gaining increasing relevance in light of shifting dietary patterns, particularly among children and adolescents. Available national and local data indicate a transition toward higher consumption of snacks, sugar-sweetened beverages, and other convenience foods, which may contribute to sustained and repeated exposure to food additives through routine dietary behaviors (Kodra *et al.* 2018; Institute of Public Health, 2021).

Taken together, these findings highlight processed foods as a critical domain in the assessment of additive exposure, dietary quality, and food safety monitoring.

For clarity, representative processed food categories and the additives commonly reported within them are summarized in Table 3.

Table 3. Representative processed food categories and commonly reported additives

Processed food category	**Commonly reported additives**	**Main technological purpose**
Processed meats	Nitrites/nitrates, antioxidants, stabilizers	Preservation, color stabilization, shelf life
Sweetened beverages	Colorants, benzoates, sweeteners, acidity regulators	Color, flavor profile, preservation, palatability
Sugar-free products	Aspartame, sucralose, saccharin, stabilizers	Sweetness without added sugar, texture

Packaged snacks	Flavor enhancers, colorants, antioxidants, emulsifiers	Taste enhancement, appearance, product stability
Industrial bakery products and desserts	Emulsifiers, preservatives, colorants, thickeners	Texture, shelf life, consistency, visual appeal

3.4. Interaction of Food Additives with Heavy Metals and Other Environmental Contaminants

An additional aspect addressed in the literature concerns the potential interaction between food additives and other environmental contaminants, including heavy metals such as lead, cadmium, mercury, and arsenic. This issue is of particular relevance because dietary exposures occur within complex mixtures, and the biological effects of food additives may be modified by concurrent exposure to toxic agents present in food, water, or the broader environment (Heindel and Blumberg, 2019; WHO, 2019).

Experimental and review-based evidence suggests that certain additives—particularly synthetic colorants and preservatives—may influence oxidative balance, inflammatory pathways, and cellular stress responses. Heavy metals are likewise well established as contributors to oxidative stress, tissue damage, and immune and neurotoxic effects. Accordingly, the potential for additive–heavy metal interactions has attracted increasing scientific attention, particularly in relation to long-term metabolic, neurological, and immunological outcomes (Albani *et al*. 2018; WHO, 2019).

However, the current body of evidence should be interpreted with caution. Much of the existing knowledge regarding additive–contaminant interactions is derived from toxicological models, in vitro studies, or mechanistic hypotheses, rather than from robust human epidemiological or clinical data. Consequently, these interactions should be considered a plausible but not yet conclusively established pathway contributing to disease risk (Buttriss, 2018; Heindel and Blumberg, 2019).

In Albania, this issue is particularly relevant from a public health perspective, given the limited availability of comprehensive national data on combined dietary exposures. Although direct evidence on additive–heavy metal interactions in the local context remains scarce, this topic warrants further investigation through targeted analytical, toxicological, and epidemiological studies, particularly among vulnerable populations such as children and adolescents, who may be more susceptible to cumulative environmental exposures (Ministry of Health and Social Protection, 2020; Institute of Public Health, 2021).

3.5. Reported Long-Term Health Effects

Beyond acute adverse reactions, repeated exposure to additive-rich dietary patterns has been discussed in relation to a range of potential long-term health outcomes. The reviewed literature most frequently addresses gastrointestinal effects, allergic and hypersensitivity responses, neurobehavioral outcomes, metabolic disturbances, and potential carcinogenic risks, although the strength and consistency of evidence vary across these domains (Albanese *et al*. 2009; Nigg *et al*. 2012; Heindel and Blumberg, 2019).

With respect to gastrointestinal and immune-related effects, certain emulsifiers, preservatives, and synthetic additives have been reported to influence intestinal permeability, gut microbiota composition, and inflammatory processes. These mechanisms have raised concerns regarding their possible contribution to chronic gastrointestinal symptoms and immune dysregulation; however, much of the supporting evidence remains mechanistic and requires further validation in human studies (Albani *et al*. 2018; Heindel and Blumberg, 2019).

Neurobehavioral effects have been most consistently discussed in relation to synthetic colorants and preservative-containing foods, particularly in pediatric populations. Some experimental and meta-analytical studies suggest associations between specific additives and behavioral outcomes, including attention-related difficulties and hyperactivity in susceptible individuals. Nevertheless, findings are not uniformly consistent, and inter-individual variability in susceptibility should be considered when interpreting these associations (Albanese *et al*. 2009; Nigg *et al*. 2012).

Potential carcinogenic risk has been primarily associated with nitrites and nitrates used in processed meat products, particularly due to their role in the endogenous formation of N-nitroso compounds. In this context, risk assessment should consider not only individual additives but also broader dietary patterns characterized by frequent consumption of processed foods (WHO, 2019; EFSA, 2020).

Metabolic effects have also received increasing attention, particularly in relation to diets high in additive-rich processed foods and sugar-sweetened or artificially sweetened beverages. Such dietary patterns have been associated with obesity, insulin resistance, dyslipidemia, and related metabolic disturbances. However, it is important to distinguish between the potential effects of individual additives and the broader impact of ultra-processed dietary patterns as a whole (Kodra *et al*. 2018; Heindel and Blumberg, 2019).

Overall, the available evidence suggests that the potential long-term health implications of food additives should be interpreted within a multifactorial framework that includes cumulative exposure, mixed dietary intake, age-related susceptibility, and overall diet quality. While certain associations are supported more consistently than others, the current body of literature underscores the need for continued scientific investigation and sustained public health attention.

3.6. International Regulatory Frameworks and the Albanian Context

At the international level, the regulation of food additives is grounded in established risk assessment frameworks and clearly defined conditions of use. Within the European Union, food additives are regulated under Regulation (EC) No 1333/2008 and are subject to comprehensive safety evaluation and periodic re-evaluation by the European Food Safety Authority (EFSA). At the global level, Codex Alimentarius standards—developed jointly by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO)—provide an essential reference framework for acceptable intake levels, technological justification, and general food safety principles governing additive use (Regulation (EC) No 1333/2008; FAO, 2017; WHO, 2019; EFSA, 2020).

These regulatory systems are designed to ensure that food additives are authorized only when they are technologically justified, safe at the proposed levels of use, and appropriately communicated to consumers through labeling requirements. However, the effectiveness of such frameworks depends not solely on the existence of legislation but also on the capacity for implementation, including laboratory infrastructure, inspection and enforcement systems, surveillance mechanisms, and public awareness. Consequently, cross-country differences may arise not only from regulatory provisions but also from variability in enforcement consistency and monitoring capacity (Buttriss, 2018; WHO, 2019).

In Albania, the legal framework governing food additives has evolved in alignment with broader European and international food safety standards. National guidance on permitted additives and conditions of use has been adopted by the Ministry of Health and Social Protection (Ministry of Health and Social Protection, 2020). Nevertheless, available evidence indicates that challenges persist in key areas, including monitoring capacity, routine laboratory analysis, and the systematic collection of national data on dietary exposure (Institute of Public Health, 2021).

As a result, a gap remains between formal regulatory provisions and their practical implementation, representing an ongoing public health concern. This issue is particularly relevant in the context of increasing consumption of processed foods, snacks, sugar-sweetened beverages, and ready-to-eat meals, especially among children and adolescents. In such settings, effective food safety governance requires not only robust regulatory frameworks but also strengthened market surveillance, improved compliance with labeling requirements, enhanced laboratory support, and increased consumer awareness. A comparative overview of selected international and Albanian regulatory considerations is presented in Table 4.

Table 4. Comparative overview of international regulatory frameworks and the Albanian context for food additives

Regulatory aspect	**European Union / International framework**	**Albania**
Legal basis	Regulation (EC) No 1333/2008; Codex Alimentarius standards	National guidelines and food safety regulations
Safety evaluation	EFSA scientific assessment; international Codex/JECFA framework	Relies on national implementation of adopted standards
Use conditions	Additives permitted only under defined technological and safety conditions	Legal provisions exist, but practical implementation may vary
Labeling requirements	Clear labeling and consumer information required	Labeling rules exist, but enforcement may not always be consistent

Monitoring capacity	Structured regulatory surveillance and re-evaluation systems	Monitoring and routine laboratory control remain more limited

3.7. Traditional Albanian Foods as a Lower-Additive Dietary Alternative

An important perspective in the discussion of food additive exposure concerns the potential role of traditional dietary patterns, which are generally based on fresher and less industrially processed foods. In contrast to highly processed commercial products, traditional Albanian meals are more commonly prepared from basic ingredients and may therefore involve lower exposure to artificial colorants, preservatives, sweeteners, and other industrial additives.

Traditional foods—such as homemade soups, vegetable-based dishes, freshly prepared dairy products, bread, legumes, fruits, and seasonal vegetables—may represent dietary patterns that are both nutritionally richer and less dependent on industrial formulation. Although such foods are not inherently free of additives, particularly when commercially sourced ingredients are incorporated, they may nonetheless provide a more favorable exposure profile compared with diets characterized by frequent consumption of packaged snacks, processed meats, sugar-sweetened beverages, and convenience foods.

From a public health perspective, promoting traditional and minimally processed dietary patterns may contribute to reducing repeated exposure to additive-rich food products, particularly among children and adolescents. This approach is consistent with broader nutritional recommendations that emphasize fresh food consumption, home-based food preparation, and reduced reliance on ultra-processed products (Buttriss, 2018).

In the Albanian context, this perspective is particularly relevant given ongoing dietary transitions that have shifted consumption patterns away from traditional foods toward imported, industrially processed, and convenience products. Encouraging the preservation of traditional food practices, alongside strengthened nutrition education and improved consumer awareness, may therefore represent a culturally appropriate and practical strategy to support healthier dietary behaviors and reduce unnecessary exposure to food additives.

4. CONCLUSIONS

The findings of this review indicate that food additives constitute an important public health consideration, particularly in the context of frequent consumption of street foods, processed foods, and other convenience products. Rather than reflecting isolated exposure to individual compounds, the potential health implications of food additives should be interpreted within a framework of cumulative dietary intake, repeated exposure over time, and overall diet quality.

The available evidence demonstrates that commonly consumed processed and ready-to-eat foods often contain multiple additives, including preservatives, colorants, sweeteners, emulsifiers, and flavor enhancers. These substances

have been associated in the literature with a range of potential health outcomes, including allergic reactions, gastrointestinal disturbances, neurobehavioral effects, metabolic alterations, and possible long-term risks. However, the strength of evidence varies across outcomes, with some associations supported primarily by mechanistic and experimental data rather than robust human clinical evidence.

In Albania, this issue is of particular relevance due to evolving dietary patterns—especially among children and adolescents—characterized by increasing consumption of processed foods, sugar-sweetened beverages, and out-of-home meals. Concurrently, existing evidence indicates limitations in food additive monitoring systems, routine laboratory capacity, and the availability of comprehensive national exposure data. These factors contribute to a gap between established regulatory frameworks and their effective implementation in practice.

Taken together, these findings highlight the need for strengthened food safety monitoring systems, improved labeling compliance, enhanced laboratory and surveillance capacity, and increased public awareness regarding dietary exposure to food additives. Future research should prioritize primary analytical studies, detailed exposure assessment, and the identification of vulnerable population groups, particularly children and adolescents.

In parallel, the promotion of traditional and minimally processed dietary patterns may represent a practical and culturally relevant strategy to reduce unnecessary exposure to additive-rich foods and support improved long-term public health outcomes.

Ethics. As this study utilizes secondary, de-identified, and publicly available data, it does not constitute human or animal subjects research. Consequently, institutional review board (IRB) approval was not required.

Authors contribution. A.D., I.B.: Conceptualization, methodology, and study design; All the authors -literature review, data synthesis, and writing of the original draft; **A.D., I. B., V.I., A. M., E. F., M. S.:** revising, final editing.

All authors have read and approved the final version of the manuscript and agree to its submission for publication.

Data availability statement This study is a narrative review based exclusively on secondary data. All information synthesized in this manuscript was derived from publicly accessible sources, including peer-reviewed scientific literature, institutional reports (e.g., WHO, EFSA, IPH), and international regulatory documents (e.g., Regulation (EC) No 1333/2008). No primary datasets were generated or analyzed during this research.

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HIGH LACTOSE INTOLERANCE IN ALBANIA: A MASSIVE CLINICAL SYNDROME

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Research

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ABSTRACT

Milk is widely consumed in Albania and is considered a staple food across all age groups. Average daily consumption is estimated at 0.7–1 L per person. However, in many individuals, lactose metabolism is impaired due to a deficiency of the enzyme lactase, which is responsible for lactose hydrolysis. This study assessed the prevalence of lactose intolerance in the Albanian population using lactose intolerance testing and structured interviews. Data collected in 2024 indicate a high prevalence (59%) among tested individuals. The study included 719 participants (379 males and 340 females), of whom 426 tested positive. Age-specific results showed increasing prevalence with age: 24% (1–5 years), 36.6% (6–15 years), 43.2% (16–20 years), 49.3% (21–30 years), 54.3% (31–40 years), 63% (41–50 years), 75.6% (51–60 years), 76% (61–70 years), 77% (71–80 years), and 83.3% (81–90 years). A higher prevalence was observed in males (57.2%) compared with females (42.8%). These findings indicate that lactose intolerance represents a widespread clinical condition in Albania. This metabolic disorder negatively affects nutrient absorption, daily functioning, hydration status, and overall quality of life.

Keywords: lactose intolerance; clinical syndrome; prevalence; age groups; Albania

1. INTRODUCTION

Lactose is a disaccharide present in milk, composed of galactose linked to glucose, and serves as an important energy source for mammals. Human milk contains approximately 7% lactose, whereas the milk of domestic ruminants, which constitutes a substantial component of human nutrition, contains about 5% lactose (Darma *et al*. 2024). In nutritional terms, lactose is the primary source of energy for infants during the first year of life. It is synthesized within the Golgi apparatus of mammary epithelial cells through the condensation of glucose and galactose. Most galactose is supplied via milk through the process of hexoneogenesis. Lactose is an osmotically active molecule that does not readily cross membranes and is stored in the alveoli of the mammary gland during secretion (Angima *et al.*2024).

Lactose absorption and biochemical breakdown occur through hydrolysis into its constituent monosaccharides, mediated by the enzyme lactase. In the small intestine, lactose is hydrolysed by β-galactosidase (lactase–phlorizin hydrolase), commonly referred to as lactase. This enzyme is produced primarily in the jejunum, which represents the main site of lactose digestion. Lactase is localized in the villi of the intestinal epithelium and is more susceptible to damage from intestinal diseases than other disaccharides located deeper within the mucosa (Vesa *et al*. 2000).

