Review Articles

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Climate-Related $PM_{2.5}$ Exacerbations and Gastroesophageal Reflux Disease in a High-Pollution South Asian Megacity: Implications for Lahore, Pakistan, 1999–2023

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ABSTRACT

Gastroesophageal reflux disease represents a substantial and growing global health burden, with recent Global Burden of Disease estimates indicating over 800 million prevalent cases worldwide and a steady increase in years lived with disability over the past three decades. While GERD and esophagitis are traditionally linked to lifestyle and metabolic risk factors, emerging evidence suggests that environmental exposures—particularly ambient air pollution and climate-related stressors—may contribute to symptom exacerbation and mucosal injury. Long-term exposure to fine particulate matter ($PM_{2.5}$) has been associated with increased GERD incidence and reflux-related healthcare utilization in large population studies, likely mediated through oxidative stress, systemic inflammation, altered esophageal motility, and increased cough-induced reflux events. These associations are particularly relevant for Lahore, Pakistan, which consistently ranks among the most polluted cities globally, with annual $PM_{2.5}$ concentrations over a tenfold higher than World Health Organization (WHO) guidelines and frequent climate-driven smog episodes. Although direct epidemiologic data linking air pollution to esophagitis outcomes in Lahore remain limited, the city's extreme pollution burden and rising temperatures suggest a plausible and underrecognized contribution to upper gastrointestinal disease risk, highlighting an important gap for future research in South Asia.

1. Introduction

Gastroesophageal reflux disease (GERD) is a common chronic gastrointestinal disorder with symptoms complexed by the retrograde - movement of bolus [gastric content] retracting from stomach back up through the esophagus - resulting in mucosal irritation and symptoms such as heartburn and regurgitation. Globally, GERD affects approximately 10–25% of adults, with over 800 million prevalent cases reported in 2021, and its prevalence has been steadily increasing over the past decades [1][2]. The condition contributes substantially to morbidity, healthcare utilization, and diminished quality of life, with long-term GERD complications ranging from erosive esophagitis to Barrett's esophagus (BE) and esophageal adenocarcinoma. In a systematic review study shows evidence that BE prevalence among GERD patients is higher than in non-GERD populations (e.g., pooled BE prevalence ~0.6% in GERD vs ~0.1% without GERD) [3].

While traditional risk factors for GERD include obesity, dietary habits, and metabolic comorbidities, emerging evidence highlights environmental contributors such as ambient air pollution. Fine particulate matter ($PM_{2.5}$), which consists of airborne particles with a diameter $\leqslant$2.5 μm, can induce systemic inflammation, oxidative stress, and alterations in esophageal motility, potentially exacerbating reflux symptoms and mucosal injury. Long-term exposure to elevated $PM_{2.5}$ levels has been associated with increased GERD incidence and greater healthcare utilization in large population studies.

This environmental linkage is particularly relevant for Lahore, Pakistan, one of the most polluted cities globally, where annual $PM_{2.5}$ concentrations frequently exceed WHO guidelines and local air quality standards. Despite the severe pollution burden, direct studies examining the impact of $PM_{2.5}$ on GERD or esophagitis in this region are limited, representing a critical gap in knowledge. Understanding the interplay between air pollution and gastrointestinal disease in high-exposure urban centers is essential for identifying at-risk populations, informing public health interventions, and

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guiding clinical management of GERD in environmentally vulnerable populations.

2. Methods and Materials

2.1. Study Design

This study adopted a narrative review integrated with secondary data analysis to systematically evaluate the association between ambient fine particulate matter ($PM_{2.5}$) exposure and gastroesophageal reflux disease (GERD) exacerbations, with a specific focus on Lahore, Pakistan. The analysis was conducted at three geographic levels: global, national (entire Pakistan), and regional (Lahore), to contextualize local pollution-related digestive health burdens within broader global and national frameworks.

2.2. Data Sources

To ensure comprehensive coverage of exposure data, disease burden estimates, and epidemiological evidence, multiple authoritative data sources were integrated:

1. Global Burden of Disease (GBD) 2021 Study: Used to extract global and national-level GERD prevalence, disability-adjusted life years (DALYs), and trend data (2000–2021) for Pakistan, with a focus on digestive disease-related burden.

