

The Possible Effects of Common Air Pollutants on the Pathophysiology of Functional Gastrointestinal Disorders: A Narrative Review

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Abstract

There are more than seven million premature deaths every year linked to air pollution effects. The critical hazards of exposure to air pollution are the increased risk of respiratory and cardiovascular diseases, which can boost morbidity and mortality. Besides, ingested pollutants can cause gastrointestinal (GI) diseases. Functional GI disorders (FGIDs) are called gut-brain interaction disorders that influence approximately one out of every four people and have negative effects on life quality, work productivity, and medical costs. Intestinal inflammation, gut microbiota, and GI motility are the three important factors in the pathogenesis pathways of these disorders. This literature aimed to clarify the link between air pollution exposure and the pathophysiology of FGIDs. This study was conducted based on published studies in English using scientific databases, such as PubMed, Embase, Web of Science, and Google Scholar, from 1990 to 2023. We used various combinations of relevant keywords, such as air pollution, air pollutant, FGID, gut microbiota, and gut inflammation. The findings indicated that air pollution can contribute to the etiology of FGIDs through dysbiosis and intestinal inflammation. In addition, air pollution may alter the composition and diversity of gut microbiota, which in turn can play major roles in the development of these disorders. In addition to the steps taken by the government to tackle air pollution, there are some recommendations to prevent the negative effects of air pollution exposure, such as the consumption of probiotics in a diet.

Keywords: Air pollution, functional gastrointestinal disorder, gut microbiota, intestinal inflammation

INTRODUCTION

A complex heterogeneous mixture of solids, liquids, and gases is defined as air pollution,^[1] which is an important environmental issue around the world related to anthropogenic activities, such as traffic in urban areas.^[2] Air pollution is an environmental stress, which can be divided into primary (directly released) and secondary (produced in the atmosphere).^[1] There are different types of air pollutants including particulate matter (PM), volatile organic compounds, and gaseous components, such as nitrogen dioxide (NO₂), sulfur dioxide (SO₂), carbon monoxide (CO), and ozone.^[3] PM is defined as liquid droplets and solid particles with sources of organic and inorganic, including metals, nitrates, sulfates, ions, and polycyclic aromatic hydrocarbons (PAHs).^[4,5] After the inspiration, the respiratory particles localize in the

respiratory tract based on their size. In this manner, larger and smaller particles are placed in the upper respiratory tract and alveolar spaces, respectively.^[6] It is widely accepted that air pollution can increase the risk of respiratory and cardiovascular diseases, which can boost morbidity and mortality.^[7] Studies have shown that air pollution can cause inflammation as an

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oxidative stress factor and affect airway epithelium. The relation between air pollution and nonpulmonary diseases, such as colon cancer and rheumatoid arthritis indicates that not only air pollution can develop pulmonary diseases, but also contribute to nonrespiratory diseases due to systemic inflammation.^[8] Besides, short-term exposure to various air pollutants can be related to gastrointestinal (GI) diseases. In this regard, the relationships between PM_{2.5} and gastric ulcers, ozone and appendicitis, CO, and gastroenteric disorders have been suggested.^[9]

Functional GI disorders (FGIDs) are a group of disorders that include variable combinations of chronic, recurrent GI manifestations in the absence of identifiable organic causes or biochemical abnormalities.^[10] It is estimated that these disorders have a global prevalence of 10%–45%.^[11] Common subtypes of FGIDs include irritable bowel syndrome (IBS), functional dyspepsia (FD), gastroesophageal reflux disease, functional dysphagia, gastroparesis, functional constipation, diarrhea, and fecal incontinence.^[12] However, IBS and FD are the most frequent subtypes of FGIDs.^[13] It is thought that FGIDs are a group of complex and multifactorial disorders without distinct pathophysiology.^[14] On the other hand, genetic, gut-brain dysfunction, low-grade mucosal inflammation, intestinal microbiota, GI motility alterations, and environmental factors, such as diet and stress may be the key factors in the development of these disorders.^[15] Figure 1 illustrates some etiologies of FGID. Moreover, bacterial, protozoal, or viral gastroenteritis and the pathogens, such as *Campylobacter jejuni*, *Shigella sonnei*, *Salmonella enterica*, and *Escherichia coli* may play roles in the postinfectious FGIDs.^[16,17] The diagnosis of these disorders is based on patient-reported symptoms. Different criteria illustrate the recognized subtypes of FGIDs with obvious symptom profiles. However, there is considerable overlap between the symptom profiles in clinical practice.^[18] In addition to GI symptoms, patients with these disorders exhibit nonspecific symptoms,

such as poorer sleep and sexual dysfunction. Consequently, these disorders can increase medical costs,^[14] and reduce the quality of life, particularly psychological health and physical activities.^[19] Of note, the total direct cost for every patient with IBS is approximately USD 348–8750 per year. Furthermore, IBS is a common cause of patients’ absence from work. In this regard, the average number of sick leave per year by the cause of IBS was about 8.5–21.6.^[16]