Lactase activity begins during intrauterine development and may persist throughout life; however, the capacity to digest lactose varies depending on genetic background. Congenital lactase deficiency can occur in infancy or later in life (Liebert *et al.* 2017). In most individuals, lactase activity declines after weaning, and in some cases may decrease to very low or undetectable levels. The inability to digest lactose results from reduced or absent lactase activity and is associated with lactose intolerance. This condition leads to gastrointestinal disturbances, including osmotic diarrhoea and bacterial fermentation in the colon, which produces gas, increases intestinal peristalsis, and causes abdominal pain (Zhao *et al.* 2010).

Lactose fermentation by the colonic microbiota generates gases such as hydrogen, carbon dioxide, and methane, contributing to symptoms such as bloating, abdominal pain, and flatulence. A wide diversity of commensal intestinal bacteria are involved in lactose fermentation. These include *Bacteroides* species (e.g., *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, and *Bacteroides ovatus*) and *Clostridium* species (e.g., *Clostridium perfringens*, *Clostridium fallax*, *Clostridium paraputrificum*, *Clostridium histolyticum*, and *Clostridium septicum*). Members of the family *Veillonellaceae* produce carbon dioxide during lactose fermentation, while *Methanobrevibacter smithii* produces methane (Arnold *et al.* 2018; Angima *et al.* 2024).

Depending on the amount of lactose ingested and residual lactase activity, individuals may experience gastrointestinal symptoms such as diarrhoea, bloating, nausea, abdominal distension, and pain, as well as systemic symptoms including headache. Clinicians should therefore carefully assess patient symptoms to determine the underlying cause and provide appropriate dietary guidance.

Lactose malabsorption refers to the impaired digestion of lactose due to low lactase activity, whereas lactose intolerance describes the clinical manifestation of this condition, characterized by symptoms such as gas, pain, and diarrhoea resulting from undigested lactose in the colon (Heyman, 2006). Although both conditions occur across all age groups, malabsorption represents a pathophysiological process, while intolerance refers to the clinical syndrome. Confusion between these terms has led to misinterpretation among patients and clinicians (Gallo *et al.* 2024).

Individuals who consume dairy products with high lactose content may develop symptoms of lactose intolerance. Products such as soft cheeses (e.g., mozzarella), hard cheeses (e.g., Parmigiano), and fermented products such as kefir may contain varying amounts of lactose and can trigger symptoms in sensitive individuals.

Over time, genetic adaptations have enabled certain populations to tolerate lactose beyond infancy. Mutations associated with lactase persistence have been identified in Northern European populations and among some African pastoralist groups, allowing continued lactose digestion into adulthood. Genotyping methods can be used to assess lactase persistence; however, they are most effective when combined with tolerance tests to improve diagnostic accuracy (Ridefelt and Håkansson, 2005).

Technological advances in milk processing and fermentation have also contributed to the availability of low-lactose products, such as certain cheeses and yogurts. In addition, adaptation of the gut microbiota may enable some lactose-intolerant individuals to tolerate limited amounts of lactose. However, modern food processing has also introduced products with variable fermentation profiles, some of which may be less suitable for lactose-intolerant individuals. At the same time, increased consumption of dairy products due to taste preferences has led to greater exposure to lactose. A lack of public awareness regarding lactose content in dairy products further complicates this issue. Therefore, it is essential to improve public knowledge and provide dietary guidance for lactose-intolerant individuals. Current evidence suggests that limiting lactose intake to approximately 12 g per meal may help reduce symptoms and improve tolerance.

2. MATERIALS AND METHODS

Data on lactose malabsorption and the prevalence of lactase persistence were assessed in adults and children aged ≥1 year using hydrogen breath tests, lactose tolerance tests, and complementary diagnostic methods. For children under 5 years of age, parent-reported information was collected alongside clinical assessment.

The study was conducted in 2024 and included 719 individuals of different age groups who presented for evaluation at two nutrition clinics in Tirana. The study population ranged from infants to elderly individuals and was categorized into the following age groups: 1–5, 6–15, 16–20, 21–30, 31–40, 41–50, 51–60, 61–70, 71–80, and 81–90 years. For children aged 1–5 years, data were obtained through parental interviews (primarily from mothers), and hydrogen levels in exhaled breath were measured. In older age groups, lactose challenge tests were performed by administering either lactose monohydrate orally or approximately 1 L of milk, followed by measurement of hydrogen concentration in exhaled breath.

Lactose malabsorption was primarily assessed using the hydrogen breath test. Participants received 50 g of lactose orally, and breath hydrogen levels were subsequently measured at regular intervals. A test was considered positive when the hydrogen concentration in exhaled breath exceeded 20 parts per million (ppm). In addition, an increase of ≥10 ppm above baseline for at least two consecutive measurements at 15-minute intervals was considered indicative of lactose malabsorption. In some cases, a 25 g lactose dose was used, with a threshold of >20 ppm for diagnosis. Lactose tolerance was also evaluated using blood glucose measurements. In individuals with lactose intolerance, the rise in blood glucose following lactose ingestion is typically limited, not exceeding 20 mg/dL (Corgneau *et al*. 2017). Additional biochemical assessments, including urinary glucose and protein-related markers, were considered where necessary to support diagnosis. Clinical symptoms associated with lactose intolerance were assessed through structured interviews (anamnesis) based on a standardized questionnaire. Participants were asked about common symptoms, including bloating, abdominal pain, diarrhoea, headache, and increased intestinal peristalsis. Data collected during the study were analysed across predefined age groups. Statistical analyses were performed to evaluate the reliability of the findings and to explore potential associations between variables.

3. RESULTS AND DISCUSSIONS

A total of 719 individuals were included in the study, of whom 426 (58.5%) were diagnosed with lactose intolerance. The prevalence increased progressively with age, from 24% in the 1–5-year age group to 83.6% in individuals aged 81–90 years. A notable increase was observed after the age of 40, with prevalence exceeding 60% and reaching over 75% in individuals older than 50 years. Across all age groups, males exhibited a higher prevalence (244 cases; 57.2%) compared with females (182 cases; 42.8%). These findings indicate a clear age-related trend, with lactose intolerance becoming increasingly common in older populations (table 1).

Table 1. Data from 2024 on the number of people included in the study and individuals confirmed positive for the lactose intolerance

Age in years	Number of people checked	Confirmed Lactose Intolerant	Confirmed negative	Lactose Intolerant (%)	Male positive	Female positive
1 to 5	54	13	41	24%	8	5
6 to 15	71	26	45	36.6%	14	12
16 to 20	67	29	38	43.2%	18	11
21 to 30	75	37	38	49.3%	20	17
31 to 40	81	44	37	54.3%	26	18
41 to 50	86	54	32	63%	28	26
51 to 60	90	68	22	75.6%	44	24
61 to 70	72	55	17	76.4%	30	25

71 to 80	62	49	13	79%	28	21
81 to 90	61	51	10	83.6%	28	23
Total	719	426	293	58.5%	244	182

The present findings confirm a high burden of lactose intolerance in the Albanian population across all age groups. In early childhood (1–5 years), the observed prevalence of 24% suggests that a subset of individuals may present with congenital or early-onset lactase deficiency. Although lactase activity is typically highest during infancy to support breast milk digestion, congenital lactase deficiency (CLD), an autosomal recessive disorder caused by mutations affecting lactase-phlorizin hydrolase (LPH), may result in early clinical manifestations (Liebert *et al*. 2017; Wanes *et al*. 2019). Differentiation from cow's milk protein allergy is clinically important due to overlapping gastrointestinal symptoms, and lactose-reduced or lactose-free formulas are commonly used in affected infants (Darma *et al*. 2024).

In school-age children (6–15 years), prevalence increased to 36.6%, reflecting the known physiological decline in lactase activity after early childhood. Reduced milk consumption and decreased substrate stimulation may further contribute to downregulation of lactase expression (Heyman, 2006). This trend continued in adolescents (16–20 years), where prevalence reached 43.2%, consistent with the progressive manifestation of lactase non-persistence during growth and hormonal maturation (Theodore and Bayless, 1982).

Among young adults (21–30 years), prevalence further increased to 49.3%, aligning with the established pattern of adult-type hypolactasia, where lactase activity may decline to approximately 10% of neonatal levels (Savilahti *et al.* 1983). A continuous increase was observed in middle-aged individuals, reaching 54.3% in the 31–40-year group and 63% in the 41–50-year group. In older adults, prevalence rose sharply to 75.6% (51–60 years), 76.4% (61–70 years), 79% (71–80 years), and 83.6% (81–90 years), confirming a strong age-related decline in lactose tolerance. This pattern is consistent with genetically determined lactase non-persistence and possible cumulative effects of gastrointestinal and metabolic changes over time (Corgneau *et al*. 2017).

Lactose intolerance symptoms are primarily driven by colonic fermentation of undigested lactose, producing hydrogen, carbon dioxide, and methane. This process involves diverse gut microbiota, including *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Clostridium perfringens*, and *Methanobrevibacter smithii*, which contribute to gas production and gastrointestinal symptoms such as bloating, abdominal pain, and diarrhoea (Arnold *et al*. 2018; Angima *et al.* 2024).

The study also revealed a slightly higher prevalence in males (57.2%) compared with females (42.8%), which may reflect differences in dietary habits, milk consumption patterns, or health-seeking behaviour rather than a direct biological effect.

Overall, the findings demonstrate that lactose intolerance is highly prevalent in Albania and increases significantly with age. This condition may contribute to impaired nutrient absorption, gastrointestinal discomfort, dehydration, and reduced quality of life. The results highlight the need for improved public awareness, dietary education, and early identification strategies, particularly in vulnerable groups such as children and the elderly. Special attention should also be given to maternal education to prevent misinterpretation of symptoms in early childhood.

4. CONCLUSIONS

The results of this study indicate a high prevalence of lactose intolerance in the Albanian population. This condition is widely distributed across all age groups, with a markedly higher frequency in elderly individuals. Despite its long-standing presence, lactose intolerance has not received sufficient public health attention in Albania, although it significantly affects nutritional status and quality of life. The findings highlight the need for targeted public health interventions, including awareness and education campaigns focused on metabolic and nutritional disorders. Such initiatives are essential to improve population knowledge and to promote appropriate dietary practices that can reduce symptom burden and prevent complications associated with lactose intolerance. Dietary adaptation, particularly the use of fermented dairy products with reduced lactose content, represents a practical preventive strategy. In addition, broader screening and clinical awareness of lactose intolerance should be considered as part of national health strategies. This is particularly important for vulnerable groups, including young children, older adults, and individuals with comorbid conditions, in order to improve health outcomes and overall well-being.

Declaration of AI use. The authors used AI-based tools (ChatGPT and Grammarly) to assist with language editing and grammar checking. All content was critically reviewed and revised by the authors, who take full responsibility for the accuracy and originality of the manuscript.

Authors' contributions. K.S.: study perception, conceived and led the study, coordinated data collection, and drafted the manuscript. V.G. contributed to data collection, interviews across age groups, and data processing. S.Z.: contributed to interviews, comparative analysis with previous studies, and the literature review. A.S.: conducted interviews with parents of young children and contributed to data collection and analysis.

All authors have read and approved the final version of the manuscript and agree to its submission to the *Albanian Journal of Natural & Technical Sciences*.

Ethics This study was conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments. Since the study involved non-invasive diagnostic procedures (hydrogen breath tests and structured interviews) as part of standard nutritional assessment, formal ethical approval was waived by the relevant institutional board. Informed consent was obtained from all individual participants included in the study. For participants under the age of 18, informed consent was obtained from their parents or legal guardians.

Conflict of interest declaration. We declare we have no competing interests

Ethics: This work did not require formal ethical approval from a human subject committee as it utilized non-invasive testing methods and standard clinical interview protocols. However, informed consent was obtained from all participants (or their guardians) prior to data collection.

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NEXT GENERATION ENVIRONMENTAL EPIDEMIOLOGY: INTEGRATING REMOTE SENSING, MOBILITY DATA, AND BIG DATA ANALYTICS

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Research

Subject Category: **Natural Sciences and Applied Sciences subject:** Environmental Epidemiology / Data Science

ABSTRACT

Environmental epidemiology is currently facing significant challenges, particularly the need for exposure assessment methods that are not only accurate and precise but also accessible and cost-effective. In this context, the implementation of real-time measurements and predictive modelling represents a key opportunity to improve exposure assessment and to manage increasingly large datasets. These approaches may expand populations, reduce selection bias, and enable analyses at broader spatial and temporal scales. This commentary aims to discuss emerging methodologies that address the evolving needs of modern environmental epidemiology, highlighting their advantages and limitations. The focus is placed on methods applied to air pollution, land use and light pollution analyses. Among these, dispersion models remain reliable tools, although their precision may decrease over large geographical areas. In contrast, satellite-based data provide high spatial and temporal resolution, offering greater exposure assessment capabilities. Additionally, remote sensing techniques are increasingly used to evaluate human mobility, enabling access to data that were previously difficult or impossible to obtain. Despite these advantages, several challenges remain, including data privacy concerns, the integration of real-time mobility data, the assessment of multi-exposure scenarios, and the need for standardized, robust and analytical methodologies. Addressing these issues requires strong interdisciplinary collaboration among public health professionals, physicists, mathematicians, engineers, biologists, biotechnologists and architects. Overall, emerging methodologies offer remarkable opportunities to advance environmental epidemiology, provided their limitations are carefully addressed.

Keywords. environmental epidemiology; modelling; satellite data; mobility data; big data

1. INTRODUCTION

Environmental epidemiology is facing increasing challenges (Tonne e*t al*. 2017; Deglin *et al*. 2021; Huang *et al*. 2024). A key issue is the need for exposure measurement methods that are not only accurate and precise,but also easily accessible, practical, and cost-effective. In this context, the implementation of real-time measurements, reliable predictive modelling,and big data management represents a promising pathway to address these needs (Badaloni *et al.* 2018; Wang *et al.* 2023). The potential of these approaches lies in their ability to increase the number of study participants,thereby reducing selection bias and enabling analyses at larger spatial and temporal scales, while maintaining high resolution at lower costs. Consequently, the development of new methodologies that go beyond traditional epidemiological approaches has become a priority in environmental health, with the aim of achieving substantial advancements in the field (Sciannameo *et al.* 2022; Palandri *et al.* 2025). This commentary aims to provide a concise overview of emerging methodologies that can address the evolving needs of modern epidemiology, highlighting their advantages and limitations. Among the main challenges currently faced in environmental epidemiology there are accurate exposure assessment, the low costs constraints, limited voluntary participation, and the need for broad spatial and temporal coverage. The present work focuses on methodological approaches used in environmental epidemiology, particularly those applied to air pollution and forecasting, as well as land use and light pollution analyses.