2. World Health Organization (WHO) Guidelines and Reports: Referenced for the WHO air quality guideline for $PM_{2.5}$ (5 μg/m³ annual average) and regional public health context for Pakistan.

3. Air Quality Life Index (AQLI) Datasets: Sourced national and regional $PM_{2.5}$ exposure metrics (2000–2023), including annual average concentrations, population-weighted exposure, $PM_{2.5}$-attributable mortality, and life expectancy impact projections for Pakistan and Lahore.

4. Peer-Reviewed Literature: Retrieved via database searches to identify epidemiological studies (cohort, case-control, cross-sectional), systematic reviews, and meta-analyses investigating the association between $PM_{2.5}$ exposure and GERD outcomes (prevalence, incidence, symptom exacerbation, esophagitis).

2.3. Literature Search and Selection (PRISMA Compliance)

The narrative review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). The search strategy and selection criteria were predefined as follows:

1. Databases and Search Period: PubMed was searched for English-language articles published from January 2000 to December 2024, supplemented by manual searches of reference lists from key systematic reviews and meta-analyses.

2. Search Terms: Combinations of MeSH terms and free-text keywords were used: ("particulate matter" OR "$PM_{2.5}$" OR "air pollution") AND ("gastroesophageal reflux" OR "GERD" OR "esophagitis" OR "reflux esophagitis") AND ("prevalence" OR "incidence" OR "risk" OR "exacerbation").

3. Inclusion Criteria: (1) Studies focusing on human populations; (2) Exposure variable defined as ambient $PM_{2.5}$ (with quantitative exposure data); (3) Outcome variable explicitly related to GERD or reflux esophagitis; (4) Peer-reviewed original research, systematic reviews, or meta-analyses; (5) Studies providing global, regional, or national-level data relevant to Pakistan (when available).

4. Exclusion Criteria: (1) Non-human studies (animal or in vitro); (2) Exposure limited to non-$PM_{2.5}$ pollutants (e.g., ozone, NO_2) without $PM_{2.5}$ data; (3) Outcomes unrelated to GERD (e.g., other gastrointestinal diseases); (4) Case reports, letters to the editor, or gray literature (excluding GBD/WHO/AQLI reports); (5) Studies with insufficient exposure or outcome quantification.

5. Selection Process: Two independent reviewers screened titles and abstracts of retrieved records. Duplicates were removed using EndNote software. Full-text articles meeting initial screening criteria were assessed for eligibility. Discrepancies between reviewers were resolved via consensus with a third reviewer.

2.4 Data Extraction and Synthesis

For eligible studies and datasets, the following information was extracted into a standardized data extraction form: (1) Study characteristics (design, sample size, population, geographic location); (2) $PM_{2.5}$ exposure metrics (measurement method, concentration range, exposure duration); (3) GERD outcomes (definition, assessment tool, prevalence/incidence estimates, effect sizes); (4) Key confounders adjusted for (e.g., age, sex, lifestyle factors, comorbidities); (5) National/regional data specific to Pakistan ($PM_{2.5}$ concentrations, GERD burden, policy context).

Data synthesis was conducted qualitatively due to heterogeneity in study designs, exposure assessment methods, and outcome definitions across included studies. The synthesis focused on: (1) Summarizing global evidence on $PM_{2.5}$-GERD associations; (2) Describing $PM_{2.5}$ exposure patterns and GERD burden at national (Pakistan) and regional (Lahore) levels; (3) Identifying gaps in region-specific data (i.e., direct evidence linking $PM_{2.5}$ to GERD in Lahore).