According to the World Health Organization, approximately 90% of people around the world are exposed to air pollution due to urbanization.^[3] Notably, the daily intake of PM in a typical Western diet is predicted to be between 10¹² and 10¹⁴ particles per person.^[16] Moreover, gaseous pollutants can affect the GI tract via promotion of systemic inflammation. Hence, the GI tract is likely an essential organ system in which air pollution can cause dysbiosis and intestinal diseases along with alterations in the gut flora diversity.^[6] Several studies have been conducted on the impact of air pollution on human health, particularly its impact on respiratory and cardiovascular diseases. However, the role of air pollution in the pathogenesis of GI diseases, such as FGIDs, is still largely unknown and needs more studies. The studies included in this narrative review reveal that air pollution can also be associated with FGIDs. In the current study, we reviewed the possible impact of air pollution on two common types of FGIDs (IBS and FD) from the perspective of intestinal inflammation, gut microbiota, and GI motility.

METHODS

Eligibility criteria

We concentrated on the research studies on the link between common air pollutants and the pathophysiology of FGIDs. Studies were excluded if they were not related, or were carried out on other GI diseases, in the process of reading the titles and abstracts (MH, BD).

Inclusion and exclusion criteria

Studies were included that were available in English, published between 1990 and 2023, full-text available, and having a distinct correlation with the subject of the study. All qualitative, quantitative, or combined research methodologies were selected. Studies were excluded if they did not meet the mentioned criteria.

Search strategy

This literature seeks to illuminate the link between air pollution and FGIDs based on information collected using scientific databases, such as PubMed, Embase, Web of Science, and Google Scholar, from 1990 to 2023. In this narrative review literature, the following set of keywords have been used: air pollution, air quality, air pollutant, air contaminant, air pollutant substance, FGIDs, functional bowel disorder, intestine flora, gut bacteria, gut microbe, human gut microbe, intestinal bacteria, GI flora, bowel microbiota, gut inflammation, intestinal inflammation, and metabolome. All

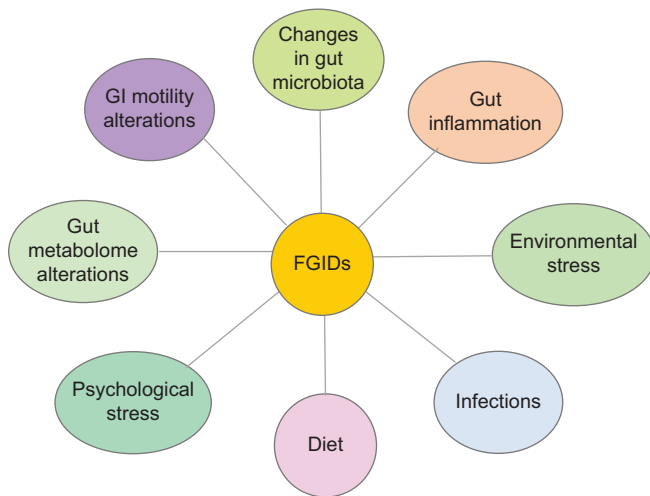


Figure 1: Etiology of functional gastrointestinal disorders. FGIDs: Functional gastrointestinal disorders, GI: Gastrointestinal

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English articles (500) were investigated. Eventually, an amount of 44 documents were cited. The complete search strategies are presented in Table 1. The search process covered the terminal date until March 2023. Literature searches were performed by two authors (MH, BD).