2. METHODOLOGIES FOR ENVIRONMENTAL EXPOSURE MODELLING

Pollution and air quality modelling

Among the methodologies currently available in environmental monitoring and health research, dispersion models remain efficient and reliable tools, although their precision may decrease when applied to extensive areas (Esmen and Marsh, 1996; Beyea, 1999). In parallel, satellite-based data have emerged as a powerful complementary resource, offering high spatial and temporal resolution for exposure assessment.

With regard to air pollution modeling, CALINE-4, a stationary plume dispersion model designed for roadways and other linear emission sources, represents a well-established approach for estimating the dispersion and deposition of air pollutants and particulate matter (Wu *et al*. 2011). By integrating various input parameters, including traffic emissions, emission variability, and meteorological conditions, the model generates concentration maps at different temporal scales, such as annual averages or daily maxima. An example of these outputs is shown in Fig. 1. The application of CALINE-4 provides a valuable tool for investigating association between exposure to traffic-related air pollution and the risk of developing specific diseases (Vinceti *et al.* 2012; Vinceti *et al*. 2016).

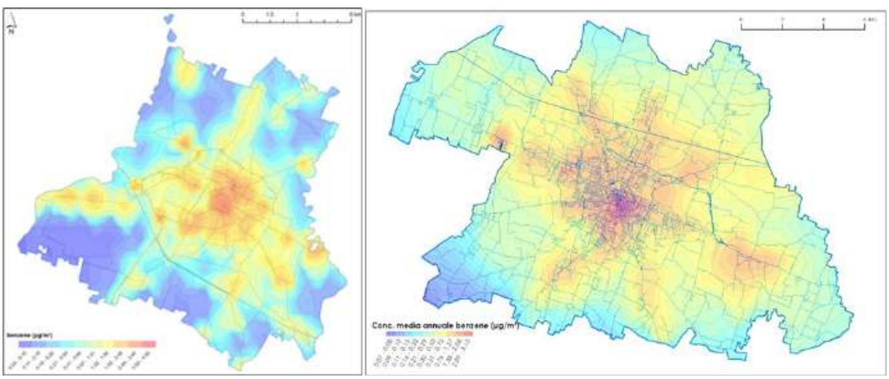


Fig. 1: Maps of the estimated annual mean atmospheric concentrations of benzene in the Municipalities of Modena and Reggio Emilia obtained through the CALINE 4 dispersion model (Vinceti *et al*. 2012).

In the context of air quality assessment, satellite-based data represent an important and increasingly used resource. An outstanding example is the Copernicus Atmosphere Monitoring (CAMS) project, which provides global and European re-analyses of aerosols, chemical species and greenhouse gases, along with daily air quality analyses and forecasts of pollutants, pollens and aerosol tracers at European level (Fig.2). These data are collected through constellations of satellites, called Sentinel missions, which provide large amounts of observations with enhanced spatial and temporal resolution. Owing to these characteristics, satellite-based remote sensing offers a valuable approach for studies investigating the relation between diseases patterns, air pollution levels, and meteorological factors (Filippini *et al*. 2020; Balboni *et al.* 2023).

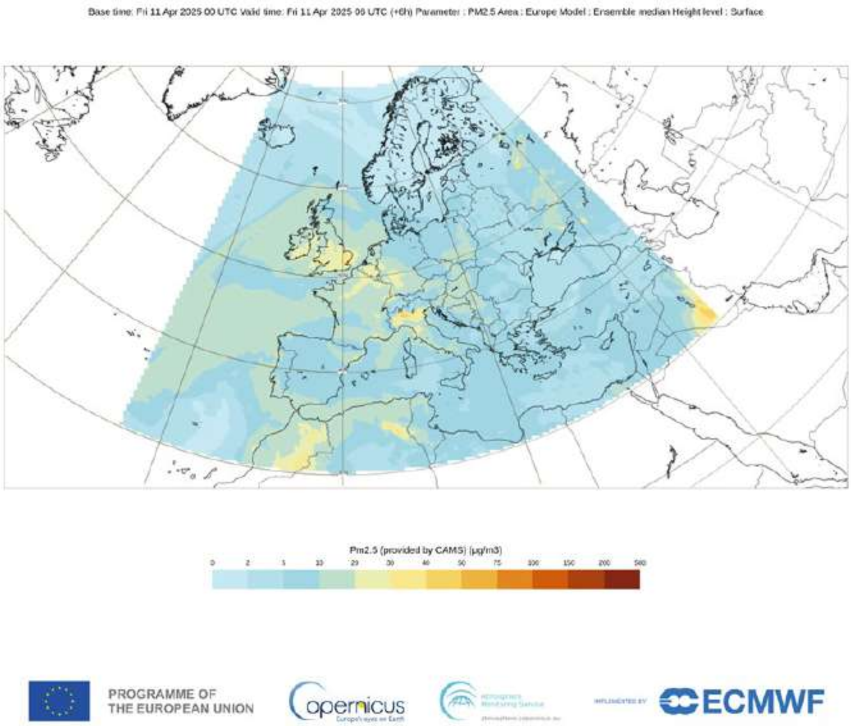


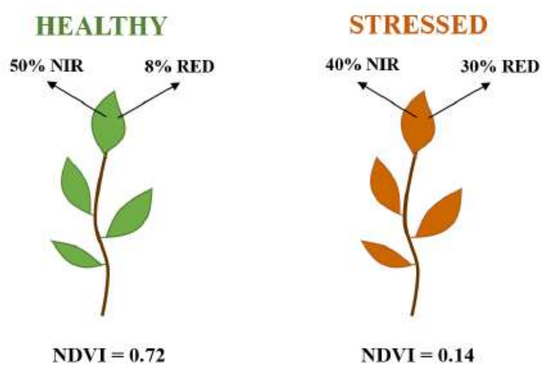
Fig.2: Forecasts of PM 2.5 in Europe in April 2025. Copernicus Atmosphere Monitoring Service (2020): CAMS European air quality forecasts. Copernicus Atmosphere Monitoring Service (CAMS) Atmosphere Data Store, https://atmosphere.copernicus.eu/european-air-quality-forecast-plots (Accessed on 11-04-2025). (Copernicus Atmosphere Monitoring Service, CAMS) (Copernicus Atmosphere Monitoring Service 2020).

Green spaces and light at night

Satellite data also provide remarkable opportunities for the analysis of green spaces, land use and light pollution. Major contributions in these areas are made by large-scale monitoring initiatives such as Copernicus, NASA programs, and Google Earth Engine platforms.

In terms of land use, the CORINE (Coordination of Information on the Environment) program, part of the Copernicus Land Monitoring Service, provides a standardized methodology for land cover maps production. These datasets support a wide range of applications, including environmental monitoring, land use planning, climate change assessments, and emergency management, all at European scale.

Remote sensing techniques further enable the assessment of vegetation quantity and health through indices such as the Normalized Difference Vegetation Index (NDVI), a standardized index which ranges from -1 to 1. This index is based on the differential reflectance of red and near-infrared radiation by vegetation: plants absorb red light for photosynthesis while reflecting near-infrared light. By analyzing this spectral behavior, NDVI provides valuable information on vegetation density and condition across specific areas (Fig. 3).



$$NDVI = \frac{NIR - RED}{NIR + RED}$$

Fig. 3: NDVI (Normalized Difference Vegetation Index) standardized index used in remote sensing to assess the health and density of vegetation.

Satellite imagery of the Earths' surface, used to derive these and other measurements, is provided by several long-standing observational programs. Among these, the NASA's Landsat program is particularly significant, representing the longest continuous archive of satellite data, with operations dating back to 1972. Landsat imagery is also accessible through platforms such as Google Earth Engine, which enables large-scale, cloud-based geospatial analysis. An example of such imagery is presented in Fig. 4.

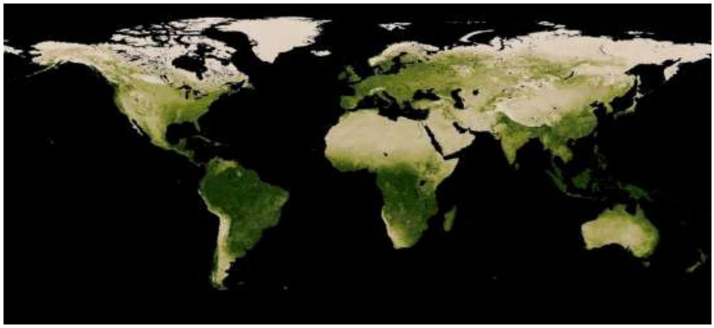


Fig. 4: NASA Earth Observations, Vegetation Index (NDVI) March 2025. Imagery produced by the NASA Earth Observations team using data taken by the MODIS/Terra Vegetation Indices L3 Global 0.05 Deg CMG V006 (MOD13C1 and MOD13C2),https://neo.gsfc.nasa.gov/view.php?datasetId=MOD_NDVI_16&date=2025-03-22. Accessed 22 March 2025 (NASA Earth Observations NEO).

Remote sensing also plays a key role in the assessment of light pollution, an issue of growing environmental and public health concern. The acquisition and analysis of nighttime light data rely on satellites sensors capable of detecting visible and infrared radiation emitted by artificial sources. In this context, data from NASA's Visible Infrared Imaging Radiometer Suite (VIIRS) provide valuable insights into spatial and temporal patterns of light pollution. An example of light pollution images is shown in Fig. 5.

Fig. 5: Light at night pollution image collected by the VIIRS instrument. This map layer was created by the U.S. National Aeronautics and Space Administration (NASA) with data collected by satellites then corrected for factors such as cloud cover, vegetation, and land cover type. The data has been validated with measurements (NASA Earth Observations NEO).

Mobility data

The use of remote sensing and digital technologies for mobility assessment is rapidly expanding, enabling access to data that were previously difficult or impossible to obtain. Mobility data offer a wide range of applications in environmental epidemiology, particularly in tracking the spread of infectious diseases, as illustrated in Figures 6 and 7 (Vinceti *et al*. 2020; Vinceti *et al*. 2022). Beyond disease surveillance, these data support environmental exposure assessments, spatial epidemiology and disease hotspots identification, mHealth, geofencing,wearable devices, real time data acquisition and predictive modeling. Furthermore, mobility data contribute to a better understanding of the social determinants of health by capturing population movement patterns and behavioral dynamics.

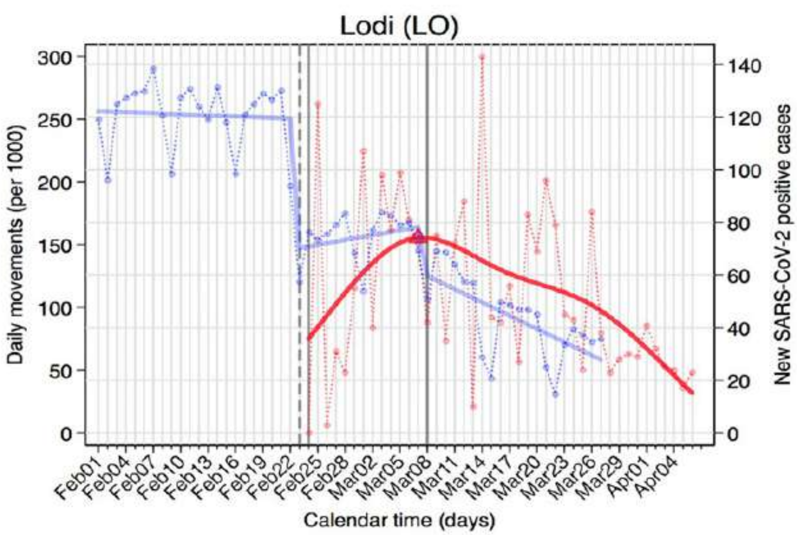


Fig. 6: Day-specific absolute numbers of people movements (blue dots) and SARS-CoV-2 positive cases (red dots) in in Lodi province (Lombardy region) from February 1, 2020-April 6, 2020 (Vinceti *et al*. 2020).

The field of digital epidemiology is rapidly emerging, aiming to leverage big data from various digital sources to detect and monitor disease dynamics, particularly viral epidemics (Fallatah and Adekola, 2024). The potential of these approaches is considerable; however, several barriers must be addressed to enable their optimal application. Similar limitations also apply to satellite-based methodologies (Barreras and Watts, 2024; Potts *et al*. 2024).

Key challenges include data privacy concerns, the reliability and the completeness of mobility data, the need for robust exposure validation and advanced analytical techniques, and the limited availability and integration of real-time mobility data.

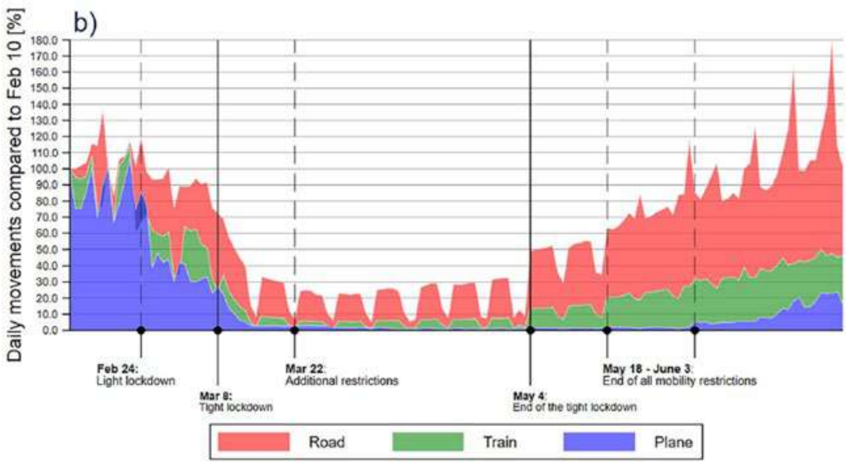


Fig. 7: Lockdown timeline and daily number of people movements according to means of transport in Italy during February–June 2020 (Vinceti *et al*. 2022).

3. DISCUSSIONS

Traditional approaches in environmental epidemiology rely on data collected from public or governmental sources (e.g., population censuses, mortality registries, etc.), monitoring stations or in situ sensors, and surveys to study participants. While these methods remain valid and reliable for exposure assessment, they present inherent limitations, including limited spatial and temporal resolution, restricted data availability, and often a localized scope that may reduce comparability and reproducibility across studies.