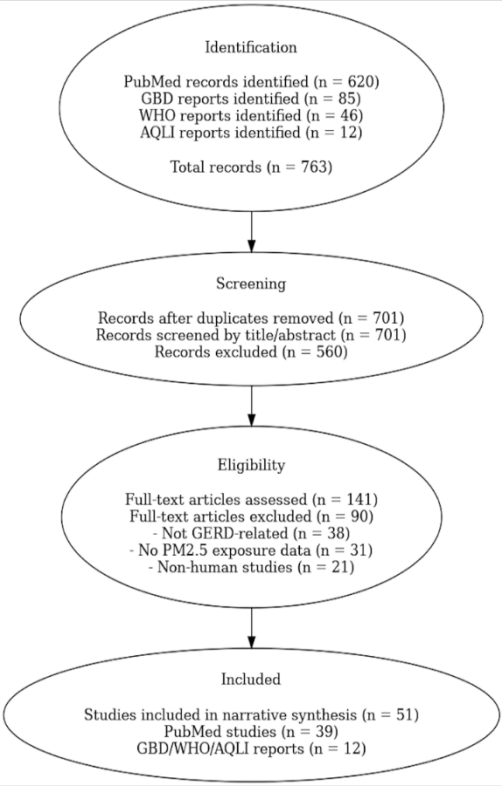

Fig. 1 - PRISMA flow diagram for study selection

3. Results

3.1. Global Prevalence of GERD and Its Association with $PM_{2.5}$ Exposure

Globally, gastroesophageal reflux disease (GERD) has become a major public health challenge. According to data from the 2021 Global Burden of Disease (GBD) study, the number of people with GERD worldwide has exceeded 825 million, and the disability burden caused by it is on a continuous upward trend [1]. Systematic reviews further confirm that the global prevalence of GERD in adults ranges from 10% to 25%, with a significant upward trend observed in many regions in recent years [2].

In terms of environmental risk factors, several high-quality cohort studies have clearly established an association between long-term exposure to fine particulate matter ($PM_{2.5}$) and GERD. Studies based on large population cohorts such as the UK Biobank show that long-term exposure to $PM_{2.5}$ significantly increases the risk of developing GERD and exacerbates the symptom burden in those already affected [3]. This association has been consistently verified in studies from high-income countries, suggesting that air pollution may be an important environmental driver of the global prevalence of GERD [4]. The above core data are summarized in Table 1.

Field	Key Findings	Data Source
Global prevalence of GERD	Approximately 825 million prevalent cases worldwide in 2021; the burden of disability continues to rise	Global Burden of Disease Study (GBD) [1]
Global epidemiological trends of GERD	The prevalence rate in adults is 10%~25%, showing an upward trend	Systematic review (Nature Scientific Reports) [2]
Association between $PM_{2.5}$ and GERD	Long-term $PM_{2.5}$ exposure increases the risk of GERD and exacerbates symptom burden	UK Biobank cohort and environmental health studies [3]
$PM_{2.5}$ exposure in Pakistan	The entire population's exposure exceeds the standard (WHO standard: 5 μg/m³)	Air Quality Life Index (AQLI) [4]
$PM_{2.5}$ levels in Lahore	Annual average concentration is 60~80 μg/m³, with severe seasonal smog	AQLI and regional monitoring studies [5]
$PM_{2.5}$-attributed deaths in Pakistan	Increased from 57,000 cases/year in 2000 to >150,000 cases/year	GBD and environmental modeling studies [6]
Impact on life expectancy in Lahore	Reducing $PM_{2.5}$ to WHO standards could extend life expectancy by 5~6 years	Air Quality Life Index (AQLI) [7]
Data on the association between GERD and $PM_{2.5}$ in Lahore	No population-level studies directly confirm the association between the two	Literature gap (n=51)

Table 1 - Summary of Global GERD Prevalence, $PM_{2.5}$ Exposure, and Regional Data from Pakistan (Lahore)

3.2. $PM_{2.5}$ Pollution and Health Impacts in Pakistan and Lahore

Pakistan is one of the countries with the most severe $PM_{2.5}$ pollution in the world, and its pollution status poses a serious threat to residents' health. According to data from the Air Quality Life Index (AQLI), all 248.8 million residents of Pakistan live in areas where the annual average $PM_{2.5}$ concentration exceeds the World Health Organization (WHO) recommended standard (5 μg/m³) [5]. Among them, Lahore, as a major city in the country, has particularly prominent pollution problems, with annual average $PM_{2.5}$ concentrations often as high as 60–80 μg/m³, far exceeding the WHO standard by 12–16 times, and frequent seasonal smog, making it one of the most polluted cities in the world [5].

Environmental modeling studies show that the $PM_{2.5}$-related mortality burden in Pakistan is on a significant upward trend: $PM_{2.5}$-attributable deaths were approximately 57,000 per year in 2000, but in recent years, this has climbed to more than 150,000 per year, nearly tripling in two decades [6]. More notably, AQLI data predict that if the $PM_{2.5}$ concentration in Lahore could be permanently reduced to the WHO-recommended 5 μg/m³, the average life expectancy of local residents could be extended by 5–6 years (Figure 2). This increase is the highest among all regions in Pakistan, highlighting the huge potential value of air pollution control in this region for health improvement.