Table 1: Scientific database search strategies

PubMed

((((((((((Air Pollution[MeSH Terms]) OR (Air Pollution*[Title/Abstract]) OR (Air Quality[Title/Abstract]) OR (Air contaminant*[Title/Abstract]) OR (air pollutant substanc*[Title/Abstract]) OR (air pollutant*[Title/Abstract]) OR (air particul* matter*[Title/Abstract]) OR (air chemical*[Title/Abstract]) OR (air contamina*[Title/Abstract]) OR (air pollut*[Title/Abstract]) OR (pollut* atmosphere[Title/Abstract]) OR (airborne particulate matter[Title/Abstract]) OR (particulate air pollutant[Title/Abstract]) AND (((((((((((Irritable Bowel Syndrome[MeSH Terms]) OR (Irritable Bowel Syndrome*[Title/Abstract]) OR (Irritable Colon[Title/Abstract]) OR (functional bowel disorder[Title/Abstract]) OR (intestine flora[Title/Abstract]) OR (gut bacteria[Title/Abstract]) OR (gut microb*[Title/Abstract]) OR (human gut microb*[Title/Abstract]) OR (intestinal bacteria[Title/Abstract]) OR (gut inflammation[Title/Abstract]) OR (metabolome[Title/Abstract]) OR (intestinal microbe*[Title/Abstract]) OR (bowel microbiota[Title/Abstract]) OR (gastro intestinal flora[Title/Abstract]))))))))))))))))))

Embase

("air pollution" OR "air pollution":ti, ab OR "air quality" OR "air quality":ti, ab OR "air contaminant":ti, ab OR "air pollutant substanc":ti, ab OR "air pollutant" OR "air pollut":ti, ab OR "air particul* matter":ti, ab OR "air chemical":ti, ab OR "air contamina":ti, ab OR "pollut* atmosphere":ti, ab OR "atmospheric particulate matter" OR "airborne particulate matter":ti, ab OR "particulate air pollutant":ti, ab) AND ("irritable bowel syndrome":ti, ab OR "irritable colon" OR "irritable colon":ti, ab OR "functional bowel disorder" OR "functional bowel disorder":ti, ab OR "intestine flora" OR "intestine flora":ti, ab OR "gut bacteria":ti, ab OR "gut microb":ti, ab OR "human gut microb":ti, ab OR "intestinal bacteria":ti, ab OR "gut inflammation" OR "gut inflammation":ti, ab OR "metabolome" OR "metabolome":ti, ab OR "intestinal microbe":ti, ab OR "bowel microbiota":ti, ab OR "gastro intestinal flora":ti, ab)

Web of Science

(TS=("Air Pollution*" OR "Air Quality*" OR "Air Contaminant" OR "Air Pollutant Substance*" OR "Air Pollutant" OR "Air Chemical" OR "Ultrafine Particle*") OR TI=("Particulate Matter*" OR "Ultrafine Fiber*" OR "Airborne Particulate Matter" OR "Particulate Air Pollutant*" OR "Ambient Particulate Matter" OR "Ultrafine Particulate Matter" OR "Ultrafine Particle*") OR AB=("Particulate Matter*" OR "Ultrafine Fiber*" OR "Airborne Particulate Matter" OR "Particulate Air Pollutant*" OR "Ambient Particulate Matter" OR "Ultrafine Particulate Matter" OR "Ultrafine Particle*")) AND (TS=("Irritable Bowel Syndrome*" OR "Irritable Colon" OR "functional bowel disorder" OR "intestine flora" OR "gut bacteria" OR "gut microb*" OR "human gut microb*" OR "intestinal bacteria" OR "gut inflammation" OR "metabolome" OR "intestinal microbe*" OR "bowel microbiota" OR "gastro intestinal flora" OR "gastrointestinal motilit*") OR TI=("Irritable Bowel Syndrome*" OR "Irritable Colon" OR "functional bowel disorder" OR "intestine flora" OR "gut bacteria" OR "gut microb*" OR "human gut microb*" OR "intestinal bacteria" OR "gut inflammation" OR "metabolome" OR "intestinal microbe*" OR "bowel microbiota" OR "gastro intestinal flora" OR "gastrointestinal motilit*") OR AB=("Irritable Bowel Syndrome*" OR "Irritable Colon" OR "functional bowel disorder" OR "intestine flora" OR "gut bacteria" OR "gut microb*" OR "human gut microb*" OR "intestinal bacteria" OR "gut inflammation" OR "metabolome" OR "intestinal microbe*" OR "bowel microbiota" OR "gastro intestinal flora"))

Study selection

Two authors separately screened the titles and abstracts based on the inclusion and exclusion criteria to determine relevant studies. Secondly, the full text of potentially eligible studies was reviewed. For studies that did not consist of abstracts available, the total publications were investigated to find out eligibility. If full papers were not available even after trying to contact the first author, they were excluded from the study.