In this context, the integration of modern technologies, such as dispersion models, satellite imagery, remote sensing and big data, has become essential to overcome the constraints of traditional methodologies. These approaches enable large-scale applications and support more adaptive and effective public health strategies. The expansion of data sources enables accessibility to previously unavailable information, allowing more comprehensive exposure assessments at both local and national levels. Access to international datasets further strengthens research capacity, particularly in countries undergoing technological development. Moreover, the use of standardized and validated methodologies improves reproducibility and facilitates cross-country comparisons. Big data approaches may also enhance population engagement while reducing data collection costs. Despite these advantages, several challenges remain, including the selection of appropriate methodological approaches, the complexity of data integration, and issues related to data quality and management. Such challenges underscore the need for interdisciplinary collaboration among experts from fields including public health, physics, mathematics, engineering, and related disciplines.

4. CONCLUSIONS

A wide range of emerging methodologies offers significant opportunities for environmental epidemiology advancement. However, several critical challenges must still be addressed, including data privacy, real-time mobility data, integration of multi-exposure scenarios, and standardized and robust analytical frameworks. Addressing these issues requires strong interdisciplinary collaboration among public health professionals and experts from different fields such as physics, mathematics, engineering, biology, biotechnology, and architecture.

Ethics. Ethical approval was not required for this study, as it was based on aggregated, publicly available data.

Data accessibility (websites, platforms).
https://atmosphere.copernicus.eu/european-air-quality-forecast-plots; https://neo.gsfc.nasa.gov/view.php?datasetId=MOD_NDVI_16&date=2025-03-22; https://www.earthdata.nasa.gov/data/instruments/viirs/land-near-real-time-data#toc-viirs-land-data-and-information.

Declaration of AI use. There has been no use of AI when writing the actual paper.

Author Contributions. A.S., M.M., T.F., M.V.: conceptualization; A.S., M.V.: investigation; : A.S., M.M., T.F., M.V.: methodology; M.M., M.V.: supervision; A.S: writing – original draft; all the authors: writing – review and editing

All the authors have approved the final version of the manuscript.

Conflict of interest declaration. The authors declare that they have no conflict of interest related to this work.

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SPATIAL AND TEMPORAL PATTERNS OF RESPIRATORY, CARDIOVASCULAR, AND MALIGNANT DISEASES IN RELATION TO AMBIENT AIR POLLUTION IN INDUSTRIAL AREAS OF ALBANIA (2021–2024): AN ECOLOGICAL EPIDEMIOLOGICAL STUDY

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ABSTRACT

Non-communicable diseases (NCDs), particularly respiratory, cardiovascular, and malignant diseases, represent a major public health challenge, especially in industrial areas where environmental exposures may increase health risks. In Albania, evidence linking morbidity patterns with air pollution in industrial settings remains limited. This study aimed to assess temporal trends in selected NCDs in industrial areas of Albania from 2021 to 2024 and to explore their potential association with ambient air pollution. A retrospective ecological study was conducted using routinely collected health data from Local Directorates of Public Health in two districts. Disease prevalence rates were calculated for selected industrial municipalities and stratified by age group. Data on ambient air pollutants (PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, CO, and benzene) were obtained from the National Environmental Agency and compared with World Health Organization (WHO) guideline values. Descriptive statistical analyses were used to evaluate spatial and temporal trends. Respiratory and cardiovascular diseases showed increasing trends in several industrial areas, particularly in Elbasan and Mallakastër, while malignant diseases displayed relatively stable but geographically variable patterns. Disease prevalence increased markedly with age, with the highest rates observed among individuals aged ≥65 years. Air quality data indicated that PM_{10} and NO_2 levels approached or exceeded recommended thresholds in certain areas, especially Elbasan and Fier. The findings suggest geographic disparities in disease burden across industrial regions and indicate a possible association between long-term air pollution exposure and increased NCD prevalence. However, due to the ecological design and the absence of individual-level exposure data, causal relationships cannot be established. Strengthening integrated environmental and health monitoring systems is essential for improving risk assessment and public health protection in Albania.

Keywords: respiratory diseases; cardiovascular diseases; malignant diseases; air pollution; industrial areas; Albania; epidemiology; public health

1. INTRODUCTION

Air pollution is widely recognized as a major environmental risk factor for human health, contributing significantly to global morbidity and mortality from both chronic and acute diseases. The World Health Organization identifies ambient air pollution as a key determinant of non-communicable diseases (NCDs), with fine particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2), ozone (O_3), sulphur dioxide (SO_2), carbon monoxide (CO), and volatile organic compounds such as benzene among the most relevant pollutants affecting health outcomes (WHO, 2021).

Over the past decade, an expanding body of epidemiological evidence has demonstrated robust associations between long-term exposure to air pollution and an increased risk of respiratory diseases, including chronic obstructive pulmonary disease and asthma, as well as cardiovascular conditions such as ischemic heart disease and stroke (EEA, 2023; Mahiyuddin *et al*. 2023). Among these pollutants, $PM_{2.5}$ is considered particularly harmful due to its ability to penetrate deep into the respiratory tract and enter the bloodstream, contributing to systemic inflammation and oxidative stress—mechanisms that play a central role in the pathogenesis of cardiovascular and respiratory diseases (Brook *et al*. 2017; Pope *et al*. 2019).

In addition, exposure to NO_2 and PM_{10} has been consistently associated with increased hospital admissions and mortality related to cardiorespiratory conditions (Huang *et al.* 2021; Requia *et al*. 2025). Air pollution has also been classified as a Group 1 carcinogen by the International Agency for Research on Cancer, with long-term exposure linked to an elevated risk of lung cancer and other malignancies (IARC, 2016; Raaschou-Nielsen *et al.* 2016)

Industrial regions represent areas of particular concern due to concentrated emissions originating from manufacturing activities, energy production, and transport systems (Beelen R *et al.* 2014). Despite substantial global evidence, studies integrating environmental exposure data with disease burden remain limited in Southeastern Europe, including Albania. Industrial zones in Albania are characterized by heterogeneous emission sources and limited continuous air quality monitoring, which constrain comprehensive environmental health assessments.

In this context, evaluating the spatial and temporal distribution of respiratory, cardiovascular, and malignant diseases in relation to environmental conditions is essential for understanding potential public health impacts. This study aims to address this gap by analyzing disease prevalence trends in selected industrial areas of Albania during the period 2021–2024 and examining their relationship with available air quality data.

2. MATERIALS AND METHODS

Study design and setting

This study employed a retrospective ecological time-series design to assess spatial and temporal patterns in the prevalence of respiratory, cardiovascular, and malignant diseases in industrial areas of Albania over the period 2021–2024. The analysis included seven municipalities—Fier, Elbasan, Mallakastër, Kuçovë, Patos, Roskovec, and Belsh—selected based on their industrial activity profiles, documented emission sources, and population characteristics.

Data sources and data quality assurance

Health outcome data were obtained from the Local Directorates of Public Health, which systematically compile aggregated morbidity data from primary healthcare centers, hospital discharge records, and specialist outpatient services. Annual counts of clinically diagnosed respiratory, cardiovascular, and malignant diseases were extracted using ICD-based classification systems where available.

Data quality assurance procedures included the removal of duplicate records across reporting facilities, cross-validation between primary care and hospital registries, and exclusion of incomplete or inconsistent entries. Population denominators were harmonized using official municipal population estimates to ensure comparability across study areas.

Environmental exposure data were retrieved from the National Environmental Agency monitoring network and included PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, CO, and benzene. Due to limitations in spatial monitoring coverage, measurements were aggregated at the municipal level.

Exposure assessment

Air pollution exposure was assessed using annual mean concentrations and, where available, short-term averages depending on pollutant type. Observed values were compared with WHO air quality guideline thresholds to contextualize exposure levels. Given the limited spatial resolution of monitoring data, exposure was defined at the area level and used as a proxy for population-level exposure, consistent with ecological study design principles.

Outcome definitions and standardization

Disease outcomes were expressed as annual prevalence rates per 10,000 population, calculated as the number of registered cases divided by the total population and multiplied by 10,000. Age-specific analyses were conducted using stratified population denominators to account for demographic variation across municipalities. Where appropriate, indirect age standardization was applied to improve comparability between regions with differing age structures.

Confounding and bias considerations

Given the ecological nature of the study, adjustment for individual-level confounders was not feasible. However, key contextual factors were considered in the interpretation of findings, including differences in age structure, regional smoking prevalence, occupational exposure patterns related to industrial activity, socioeconomic variability, and access to healthcare services. Potential sources of bias—including ecological fallacy and exposure misclassification—were acknowledged, particularly in relation to the use of aggregated environmental data.

Statistical analysis

A descriptive analytical framework was applied. Temporal trends were assessed through year-to-year percentage changes in prevalence rates, while spatial heterogeneity was evaluated by comparing standardized prevalence estimates across municipalities. No inferential statistical testing was performed, as the dataset represents near-complete population coverage within the selected areas rather than a sampled population. This approach is consistent with ecological surveillance studies focused on population-level burden estimation.

Sensitivity and robustness considerations

Several analytical steps were undertaken to enhance the robustness of the findings. Age-stratified analyses were used to reduce confounding related to demographic structure. Multi-year trend assessment (2021–2024) was applied to minimize the influence of random annual variation. Cross-disease comparisons across respiratory, cardiovascular, and malignant conditions were conducted to evaluate the internal consistency of observed patterns. Environmental exposure levels were interpreted in relation to WHO guideline thresholds to support external comparability.

Ethical considerations

All data used in this study were secondary, aggregated, and anonymized at the municipal level, with no access to individual identifiers. Ethical approval was therefore not required, in accordance with national regulations governing the use of secondary public health data.

3. RESULTS AND DISCUSSIONS

The empirical data compiled in Tables 1–8 and Figures 1–3 reveal distinct spatial and temporal heterogeneity in the prevalence of respiratory, cardiovascular, and malignant pathologies across the designated industrial municipalities of Albania during the 2021–2024 observation window. Mechanistically, elevated disease burdens correlated consistently with municipalities characterized by intensive industrial profiles—specifically Elbasan, Fier, Mallakastër, and Roskovec. Conversely, lower, highly stable baseline prevalence rates were sustained in Patos, Kuçovë, and Belsh.

As delineated in Table 1 and Figure 1, respiratory conditions exhibited the most acute temporal escalation. Mallakastër demonstrated the sharpest positive trajectory, with prevalence rates surging from 72.4 cases per 10,000 population in 2021 to 427.4 per 10,000 in 2024, quantifying an approximate sixfold increase. Roskovec consistently registered among the highest baseline and longitudinal respiratory disease prevalence rates throughout the study period, while Elbasan exhibited a monotonic upward trend. In contrast, Fier exhibited a non-monotonic pattern characterized by an initial decline followed by a moderate rebound, whereas Patos and Kuçovë maintained low prevalence rates with negligible annual variance. Figure 1 further illustrates a widening longitudinal divergence between high- and low-prevalence municipalities, indicating intensifying spatial inequality in regional respiratory disease burdens.

Table 1. Prevalence of respiratory diseases (per 10,000 population) in selected industrial areas of Albania, 2021–2024

	Year			
Region	**2021**	**2022**	**2023**	**2024**
Mallakaster/10000	72.4	118.3	385.7	427.4
Kucove/10000	18.1	18.5	23.1	24.3
Fier/10000	92.9	41.2	52.4	57.2
Patos/10000	4.9	8.5	7.1	7.4
Roskovec/10000	246.3	254.6	274.6	346.7
Elbasan/10000	156.1	175.9	189.3	218.7
Belsh/10000	8.4	16.3	21.5	18.5

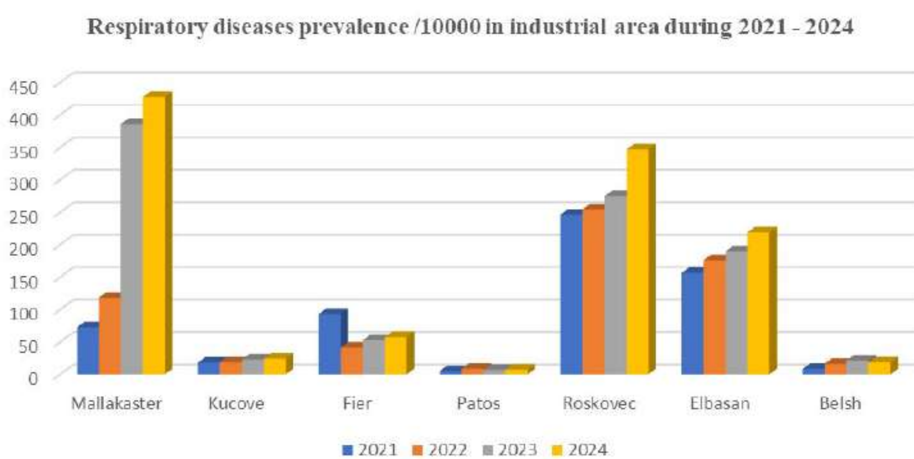

Fig. 1. Temporal trends in respiratory disease prevalence (per 10,000 population) across selected industrial areas, Albania, 2021–2024.

The escalating respiratory disease burden observed in heavily industrialized municipalities aligns with international epidemiological data linking long-term ambient exposure to particulate matter (PM_{10}, $PM_{2.5}$) and nitrogen oxides (NO_x) with adverse pulmonary outcomes (Beelen *et al.* 2014; WHO, 2021). However, given the ecological architecture of this study and the concomitant absence of individual-level dosimetry, these spatial associations must be interpreted with caution to avoid ecological fallacy, and cannot be construed as definitive evidence of direct causality (Morgenstern, 2021).

Table 2 and Figure 2 illustrate a persistently elevated prevalence of cardiovascular diseases (CVD) across all monitored cohorts, with Elbasan consistently exhibiting the highest absolute burden. CVD prevalence in Elbasan expanded from 630.7 per 10,000 population in 2021 to 872.0 per 10,000 in 2024, while Fier demonstrated a continuous linear increase from 312.5 to 416.5 per 10,000 population. Mallakastër and Roskovec similarly displayed positive secular trends, whereas Patos and Kuçovë remained comparatively stationary. Figure 2 highlights these stark geographic disparities and the progressive longitudinal amplification of CVD, particularly within the Elbasan and Fier enclaves.