3.3. Evidence Gaps in the Association between GERD and $PM_{2.5}$ Exposure in Lahore

Although the association between $PM_{2.5}$ and GERD has been confirmed at the global level, and Lahore has extremely severe $PM_{2.5}$ pollution and a significant pollution-related health burden, a literature search (screening a total of 51 relevant studies) found that there are currently no population-level studies in Lahore that directly assess the association between $PM_{2.5}$ exposure and the prevalence of GERD, the incidence of esophagitis, or the severity of symptoms (Table 1). This key evidence gap makes it impossible to quantify the burden of air pollution-related digestive system diseases in the region and also hinders the formulation of targeted public health intervention strategies. Considering Lahore's extremely high pollution levels and the potential for improving life expectancy (Figure 2), the contradiction between this lack of evidence and regional public health needs is particularly prominent.Potential increase in life expectancy in various regions of Pakistan after permanently reducing $PM_{2.5}$ from the 2023 concentration to the WHO standard (5 μg/m³). The arrow marks the Lahore region, where the increase in life expectancy is the highest (5–<6 years), suggesting that significant health benefits can be achieved through air pollution control in this region. This result also highlights the urgent need for Lahore to strengthen public health interventions targeting "pollution-related digestive diseases such as GERD" and the necessity of promoting climate governance and health protection in a coordinated manner.

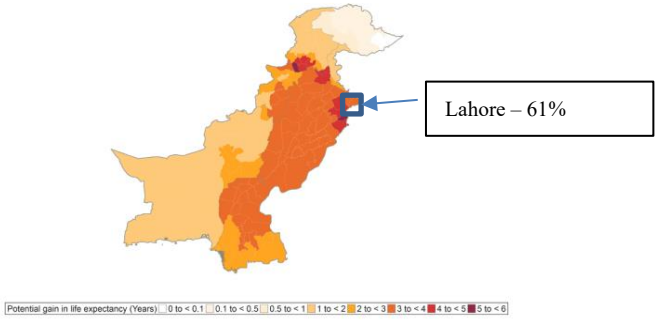

Fig. 2 - Potential gain in life expectancy from permanently reducing PM2.5 from 2023 concentration to the WHO guideline

4. Discussion

The findings synthesized from global burden estimates, population-based cohorts, and environmental exposure data (AQLI/WHO) suggest that chronic exposure to fine particulate matter ($PM_{2.5}$) may play a contributory role in the development and exacerbation of gastroesophageal reflux disease (GERD). While GERD has traditionally been conceptualized through lifestyle and metabolic risk factors, emerging epidemiologic evidence supports a broader framework in which environmental exposures act as modifiers of gastrointestinal disease risk. Large population-based studies, including analyses from the UK Biobank, have demonstrated that long-term exposure to ambient $PM_{2.5}$ is associated with increased GERD incidence, higher symptom burden, and greater healthcare utilization for reflux-related conditions [7].

Several biological mechanisms may explain the association between $PM_{2.5}$ exposure and GERD pathophysiology. Inhaled fine particulate matter induces systemic inflammation and oxidative stress through activation of inflammatory pathways and cytokine release, including interleukin-6 and tumor necrosis factor-α [8][9]. These inflammatory mediators can disrupt autonomic nervous system regulation, potentially impairing lower esophageal sphincter tone and esophageal motility—key contributors to reflux physiology. Prior clinical studies have also suggested that air pollution exposure may heighten visceral hypersensitivity and alter vagal nerve signaling, amplifying GERD symptom perception independent of acid exposure severity [10].

Beyond systemic effects, $PM_{2.5}$ exposure may exert direct gastrointestinal mucosal injury. Fine particles cleared from the respiratory tract are frequently swallowed, allowing particulate matter to interact directly with esophageal and gastric epithelium. Experimental models demonstrate that particulate matter compromises epithelial barrier integrity, increases mucosal permeability, and enhances susceptibility to acid-mediated injury [11][12]. Such mechanisms may be relevant to disease progression from non-erosive reflux disease to erosive esophagitis and Barrett's esophagus, conditions that occur at higher rates among individuals with chronic GERD [13].