Table 2. The Prevalence of Cardiovascular Diseases (per 10,000 population) in selected industrial areas of Albania, 2021–2024

	Year			
Region	**2021**	**2022**	**2023**	**2024**
Mallakaster/10000	140.1	186.6	182.9	200.5
Kucove/10000	43.5	40.6	42.1	50.7
Fier/10000	312.5	341.8	399	416.5
Patos/10000	24.5	19.3	22.7	24.1
Roskovec/10000	28.6	40.5	60.2	64.6
Elbasan/10000	630.7	663	693.6	872
Belsh/10000	173.8	161.7	210.7	163.8

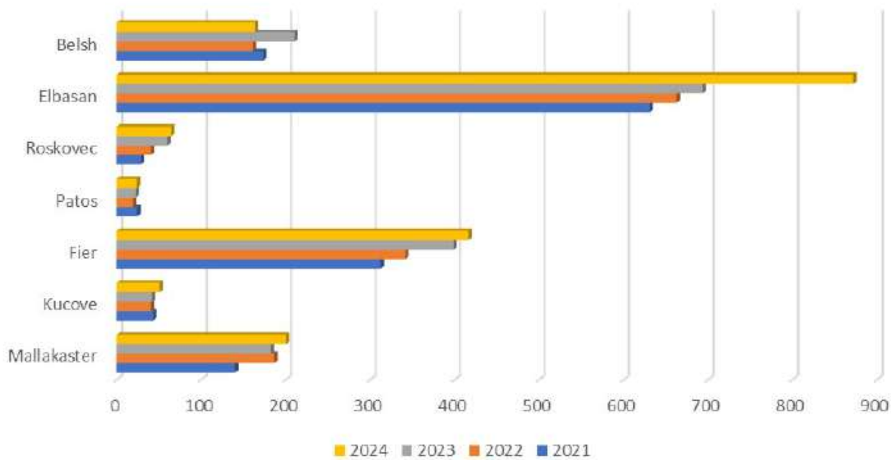

Fig. 2. Temporal trends in cardiovascular disease prevalence (per 10,000 population) across selected industrial areas, Albania, 2021–2024

The synchronous escalation of respiratory and cardiovascular morbidities in high-exposure municipalities strengthens the biological plausibility of these data. Both pathophysiological clusters share overlapping etiologics linked to chronic ambient air pollution, mediated primarily via systemic inflammation, oxidative stress, endothelial dysfunction, and accelerated pulmonary-cardiovascular remodeling (Brook *et al*. 2017; Pope *et al*. 2019). The multi-year replication of these spatial configurations further substantiates the epidemiological robustness of the observed associations.

As summarized in Table 3 and Figure 3, malignant neoplasms displayed lower absolute prevalence and attenuated temporal variability relative to respiratory and cardiovascular conditions. Fier consistently recorded the highest oncological prevalence, rising from 45.1 cases per 10,000 population in 2021 to 61.0 per 10,000 in 2024, while Elbasan exhibited a gradual, low-slope upward trend. The remaining municipalities exhibited stationary or fluctuating baseline patterns with minor annual deltas. Figure 3 underlines the protracted temporal variation of malignant diseases compared to the acute vectors seen in respiratory and cardiovascular metrics. These stable longitudinal trends are epidemiologically congruent with the extended latency periods intrinsic to carcinogenesis.

Table 3. Prevalence of Malignant Diseases (per 10,000 population) in Selected Industrial Areas of Albania, 2021–2024

	Year			
Region	**2021**	**2022**	**2023**	**2024**
Mallakaster/10000	13.2	12	13.2	10.1
Kucove/10000	6.5	3.8	5.7	9.1
Fier/10000	45.1	43.5	55	61
Patos/10000	6.8	6.8	10.9	9.2
Roskovec/10000	8.6	40.5	8.5	13.3
Elbasan/10000	28.7	29	27.8	1.6
Belsh/10000	25.2	2.81	1.6	4.6

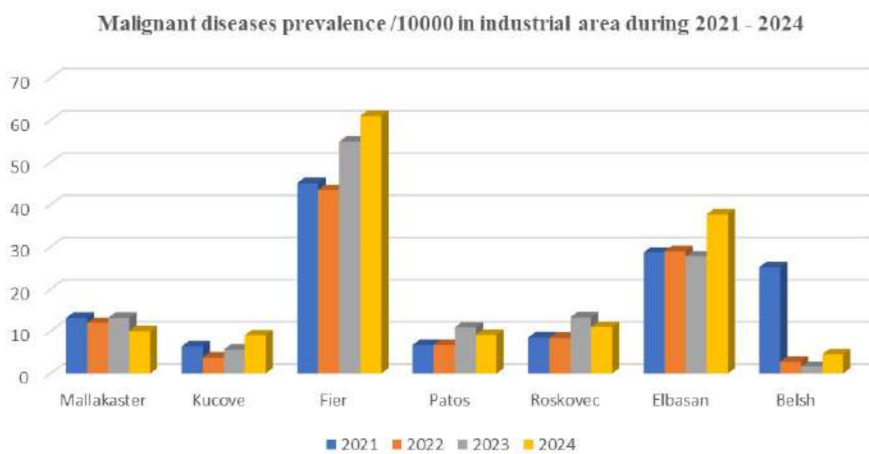

Fig. 3. Temporal trends in malignant disease prevalence (per 10,000 population) across selected industrial areas, Albania, 2021–2024.

The elevated prevalence of malignant diseases within these industrial hubs is coherent with established toxicological frameworks classifying ambient air pollution as a Group 1 human carcinogen (IARC, 2016; Raaschou-Nielsen *et al.* 2016). Nevertheless, oncological prevalence is highly confounded by unmeasured lifestyle and endogenous variables—including tobacco use, occupational carcinogen exposure, genetic predisposition, and differential diagnostic screening practices—which could not be statistically controlled for in this aggregate analysis.

Age-stratified analyses (Tables 4–6) confirm that age remains a dominant determinant of morbidity across all diagnostic categories. Table 4 demonstrates that respiratory diseases consistently peaked within the cohort aged ≥65 years across all jurisdictions, with maximum expression in Elbasan, Roskovec, and Mallakastër. Similarly, Table 5 reveals a steep, age-dependent escalation in CVD, characterized by exceptionally high prevalence among the elderly strata of Elbasan and Fier. Notably, in Elbasan, CVD prevalence within the ≥65 age group advanced from 2806.8 per 10,000 population in 2021 to 3395.7 per 10,000 in 2024. Table 6 indicates that malignant neoplasms were likewise heavily skewed toward older age brackets, concentrated primarily in the ≥55 and ≥65 cohorts, matching established biodemographic models of cancer incidence.

Table 4. Age-specific prevalence of respiratory diseases (per 10,000 population) across selected industrial areas of Albania, 2021–2024

	Respiratory diseases prevalence by age-group – Mallakaster								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	30.24	28.2	75.5	54.84	67.58	79.01	218.24
2022	152.5	88.24	136.08	23.5	23.73	85.55	154.48	139.58	303.1
2023	196.1	898.51	758	63.44	140.21	289.54	277.58	424.02	640.16
2024	108.9	417.17	616.9	162.13	211.39	232.51	477.92	447.72	979.63
	Respiratory diseases prevalence by age-group - Kucova								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	3.22	1.81	0	1.49	26.23	29.44	47.16
2022	0	0	0	0	0	2.96	19.85	26.1	70.29
2023	0	0	0	0	0	4.81	33.91	30.17	59.93
2024	0	0	0	0	0	7.56	67.09	38.37	71.22
	Respiratory diseases prevalence by age-group - Fier								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	17.3	14.99	12.92	14.2	31.45	89.35	171.8	221.39
2022	0	8.9	4.36	11.5	0.92	22.97	27.72	61.27	111.12
2023	0	4.2	11.45	16.05	6.88	13.12	35.78	70.04	128
2024	0	9.8	8.06	16.36	10.03	33.64	44.14	82	122.6
	Respiratory diseases prevalence by age-group - Patos								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65

2021	0	0	0	0	0	0	10.94	15.54	7.11
2022	0	0	7.05	2.03	0	2.45	2.58	24.56	17.04
2023	0	0	19.92	4.3	1.2	0	6.35	13.79	13.6
2024	0	0	10.11	2.16	0	3.18	2.65	13.81	21.25
	Respiratory diseases prevalence by age-group - Roskovec								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	0	3	17	110	584
2022	0	0	0	0	0	4	20	122	603
2023	0	0	0	0	0	5	24	170	627
2024	0	0	0	0	0	6	119	182	643
	Respiratory diseases prevalence by age-group - Elbasan								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	36.73	17.02	6.39	7.52	12.22	58.11	208.28	457.21	671.2
2022	102.61	36.22	17.05	15.9	22.4	63.29	221.23	487.71	763.9
2023	46.86	43.43	17.43	18.16	31.48	69.89	217.95	455.3	857.2
2024	96.15	64.5	22.92	20.59	39.36	77.11	283.52	520.4	919.8
	Respiratory diseases prevalence by age-group - Belsh								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	3.58	1.2	12.2	11.73	64.28
2022	205.5	21.14	5.23	0	7.17	3.61	14.8	7.9	125.2
2023	125	4.53	5.57	8.25	2.04	8.82	9.79	22.44	167.8
2024	128.2	4.59	5.75	5.43	8.28	6.35	10.12	12.01	160.04

Table 5. Age-specific prevalence of cardiovascular diseases (per 10,000 population) across selected industrial areas of Albania, 2021–2024

	Cardiovascular diseases prevalence by age-group Mallakaster,								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	2.35	0	32.9	79.7	321.3	664.4
2022	0	0	0	2.35	0	48.26	115.9	571.5	739.6
2023	0	0	0	2.35	0	50.45	205.2	358.2	814.8
2024	0	0	0	2.35	2.16	89.9	176.2	408.2	887.5
	Cardiovascular diseases prevalence by age-group Kucove								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	0	6	33	61	93
2022	0	0	0	0	0	11	33	49	78

2023	0	0	0	0	0	3	25	60	91
2024	0	0	0	0	0	2	23	67	104
	Cardiovascular diseases prevalence by age-group Fier								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	4.94	1.61	1.78	4.85	18.87	453.8	596.6	797.5
2022	0	2.21	1.45	1.23	20.19	85.49	206.7	537.3	1039
2023	0	2.09	2.29	13.04	22.79	126	258	678.3	985.8
2024	26.08	0	2.48	7.73	21.6	117.3	315.2	693.6	995.6
	Cardiovascular diseases prevalence by age-group Patos								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	0	0	41.01	48.35	66.87
2022	0	0	0	0	0	0	25.76	34.39	56.79
2023	0	0	0	0	0	0	25.39	49.98	60.45
2024	0	0	0	0	0	0	26.46	50.06	70.85
	Cardiovasculary diseases prevalence by age-group Roskovec								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	69	0	4.23	2.44	0	5.75	1.33	115.9	56.14
2022	0	0	4.19	0	0	3.16	44.71	107.8	89.72
2023	0	0	3.92	0	2.12	0	48.25	142.2	164.3
2024	0	0	4.07	0	2.37	0	88.18	155.4	145
	Cardiovascular diseases prevalence by age-group Elbasan								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	146.9	42.54	23.95	65.57	227	298.3	728.4	1340.1	2806.8
2022	28	46.87	28.23	65.69	229.1	304.5	762.2	1360.8	3035.9
2023	140.6	82.73	40.67	75.32	232.3	322.1	879.9	1660.7	2742.3
2024	160.3	157.4	69.9	126.4	273.2	389.6	1088.1	2021.8	3395.7
	Cardiovascular diseases prevalence by age-group Belsh								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	129	41.58	7.83	19.39	66.23	79.34	239.2	414.4	948.2
2022	68.5	42.28	7.85	19.42	62.74	78.22	203.8	391.2	892.6
2023	125	9.05	11.14	41.22	81.37	91.92	293.7	426.3	1166.6
2024	128.2	4.59	5.75	35.3	68.31	44.44	273.3	416.3	946.5

Table 6. Age-specific prevalence of malignant diseases (per 10,000 population) across selected industrial areas of Albania, 2021–2024

	Malignant diseases prevalence by age-group - Mallakaster								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	0	0	24.14	50.04	31.52
2022	0	0	0	0	0	0	16.9	39.51	38.8
2023	0	0	0	0	0	2.19	24.14	47.41	31.52
2024	0	0	0	0	0	2.19	16.9	31.61	29.1
	Malignant diseases prevalence by age-group - Kucove								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	0	1.49	7.49	9.37	19.55
2022	0	0	0	2.01	0	1.48	4.41	9.62	5.86
2023	0	0	3.5	0	0	3.21	7.27	6.96	13.08
2024	0	0	3.1	0	0	5.04	18.64	13.35	27.06
	Malignant diseases prevalence by age-group - Fier								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	1.78	2.08	27.26	46.03	50.39	132.9
2022	0	0	0	2.47	2.76	23.39	36.83	41.7	137
2023	0	0	1.15	2.01	3.98	35.61	50.74	56.89	143.8
2024	0	0	0.62	0.91	2.32	42.31	58.29	69.54	150.4
	Malignant diseases prevalence by age-group -Patos								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	2.31	2.42	2.74	8.65	22.76
2022	0	24	0	0	0	2.46	7.73	13.1	17.04
2023	0	0	0	0	0	7.69	6.35	17.24	33.25
2024	0	0	0	0	1.2	0	2.65	8.63	40.74
	Malignant diseases prevalence by age-group - Roskovec								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0	0	3.96	2.88	2.66	14.13	28.07
2022	0	11	0	0	0	3.16	7.45	18.34	20.7
2023	0	0	0	0	0	6.89	5.38	23.7	36.88
2024	0	0	0	0	2.37	0	2.94	12.33	40.67
	Malignant diseases prevalence by age-group - Elbasan								

	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	0.53	1.25	6.79	14.08	43.2	65.59	117.9
2022	0	0	0	0.84	3.4	22.02	37.73	53.4	123
2023	0	0	0	0.77	5.5	20.6	33.74	54.69	114.1
2024	0	0	0	1.65	8.53	25.97	51.87	76.04	141.5
	Malignant diseases prevalence by age-group -Belsh								
	< 1 year	1.-4	5-14.	15-24	25-34	35-44	45-54	55-64	≥ 65
2021	0	0	2.61	2.16	17.9	13.22	43.93	70.37	88.39
2022	0	0	0	0	0	6.02	7.37	3.95	0
2023	0	0	0	0	0	3.78	4.9	0	0
2024	0	0	0	0	0	3.81	17.72	16.02	0

These age-specific data align with global gerontological and environmental health literature indicating that older populations exhibit heightened vulnerability to chronic somatic diseases due to cumulative lifetime environmental insults and senescent biological susceptibility (Landrigan *et al*. 2018; WHO, 2021). The persistence of elevated prevalence in Elbasan and Fier across multiple age cross-sections suggests that adverse environmental determinants may be compounding underlying demographic shifts to drive the local disease burden.

Environmental monitoring matrices (Table 7) provide crucial exposure context for these health outcomes. Mean ambient concentrations of PM_{10} and NO_2 in Elbasan consistently approached or breached national regulatory frameworks and WHO air quality guidelines during the study timeframe; elevated particulate concentrations were similarly recurrent in Fier. In Elbasan, annual means reached 47.85 $\mu g/m^3$ for PM_{10} and 36.6 $\mu g/m^3$ for NO_2 by 2024, critically exceeding recommended health-protective thresholds. Conversely, sulfur dioxide (SO_2), carbon monoxide (CO), and tropospheric ozone (O_3) levels generally remained within compliant margins in both municipalities. Table 8 details the specific WHO air quality guidelines utilized as reference thresholds for the comparative analyses executed in Table 7.

The high ambient concentrations of PM_{10}, PM 2.5, and NO_2 observed in Elbasan support the hypothesis that particulate matter and nitrogen oxides constitute the primary ambient stressors driving the excess respiratory and cardiovascular morbidity burdens in these industrial zones.

Identical criteria pollutant profiles have been robustly coupled with elevated cardiopulmonary morbidity and mortality in large-scale international multi-center studies (HEI, 2020; WHO, 2021).

Table 7. Concentrations of air pollutants (SO_2, O_3, CO, NO_2, PM10, PM2.5, and Benzene) in industrial areas of Fier and Elbasan, Albania, 2021–2024, compared with national standard limits (National Environmental Agency data)

Fier	**SO2 µg/m³**	**O3 µg/m³**	**CO mg/m³**	**NO2µg/m³**	**PM10 µg/m³**	**PM2.5 µg/m³**	**Benzene µg/m³**
2021	7.49	28.06					
2022							
2023		28.06	0.46		25.39	14.55	1.23
2024		43.27	0.48	32.9	23.42		0.97
Standard level	**50 (24h)**	**Average in 6 months (B) - 70 and 8-h average (A) - 120**	**24h(A) - 7**	**Annual average - 20**	**Annual average - 30**	**Annual average - 37.5**	**Annual average - 5**
Elbasan	**SO2 µg/m³**	**O3 µg/m³**	**CO mg/m³**	**NO2µg/m³**	**PM10 µg/m³**	**PM2.5 µg/m³**	**Benzene µg/m³**
2021							
2022							
2023			1.91				2.24
2024	2.93	37.2	0.57	36.6	47.85		2.54
Standard level	**50 (24h)**	**Average in 6 months (B) - 70 and 8-h average (A) - 120**	**24h(A) - 7**	**Annual average - 20**	**Annual average - 30**	**Annual average - 37.5**	**Annual average - 5**

Table 8. WHO Air Quality Standard Values Table (Levels 1–4)

Pollutant	Averaging time	Level 1	Level 2	Level 3	Level 4 (WHO guideline)
PM2.5	Annual mean	35 µg/m³	25 µg/m³	15 µg/m³	10 µg/m³
PM10	Annual mean	70 µg/m³	50 µg/m³	30 µg/m³	20 µg/m³
NO2	Annual mean	200 µg/m³	100 µg/m³	60 µg/m³	40 µg/m³
NO2	24-hour mean	400 µg/m³	200 µg/m³	150 µg/m³	120 µg/m³
SO2	24-hour mean	500 µg/m³	350 µg/m³	250 µg/m³	—
CO	8-hour mean	30 mg/m³	20 mg/m³	10 mg/m³	WHO guideline applies
O3	8-hour mean	160 µg/m³	140 µg/m³	130 µg/m³	120 µg/m³
O3	Seasonal (6-month)	100 µg/m³	90 µg/m³	80 µg/m³	70 µg/m³
Benzene (C6H6)	Annual mean	20 µg/m³	10 µg/m³	7 µg/m³	5 µg/m³

* A- The value should be 99% of the time (only 3-4 days above the norm)
B-Average value of the summer season

Despite the epidemiological coherence of these results, several systemic methodological limitations must be stated. The ecological design restricts causal inference and leaves the findings susceptible to the ecological fallacy (Morgenstern, 2021). Non-differential exposure misclassification remains possible, as municipality-level aggregate pollutant averages may not accurately mirror individual time-activity patterns or distinct occupational exposures. Furthermore, residual confounding persists due to the unavailability of individual-level data regarding smoking status, socioeconomic status (SES), occupational history, and local healthcare accessibility. Potential variations in diagnostic rigor and institutional reporting fidelity across municipalities may also introduce information bias into the prevalence estimates.

Nonetheless, the multi-tiered data presented in Tables 1–8 and Figures 1–3 demonstrate internal consistency, biological plausibility, and structural coherence with existing environmental health paradigms when evaluated through the lens of the Bradford Hill framework (Hill, 1965). While true temporality and definitive dose-response curves cannot be fully established using this design, the pronounced spatial associations underscore an urgent mandate for rigorous, analytical epidemiological investigations (e.g., case-control or prospective cohort studies).

In conclusion, this study maps critical geographic disparities in the non-communicable disease burden across Albania's industrial sectors. The data emphasize an immediate need for optimized environmental monitoring networks, enhanced interoperability between environmental and syndromic public health surveillance systems, and targeted, localized public health interventions within high-burden municipalities like Elbasan and Fier.

4. CONCLUSION

This ecological study provides a comparative assessment of the prevalence of respiratory, cardiovascular, and malignant diseases in selected industrial areas of Albania between 2021 and 2024, in relation to ambient air pollution exposure. The findings demonstrate clear spatial heterogeneity, with consistently higher burdens of respiratory and cardiovascular diseases observed in Elbasan compared to Fier and other municipalities.

Across all study areas, a strong and consistent age-dependent gradient was identified, with the highest disease prevalence among individuals aged ≥65 years, confirming age as a major determinant of non-communicable disease burden. Cardiovascular and respiratory diseases showed increasing temporal trends in several industrial areas, whereas malignant diseases remained relatively stable but exhibited persistent regional differences.

Environmental data indicate that most measured pollutants remained within national standards; however, exceedances and near-threshold levels of PM10 and NO_2 were observed, particularly in Elbasan and, to a lesser extent, Fier. These patterns are epidemiologically consistent with the observed higher disease burden in more polluted areas, although causal relationships cannot be established.

Due to the ecological design, aggregated exposure assessment, and lack of control for individual-level confounders, causal inference is not possible. Additional factors, such as smoking prevalence, occupational exposure, socioeconomic conditions, and healthcare access, may also contribute to the observed spatial differences.

In conclusion, the study provides consistent population-level evidence suggesting an association between industrial air pollution patterns and the distribution of non-communicable diseases in Albania. The findings highlight the need for integrated environmental and health surveillance systems, improved air quality monitoring, and targeted public health interventions in high-risk industrial areas, particularly Elbasan.

Ethics. Ethical approval was not required for this study, as it is based on secondary, aggregated, and anonymized data from public sources. No individual-level data or personal identifiers were accessed or analyzed.

Data accessibility. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. Due to the use of aggregated public health surveillance data, individual-level data are not publicly accessible. Data supporting the findings of this study are available from the following public sources: www.geo.edu.al and EMSC-CSEM.org. Additional datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declaration of AI use. The authors declare that artificial intelligence tools were used solely for language editing, grammar correction, and formatting support. These tools were not used for data generation, statistical analysis, interpretation of results, or the formulation of scientific conclusions.

Author Contributions. E. Mataj.: conceptualization; methodology; formal analysis; investigation; writing – original draft; E.T.: conceptualization; writing – review and editing; supervision; I. S.: methodology; data collection; data curation; investigation; writing – review and editing.

All authors have read and approved the final version of the manuscript and agree to its submission for publication.

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SARS-COV-2 IMMUNITY IN ALBANIA: LESSONS FROM THE COVID-19 PANDEMIC FOR FUTURE PUBLIC HEALTH AND ENVIRONMENTAL CHALLENGES

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Research

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ABSTRACT

The COVID-19 pandemic posed a significant public health stressor, necessitating a robust understanding of SARS-CoV-2 transmission dynamics and the longitudinal evolution of population immunity. This study evaluates anti-SARS-CoV-2 seroprevalence in Tirana, Albania, from 2020 to 2023, quantifying the relative contributions of natural infection, vaccination, and hybrid immunity. Five cross-sectional serosurveys were conducted (June 2020–April 2023) among adults aged 18–70 years. Participants were randomly selected from five primary urban healthcare centers. Serological status was determined via enzyme-linked immunosorbent assays (ELISA) detecting IgG antibodies against SARS-CoV-2 spike (S1) and nucleoprotein (N) antigens. Anti-S1 IgG seroprevalence escalated from 7.5% in June 2020 to 48.2% by December 2020. Prevalence reached 71.7% in August 2021, and plateaued at 93.1% in August 2022 and 93.9% by April 2023. Notably, hybrid immunity prevalence surged from 19.9% in 2021 to 56.0% in 2022. Mean antibody titers in 2022 were 2.4-fold higher than in 2021, indicating a potent immune response synergized by vaccination and prior infection. By late 2022, the Albanian urban population reached a high immunity threshold, primarily driven by the expansion of hybrid immunity. While these levels suggest a transition toward endemicity, targeted vaccination remains critical for vulnerable cohorts. This study provides a framework for long-term serological surveillance and informs future immunization strategies in similar epidemiological settings.

***Keywords*:** SARS-CoV-2; seroepidemiology; seroprevalence dynamics; hybrid immunity; Albania; antibody response

1. INTRODUCTION

The COVID-19 pandemic posed a globally significant public health stressor, necessitating a deep understanding of SARS-CoV-2 transmission dynamics and the development of population immunity. (Randolph and Barreiro, 2020). While molecular and antigen testing are valuable for detecting active infections, they often miss asymptomatic or mild cases, thereby underestimating the true extent of viral spread. Seroprevalence studies, which measure antibodies to SARS-CoV-2, provide a more accurate assessment of prior infections, offer insight into the relative contributions of natural and vaccine-induced immunity, and generate critical data to refine vaccination strategies (Lee *et al*. 2020). The balance between these two sources of immunity varies widely across countries, shaped by factors such as vaccine availability, campaign coverage, and the intensity of viral circulation (Vaughan *et al*. 2020).

In Albania, a middle-income country in Eastern Europe, five general population serosurveys were conducted between May 2020 and March 2023 among adults aged 18 years and older. These surveys tracked the evolution of SARS-CoV-2 seropositivity and immune responses, focusing on antibodies to the Spike-1 (S1) and Nucleoprotein (N) antigens in relation to vaccination status and prior SARS-CoV-2 infection. The findings provide a chronological account of Albania's progress toward herd immunity and offer guidance for future public health and vaccination policies, particularly in resource-limited settings.

2. MATERIALS AND METHODS

This cross-sectional observational cohort study was conducted in alignment with STROBE guidelines across five survey rounds between 2020 and 2023. Adults aged 18 years and older were randomly selected from the electronic registries of five Primary Health Centers (PHCs) in Tirana and Berat, which together cover an estimated 281,600 urban residents. Each serosurvey aimed to assess the prevalence of anti-SARS-CoV-2 antibodies over time.

A multi-stage sampling strategy was implemented to ensure representativeness across age groups and geographical areas. PHC staff used electronic family doctor registries to invite participants, collect blood samples, and conduct interviews. The sample sizes for each round were as follows: June 2020 (n=300); December 2020 (n=900); July–August 2021 and 2022 (approximately n=2,000 per round); and January–April 2023 (n=164), the latter of which were also tested for cellular immunity.

Serological testing was performed using enzyme-linked immunosorbent assays (ELISA, Euroimmun, Germany) to detect IgG antibodies against the Spike-1 (S1) and Nucleoprotein (N) antigens. Results were classified by Index Ratio (IR) as follows: IR > 1.1 was considered seropositive, 0.8–1.1 as borderline, and < 0.8 as negative.

3. RESULTS AND DISCUSSIONS

The COVID-19 seroprevalence rate, measured by anti-S1 antibodies against SARS-CoV-2, among adults in Tirana, Albania, reached 7.5% during the first six months of the pandemic. The 48.2% seroprevalence observed in December 2020 coincided with the decline of the wild-type variant and the emergence of the Alpha variant (Figure 1).

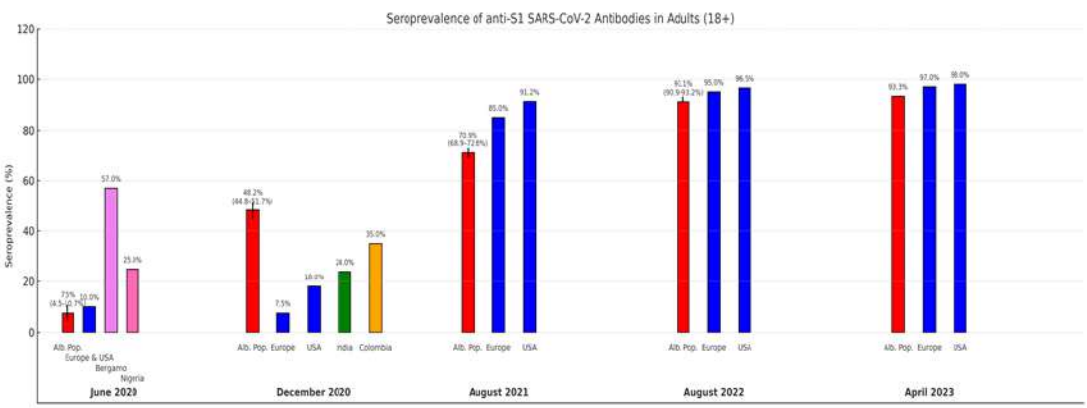

Fig.1. Anti-S1-SARS-CoV-2 IgG seropositivity data dynamic in the Albanian Population compared with other populations during all the five rounds of the study: The seroprevalence (%) of the Albanian population is shown in red, that of Europe and the USA in blue, while other populations (Bergamo, Nigeria, India, and Colombia) during June and December 2020 are presented respectively in purple, rose, green and yellow colors.

By August 2021, on the eve of the Delta wave, while immunization levels in Western Europe and the USA had exceeded 90%, due to intensive vaccination campaigns. In contrast, in Tirana, Albania, the immunization rate stood at 70%, reflecting lower national vaccination coverage. By August 2022, the combined effects of natural infection and vaccine-induced immunity led to seroprevalence exceeding 90% in Tirana, marking the transition from the pandemic phase of transmission to endemic circulation. This endemic phase, driven by widespread natural immunity to Omicron variants and increased vaccine uptake, remained stable through April 2023. (Figure 1).