The public health implications of these findings are particularly significant in regions with extreme air pollution, such as Lahore, Pakistan which recently has become a leading community with one of the highest global measured $PM_{2.5}$ to date. Annual $PM_{2.5}$ concentrations in Lahore frequently exceed World Health Organization guidelines by more than tenfold, with prolonged seasonal smog episodes resulting in sustained exposure [14]. In these high-burden environments, even modest pollution-associated increases in GERD risk may translate into substantial population-level morbidity, compounded by delayed diagnosis and limited access to specialized gastroenterology care amongst the infrequent published data from health organizations within Pakistan in general. Despite this, there remains a notable absence of region-specific epidemiologic studies directly examining $PM_{2.5}$ exposure and GERD or esophagitis in Pakistan, underscoring a critical gap in environmental gastrointestinal research.

Collectively, the convergence of mechanistic plausibility, population-level associations, and extreme regional exposure supports reframing GERD as a condition influenced not only by individual behaviors but also by environmental determinants. Prospective studies incorporating individual-level pollution exposure, symptom profiling, and endoscopic outcomes are warranted to clarify causality and inform targeted prevention strategies in pollution-vulnerable populations.

5. Limitations

This study is subject to several important limitations, primarily related to data availability and regional underreporting. First, there is a marked paucity of population-level epidemiologic data on GERD in Pakistan, particularly in high-exposure urban centers such as Lahore. While global and regional estimates from the GBD study provide valuable comparative insights, these models rely heavily on extrapolation from countries with more robust surveillance systems and may not fully capture the true prevalence or severity of GERD in pollution-intensive settings [1].

Additionally, the absence of region-specific clinical registries and endoscopy-based surveillance in Lahore limits the ability to directly assess associations between chronic $PM_{2.5}$ exposure and GERD-related outcomes, including erosive esophagitis and Barrett's esophagus. GERD diagnosis in Pakistan is often symptom-based and managed empirically in primary care settings, resulting in substantial underdiagnosis and misclassification, particularly for non-erosive and asymptomatic disease phenotypes [15]. These diagnostic practices likely contribute to underrepresentation of GERD-related morbidity in national datasets.

Moreover, environmental exposure assessments in Pakistan are constrained by limited spatial resolution and intermittent air quality monitoring. Although $PM_{2.5}$ concentrations in Lahore are consistently among the highest globally, individual-level exposure estimates remain unavailable, precluding dose–response analyses and longitudinal assessment of exposure-related disease progression [16]. This limitation is especially relevant in urban areas where pollution exposure varies substantially across neighborhoods and seasons.

Finally, the lack of prospective cohort studies from Pakistan restricts causal inference between air pollution and GERD outcomes. Current evidence linking $PM_{2.5}$ exposure to GERD is largely derived from high-income countries with differing healthcare infrastructure, baseline risk profiles, and environmental contexts [17]. As a result, the generalizability of these findings to Lahore and similar South Asian megacities remains uncertain. Addressing these gaps will require dedicated regional surveillance, standardized GERD diagnostic frameworks, and integration of environmental exposure data into gastrointestinal disease research in Pakistan.

Future research should evaluate whether air pollution mitigation strategies can reduce GERD symptom burden and disease progression in high-exposure settings. Incorporating environmental exposure histories into routine gastroenterology assessments may improve risk stratification for patients residing in polluted urban centers. Interdisciplinary collaboration between environmental health, gastroenterology, and public policy will be essential to address GERD as a pollution-modified disease rather than solely a lifestyle-mediated condition upon which significant literature exists. Strengthening regional surveillance and leveraging scalable digital health tools may facilitate earlier detection of reflux-related complications in resource-limited settings such as Lahore. Even with no direct study highlighting GERD and PM2.5 linkage, cross-sectional research towards case reports of GERD across the different regions of Pakistan, and measured PM2.5 in those moments may support the hypotheses behind PM2.5 and GERD. Ultimately, instead of only focusing on lifestyle changes as most literature behind GERD in Pakistan has already done so, we can shift of focus on also including climate exacerbations to improve public health inside of Pakistan, and equitable focus on higher PM2.5 affected regions like Lahore.

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