The 7.5% seroprevalence observed in June 2021 in Tirana was comparable to that reported in other parts of Europe and North America; however, it differed from outbreaks in certain urban hotspots, such as Bergamo, Italy, or urban regions in Nigeria (Signorelli *et al*. 2020; Jones *et al.* 2023). The sharp increase to 48% in December 2020 was consistent with findings from densely populated settings, such as those reported in Bolivia and India, where seroprevalence ranged from 24% to 35%, but contrasted with Western European countries and the United States, where rates among the adults ranged between 7.5% and 18% (Bobrovitz *et al*. 2021; Bergeri *et al*. 2022). These differences reflect the varying degrees of implementation and adherence to physical and social distancing measures across settings. The approximately 80% seropositivity observed among unvaccinated individuals in August 2022 suggests that, in the absence of vaccination, the pandemic would likely have persisted for at least an additional six months, until naturally acquired immunity approached the threshold commonly associated with herd immunity (Sulcebe *et al*. 2023; 2024). The attainment of over 90 % population-level immunity by late 2022 marks a critical transition toward endemic Sars-CoV-2 circulation in Albania.

Vaccination played a crucial role in enhancing immunity. In August 2022, over 95% of vaccinated individuals were seropositive, compared with only 80% among the unvaccinated individuals (Figure 2). In 2021, two vaccine doses were generally required to achieve a robust immune response; however, by 2022, even a single dose following prior infection was sufficient to elicit high antibody titers (Figure 3). Quantitative anti-S1 antibody levels peaked in August 2022 and remained stable into 2023, further supporting the conclusion that herd immunity was achieved in the second half of 2022 (Figures 3 and 4).

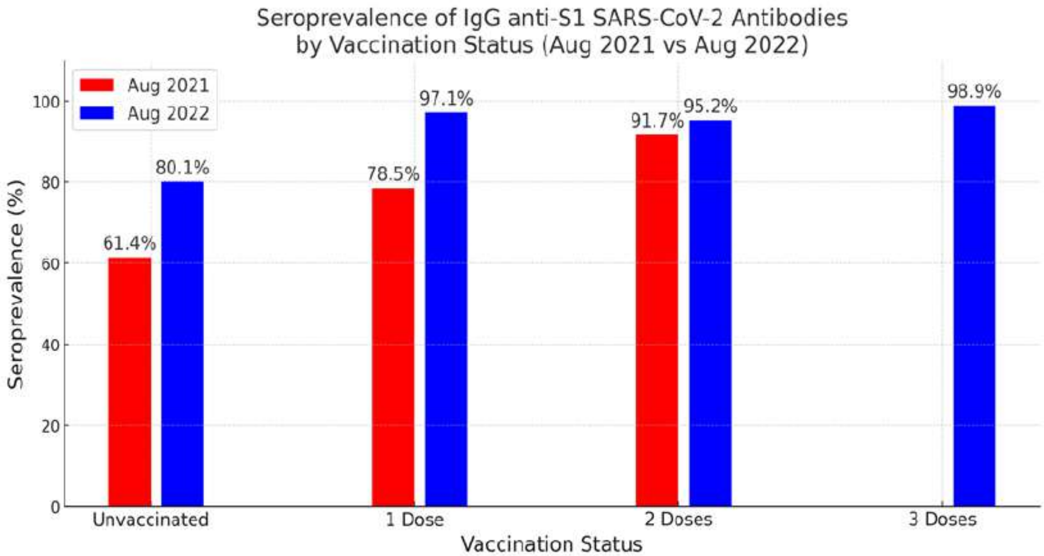

Fig. 2. Role of vaccination in the generation of COVID-19 immunity.

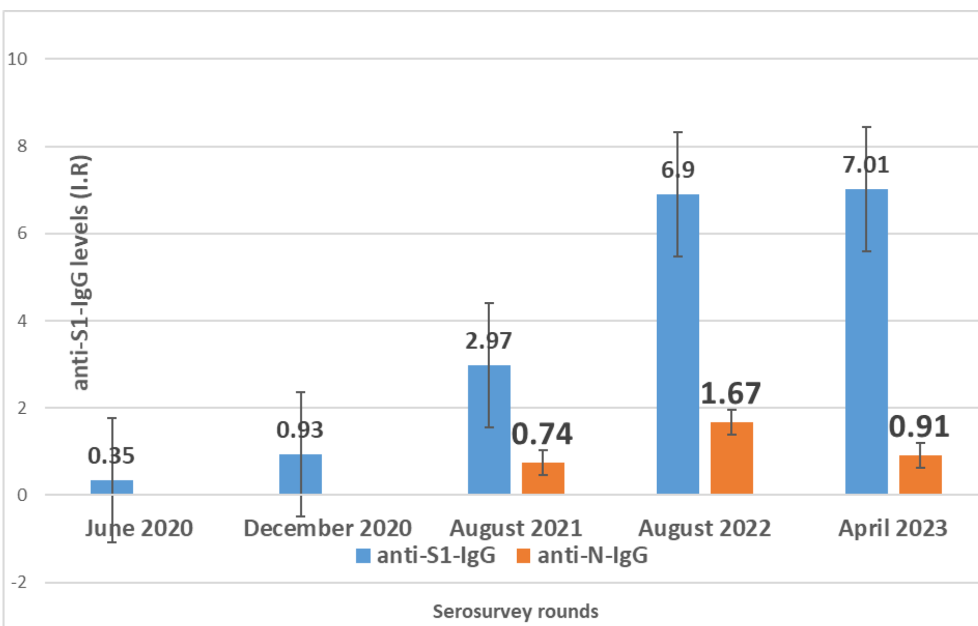

Fig. 3. Anti-S1-SARS-CoV-2 and Anti-N-SARS-CoV-2 IgG antibody levels in the Albanian Population during the five rounds of the study.

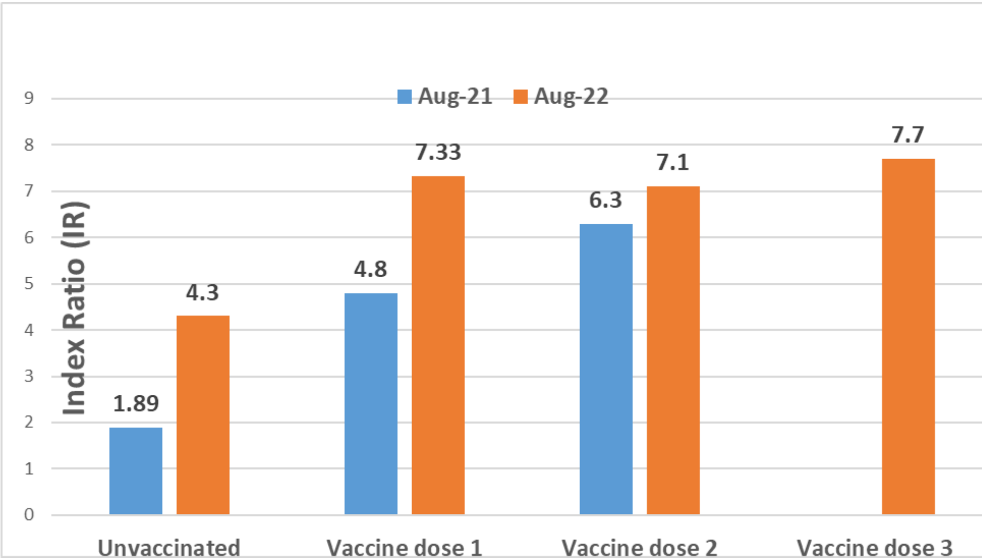

Fig. 4. Levels of Anti-S1 Antibodies (IR Values) Among Individuals with Different Vaccination Statuses in the 2021 and 2022 cohorts.

4. CONCLUSIONS

This study provides a comprehensive longitudinal analysis of SARS-CoV-2 seroepidemiology within the Albanian population from 2020 to 2023. Our findings demonstrate a non-linear increase in seroprevalence, initially catalyzed by natural infection and subsequently augmented by national vaccination campaigns. By late 2022, anti-SARS-CoV-2 antibody detection exceeded 90% in the adult urban cohort, signaling a shift from pandemic volatility toward endemic stabilization.

The data underscore the superior efficacy of hybrid immunity—the synergistic result of prior infection and vaccination. These cohorts exhibited robust antibody titers and enhanced neutralization breadth compared to those with monotypic infection- or vaccine-induced immunity. This supports global evidence that hybrid immunity confers more durable protection against evolving lineages.

Furthermore, the Albanian context illustrates the utility of seroepidemiological surveillance as a high-resolution tool for capturing asymptomatic seroconversion and monitoring long-term immunological waning. While a high population immunity threshold was likely surpassed by H2 2022, strategic immunization remains critical for high-risk demographics, including the elderly and the immunocompromised. Future public health frameworks must utilize adaptive immunization policies to mitigate the risks posed by antigenic drift and emerging viral threats.

Ethics: The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant national regulations. Ethical approval was obtained from the appropriate ethics committee in Albania prior to initiating the study. All participants were informed of the objectives and procedures of the study, and written informed consent was obtained prior to enrolment. Participation was voluntary, and all data were collected and processed anonymously to ensure confidentiality and privacy.

Data accessibility (websites, platforms). Not applicable.

Declaration of AI use. The authors declare that no artificial intelligence tools were used in the preparation of this manuscript.

Authors' contributions. G.S.: conceptualization; G.S. and A.Y.: methodology; G.S., A.Y., M.K.P.: validation; G.S., A.Y., I.S.Q., M.K.P., E.S.: formal analysis; G.S., A.Y., I.S.Q., M.K.P., E.S., M.J.P.: writing—original draft preparation; G.S., A.Y., M.K.P., and M.J.P.; writing—review and editing; G.S. and A.Y.; project administration; G.S.: funding acquisition.

All authors have read and agreed to the published version of the manuscript.

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EUROPEANIZATION OF WESTERN BALKANS AND ITS OCCUPATIONAL HEALTH AND SAFETY POLICIES

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Research

Subject Category: **Applied / Social Sciences:** Health Policy & Occupational Health

ABSTRACT

The Europeanization process is expected to influence Western Balkan health policies; however, empirical data regarding concrete developments in occupational health and safety (OHS) remains limited. This study aims to identify OHS advancements in the Western Balkans (WB) linked to Europeanization and to explore longitudinal progress trends through a cross-country comparative analysis of six nations: Albania, Bosnia and Herzegovina, Croatia, North Macedonia, Serbia, and Montenegro. We conducted a health policy analysis of 109 progress reports submitted to the European Commission over a 17-year period (2005–2022). Analysis focused on Chapter 28 ("Consumer and Health Protection") and relevant subsections containing OHS-related descriptors. Findings indicate that Europeanization significantly influences WB- OHS policies at three levels: i) Contextual: Revision of national legislation to align with the acquis; ii) Distal: Implementation of new OHS Strategic Action Plans; and ii) Proximal: Enhancement of internal coordination and institutional reorganization. While legislation has shifted positively, these countries must further leverage the EU agenda to catalyze systemic health policy improvements.

Keywords: Europeanization, Western Balkans, health policy, comparative study

1. INTRODUCTION

The Western Balkans (WB) constitute a complex and diverse region with a challenging recent history. The violent dissolution of the Socialist Federal Republic of Yugoslavia (SFRY) in the early 1990s was followed by years of turmoil, which detrimentally impacted the transition process across the region (Kubo, 2007). Beyond this conflictual history, the WB countries share a collective aspiration for European Union (EU) accession. The EU is a dynamic entity that evolves through the integration of new member states or regions required to undergo rigorous alignment as potential or candidate-member states (Fontaine, 2014). This paper focuses on six WB nations with varying EU statuses: one-member state (Croatia), four candidate countries (Albania, Serbia, Montenegro, and North Macedonia), and one potential candidate (Bosnia and Herzegovina), as categorized by the *European Neighborhood Policy and Enlargement Negotiations* framework.

Occupational health and safety (OHS) is a critical component of public health systems, particularly within transitional contexts characterized by labor-market reforms and regulatory alignment. In the WB, OHS policies are shaped by both domestic priorities and external pressures, primarily the EU integration process. Despite its significance, OHS remains underexplored within the scholarship on Europeanization and health-policy development in the region.

Europeanization is defined as "an incremental process reorienting the direction and shape of politics to the degree that European Community political and economic dynamics become part of the organizational logic of national politics and policy-making" (Ladrech, 1994). This concept provides the analytical framework for examining how EU-related dynamics influence national policy, including OHS. According to the literature, Europeanization impacts domestic change through: (a) institutional compliance, where EU policy dictates specific requirements; (b) restructuring domestic opportunity structures, which alters the "rules of the game"; and (c) cognitive framing, which shifts the beliefs and preferences of domestic actors (Knill and Lehmkuhl, 2002; Botetzagias, 2005). Within public health, the EU acts as a global actor, a health-system supporter, and a regulator (Battams *et al*. 2014).

The Europeanization process is expected to influence Western Balkan health policies (Džankić *et al*. 2019). However, empirical data regarding concrete OHS policy developments remain scarce, particularly concerning how Europeanization mechanisms translate into governance changes across different levels. This study aims to identify OHS advancements in the WB linked to Europeanization and to analyze progress trends through a cross-country comparative analysis of Albania, Bosnia and Herzegovina, Croatia, North Macedonia, Serbia, and Montenegro.

2. MATERIALS AND METHODS

We conducted a health policy analysis by examining 109 progress reports issued by the European Commission regarding the six Western Balkan countries over a 17-year period (2005–2022). The nations included in the cohort were Albania, Bosnia and Herzegovina, Croatia, the Republic of North Macedonia, Serbia, and Montenegro. This study employs a longitudinal qualitative document analysis approach, integrating elements of both policy and content analysis to systematically investigate advancements in occupational health and safety (OHS) policies over time and across diverse national contexts.

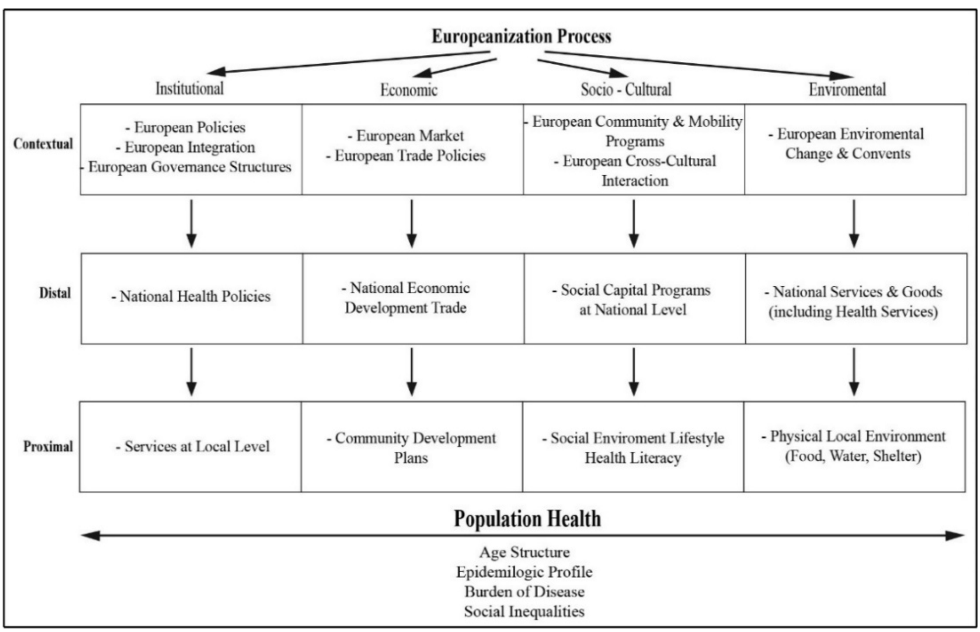

Fig. 1: determinants influencing distal factors through four primary channels: European governance structures; European market and trade policies; community and mobility programs; and European environmental change and conventions.

Inclusion criteria encompassed all European Commission progress reports for the six target nations between 2005 and 2022 that contained explicit references to health policy and OHS. Reports lacking substantive sections or lexical markers related to OHS were excluded. The primary focus was placed on Chapter 28 ("Consumer and Health Protection"), though other chapters containing the descriptors "occupational health," "safety," or "occupational health and safety" were also scrutinized.

These sections were systematically reviewed to identify policy developments, institutional shifts, and strategic actions. For the purposes of this study, the Huynen (2005) framework was adapted to account for the specificities of the European context. This analytical tool guided the tri-level categorization of data:

- Contextual: Legislative and macro-level changes;
- Distal: Strategies and policy frameworks;
- Proximal: Institutional coordination and localized service delivery.

Figure 1 illustrates the interplay of contextual determinants influencing distal factors through four primary channels: European governance structures; European market and trade policies; community and mobility programs; and European environmental change and conventions (Tresa *et al*. 2022).

The data extraction process involved isolating relevant text segments for coding according to the predefined framework, facilitating a structured cross-country longitudinal comparison. This analysis prioritized the identification of thematic patterns and associations between Europeanization processes and OHS advancements, rather than asserting direct causality.

3. RESULTS AND DISCUSSION

The findings suggest that Europeanization is associated with significant advancements in OHS policies across the Western Balkans. These developments, identified through the systematic analysis of 109 European Commission progress reports, are categorized into contextual, distal, and proximal levels (see Table 1). However, the extensity, pace, and consistency of these developments exhibit significant inter-country heterogeneity.

Table 1. Categorization of OHS policy advancements in Western Balkan Countries (2005–2022) across contextual, distal, and proximal levels

At the contextual level	At the distal level	At the proximal level
Revised national legislation based on new acquis	Have undertaken new *Occupational Safety and Health Strategy Action Plan*	Have improved internal coordination among national institutions
Have built cooperation with international institutions		Have reorganized their institutions to better address regulations related to Europeanization of health systems
		Have improved their services at local level or have built new institutions

The findings demonstrate that Europeanization is associated with substantive developments in occupational health and safety (OHS) policies across the Western Balkans. These advancements, identified through the longitudinal analysis of 109 European Commission progress reports, are categorized according to the contextual-distal-proximal analytical framework. However, the extensity, pace, and consistency of these developments exhibit significant inter-country heterogeneity.

At the contextual level, all countries demonstrate evidence of legislative alignment with the *acquis*, although the temporal onset and depth of these reforms vary. Croatia, as an EU member state, exhibited earlier and more comprehensive alignment, whereas candidate and potential candidate nations, such as Bosnia and Herzegovina, show more gradual and fragmented trajectories. Most countries report increased cooperation with international institutions, a trend that is positively correlated with the advancement of the EU integration process.

At the distal level, the development of OHS strategies and action plans is observed in the majority of nations, albeit with variation in scope. Over time, a trend toward the increased formalization of policy frameworks is evident, particularly in later reporting cycles, suggesting a strengthening of strategic planning in OHS.

At the proximal level, findings indicate improvements in institutional arrangements and service delivery, though these remain asymmetrical. Several reports highlight enhanced coordination among national institutions and the reorganization of governance structures to better accommodate regulatory mandates. While some nations established dedicated OHS units, improvements in local-level service delivery were less consistently documented and appear contingent upon national fiscal capacity and institutional resources.

Across all levels, the analysis reveals that policy developments are not uniform but reflect differences in institutional capacity, integration stage, and national priorities. These findings are consistent with the Europeanization framework, which posits that policy change occurs through mechanisms such as institutional compliance, shifts in domestic opportunity structures, and the reorientation of policy priorities (Ladrech, 1994; Knill and Lehmkuhl, 2002).

In alignment with prior research on the Western Balkans (e.g., Tresa *et al*. 2022), the results indicate that EU integration processes catalyze legislative alignment and the formalization of policy frameworks. However, the findings also suggest that Europeanization may be more effective in shaping de jure policy frameworks than in ensuring their de facto consistent implementation—a pattern frequently observed in broader health policy and governance literature.

4. CONCLUSIONS

The Western Balkan nations have demonstrated a positive trajectory in legislative alignment and the enactment of occupational health and safety (OHS) policies at both national and sub-national levels. It is imperative that these countries leverage the European integration agenda to further catalyze systemic health-policy improvements and enhance the well-being and socioeconomic conditions of their populations.

While the formalization of these frameworks marks a significant milestone, further research is required to evaluate the translation of policy into practice. Future studies should focus on assessing the measurable impact of these developments on occupational health outcomes, workforce safety metrics, and broader population health indicators.

Ethics. Formal ethical approval was deemed not applicable for this study as it did not involve clinical interventions. Data collection was based on report analysis and did not involve neither interviews nor personal data collection.

Data sharing statement. Data supporting the findings and conclusions are available upon request from the corresponding author.

Authors' contributions. E.T, G.B, K.C: conceptualization; E.T, K.C: methodology; E.T: investigation, and resources; G.P: results reporting; K.C: supervision. All authors agreed with the results and conclusions.

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AI statement. A Large Language Model (ChatGPT 5.5) was utilized exclusively for linguistic refinement and improving the quality of the English text. The authors maintain full responsibility for the data interpretation, scientific content, and final wording of the manuscript.

Declaration of Interest. The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

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PESTICIDE EXPOSURE AND MALE REPRODUCTIVE HEALTH: A COMMENTARY ON EMERGING TOXICOLOGICAL AND HUMAN STUDIES

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Review

Subject Category: Life Sciences & Applied public health subject area: Ecotoxicology and Reproductive Epidemiology

ABSTRACT

Global indicators of male reproductive health—most notably spermatozoa quality and concentration—have demonstrated a well-documented, multi-decade decline, sparking intensive public health investigation. Among a myriad of anthropogenic environmental risk factors, synthetic pesticide exposure stands out as a primary contributor to adverse spermatogenic outcomes. This commentary synthesizes a seminal presentation delivered at the Third International Conference on Public Health and Environment, evaluating global chemical trends, regional import data, and recent meta-analytic evidence linking organophosphate and N-methyl carbamate exposure to impaired semen parameters. By integrating clinical epidemiology with molecular toxicology, this paper contextualizes the mechanisms of endocrine disruption, oxidative stress, and gonadal toxicity, ultimately advocating for heightened regulatory oversight and advanced mixture-effect profiling.

Keywords: pesticides, sperm concentration, male infertility, endocrine disruption, organophosphates, carbamates, ecotoxicology

1. INTRODUCTION

The intersection of intensive agricultural production and environmental health represents one of the most pressing challenges of modern ecotoxicological science. While chemical pesticides are undeniably integral to maximizing crop yields, managing invasive vectors, and stabilizing public health frameworks, their pervasive distribution inevitably results in unintended biological consequences for non-target organisms, including humans (Shekhar *et al*. 2024).

Concurrently, global epidemiological trends reveal an alarming, secular decline in human sperm counts and overall semen quality (Levine *et al*. 2023). This phenomenon suggests that modern reproductive pathologies are heavily driven by environmental and lifestyle shifts rather than purely genetic etiologies (Han *et al*. 2025). Many contemporary-use pesticides are classified as environmental endocrine disruptors (EEDs). These agents possess the capacity to mimic, antagonize, or otherwise interfere with endogenous hormonal signaling cascades, thereby undermining the highly sensitive, homeostatically regulated process of spermatogenesis (Han *et al*. 2025).

This commentary reviews and expands upon the synthesis presented by Perry at the Third International Conference on Public Health and Environment, exploring the direct correlations between adult pesticide exposure and diminished reproductive parameters.

2. METHODOLOGICAL FRAMEWORK OF THE SOURCE EVIDENCE

The core conclusions evaluated in this commentary rest upon a rigorous systematic literature review and meta-analysis conducted by Ellis *et al*. (2023). The investigators restricted their epidemiological scope to human adult populations with quantified exposure to two widespread chemical classes: **organophosphate** and **N-methyl carbamate** insecticides.

The analytical matrix required stringently defined parameters:

- **Population:** Adult males with verified occupational, residential, or environmental exposure profiles.
- **Comparators:** Unexposed or significantly lower-exposure control cohorts.
- **Outcomes:** Direct quantitative semen analysis metrics, with a primary analytical focus on sperm concentration (millions/mL).

Methodological confounders, study design variations, and risks of bias were systematically vetted using established epidemiological evaluation tools. Stratified subgroup analyses and robust sensitivity testing were further employed to verify that the derived pooled effect sizes were not artifactual or disproportionately skewed by individual study anomalies (Ellis *et al*. 2023). For the full research report containing the comprehensive data sets and statistical adjustments, see Ellis *et al*. (2023) in *Environmental Health Perspectives* via the official PubMed record .

3. RESULTS AND MACRO-ECONOMIC DATA

Data spanning from 1999 through 2020 demonstrate that global pesticide consumption remains profoundly elevated. Despite regulatory restrictions phased in for persistent organic pollutants (POPs) under international treaties, total chemical volumes have not dropped; instead, the market has shifted toward less persistent, rapidly degrading chemical variants (Shekhar *et al*. 2024). While these contemporary compounds exhibit shorter environmental half-lives, their acute biological activity remains exceptionally high.

On a regional scale, the import dynamics of developing and transitioning economies illustrate this ongoing reliance. For instance, trade data highlighted during the conference regarding Albania revealed that between the years 2020 and 2023, the nation imported approximately 7,000 tons of pesticides, representing an economic valuation of 4.8 billion ALL. This significant chemical influx underscores the high probability of localized occupational and environmental exposure.

Summary of Meta-Analytic Outcomes

The pooled statistical metrics from the meta-analysis revealed a highly significant, negative association between elevated adult biomarker levels (or proxy exposure metrics) for organophosphates or carbamates and baseline sperm concentrations (Ellis *et al.* 2023). This downward trend held true across various geographical cohorts. Even when accounting for differences in how exposure was measured or population baselines, the core finding remained stable: higher pesticide exposure correlates with lower sperm counts.

4. DISCUSSION AND PATHOPHYSIOLOGICAL MECHANISMS

The cross-disciplinary consistency between human observational epidemiology and experimental animal models lends a high degree of biological plausibility to these findings. The pathophysiological deterioration of semen quality induced by organophosphates and carbamates can be mapped across three primary molecular pathways:

I. Endocrine Disruption Along the HPT Axis

Spermatogenesis is entirely dependent on the precise, pulsatile secretion of Gonadotropin-Releasing Hormone (GnRH), Luteinizing Hormone (LH), and Follicle-Stimulating Hormone (FSH) along the Hypothalamic-Pituitary-Testicular (HPT) axis.

- Organophosphates directly disrupt this homeostatic balance by altering acetylcholinesterase activity in the central nervous system, which indirectly suppresses gonadotropin discharge.
- At the gonadal level, these compounds inhibit Leydig cell steroidogenesis, leading to a profound drop in intratesticular testosterone—the primary driver of germ cell differentiation (Han *et al*. 2025).

II. Induction of Oxidative Stress

The membranes of human spermatozoa are uniquely rich in polyunsaturated fatty acids, making them highly susceptible to reactive oxygen species (ROS) (Qi *et al.* 2026). Both organophosphates and carbamates exhaust intracellular antioxidant reserves (such as glutathione peroxidase and superoxide dismutase). This resulting state of unchecked oxidative stress triggers lipid peroxidation, which damages sperm membrane integrity, compromises motility, and induces structural abnormalities in the head and flagellum (Qi *et al*. 2026; Tarlan *et al.* 2026).

III. Direct Testicular and Germ Cell Toxicity

Beyond hormonal interference, these chemical agents cross the blood-testis barrier, exerting direct cytotoxic and apoptotic effects on developing spermatids and supportive Sertoli cells (Han *et al.*2025). This direct damage leads to premature germ cell sloughing and a marked decrease in the overall daily output of the seminiferous tubules.

Policy and Public Health Paradigms

The persistence of these reproductive risks highlights clear gaps in current chemical regulatory frameworks. Because modern pesticides break down quickly in the environment, they are often deemed "safer." However, this quick breakdown leads to a cycle of repeated, continuous exposures for agricultural workers and surrounding communities (Shekhar *et al.* 2024).

To safeguard population-level fertility, public health policies must transition from passive monitoring to active harm reduction (Han *et al.* 2025). This includes implementing stiffer occupational exposure ceilings, establishing routine urinary biomonitoring programs for farmworkers, and offering economic incentives for Integrated Pest Management (IPM) practices that reduce chemical reliance.

5. CONCLUSION AND STRATEGIC FUTURE DIRECTIONS

Epidemiological and experimental evidence gathered over the past quarter-century establishes a clear link between pesticide exposure and diminished male reproductive capacity. The latest meta-analytic data confirms that adult exposure to organophosphates and N-methyl carbamates consistently reduces sperm concentration (Ellis *et al.* 2023).

To advance our understanding, future ecotoxicological research should prioritize:

1. **Mixture Toxicology:** Evaluating the cumulative, synergistic impact of "chemical cocktails," as human populations are rarely exposed to an isolated compound.
2. **Epigenetic Inheritance:** Investigating whether pesticide-induced changes to the sperm epigenome can pass reproductive liabilities down to unexposed future generations (Han *et al.* 2025).
3. **Dose-Response Thresholds:** Refining low-dose exposure curves to better protect vulnerable populations, including developing fetuses and adolescents.

Given the steady decline in global sperm counts, waiting for absolute causal certainty is a risky strategy. Implementing precautionary, health-protective regulations and shifting toward sustainable agriculture are essential steps to preserve reproductive health.

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