RESULTS AND DISCUSSION

Effective factors in the pathophysiology of functional gastrointestinal disorder

Intestinal inflammation

The intestinal mucosal immune system is developed as a well-organized barrier against foreign pathogens as well as a beneficial environment to keep gut tolerance to food antigens and microbiota.^[20] Chronic immune changes and low-grade mucosal inflammation have been proposed in FGID patients. The inflammatory reaction in these patients is accompanied by the release of inflammatory cytokines, like Interleukin (IL)-13 and IL-5. Of note, IL-6, tumor necrosis factor (TNF)- α , and IL-1 β may have significant roles in the development and progression of IBS. Intestinal inflammation can increase gut permeability and cause diarrhea due to decreasing the absorption of water and sodium.^[21]

Gut microbiota

The term gut microbiota is a group of bacteria, archaea, and eukarya that live in the GI tract and have many benefits to the host. The normal gut microbiome is mainly comprised of two major phyla, namely *Bacteroidetes*, and *Firmicutes*. Host immune system, genetic, and environmental factors, such as diet, smoking, location, and living in urban or rural areas contribute to the composition and diversity of gut microbiota. These beneficial microorganisms help with nutrient, xenobiotic, and drug metabolism, maintaining gut integrity, developing the immune system, and giving protection against pathogenic microorganisms. Studies have revealed that the gut microbiota regulates the release of immunoglobulin A on the mucosal surface of the GI tract, which prevents the adhesion of pathogens to the intestinal epithelium and their penetration into the gut barrier. Besides, *Bacteroides* and *Clostridium* species play an important role in preventing gut inflammation via increasing the concentration of immune mediators that maintain GI tract hemostasis, called regulatory T-cells.^[18,22-24]

On the other hand, the gut microbiome plays an essential role in the development of human diseases including IBS, inflammatory bowel disease (IBD), and metabolic diseases, like diabetes and obesity.^[22,23] On the whole, the intestinal microbiota consists of useful bacteria, such as *Bifidobacterium* and *Lactobacillus*, and pathogenic bacteria, such as *Streptococcus*, *Enterobacteriaceae*, *Clostridium*, *Escherichia*, and *Staphylococcus*. When the healthy balance between the symbionts and pathobionts is disturbed, alterations in the

diversity and composition of the gut microbiota (dysbiosis) can occur, which may lead to GI disease susceptibility.^[11]

The intestinal epithelium includes epithelial cells and tight junctions (TJ) proteins. These structures act as a barrier between the intestinal microbiome and systemic environmental factors as well as mucin secretion and protection against inflammatory response.^[25]

GI hemostasis is defined as cooperation between the intestinal epithelial layer, gut microbiota, and immune system. When the intestinal hemostatic balance is disturbed, it may lead to FGIDs.^[18]

Role of air pollution in the pathophysiology of functional gastrointestinal disorders

Air pollution and intestinal inflammation

Air pollution can cause dysbiosis and intestinal inflammation,^[25] which is illustrated in Table 2. Association between air pollution and intestinal diseases, such as IBD, appendicitis, and colorectal cancer, due to increased inflammatory conditions by air pollution, have been shown in previous studies.^[6] Intestinal inflammation may also be a possible mechanism in the development or progression of FGIDs.

The GI tract exposure to air pollution can be direct or indirect. Air pollutants may enter into the GI tract via ingestion of

contaminated food and water or are swallowed in the GI tract through the pulmonary system due to mucociliary transport of respiratory pollutants. In the GI tract, ingested pollutants may affect the intestinal epithelium via the production of intestinal oxidative lipids and reactive oxygen species (ROS), which can cause intestinal inflammation and increase gut permeability.^[3] The role of air pollution in intestinal inflammatory conditions may be due to interference in the normal metabolism of intestinal lipids. In this regard, studies demonstrated that diesel exhaust particles (DEP), which consist of numerous PMs with a diameter <100 nm, can develop intestinal disease through several mechanisms. Exposure to these pollutants can boost infiltration of immune cells, such as neutrophils and macrophages in the intestine due to increasing pro-inflammatory cytokines and oxidative lipids, like hydroxyeicosatetraenoic acids, prostaglandin D₂, and hydroxyoctadecadienoic acids. Moreover, DEP exposure can decrease the activities of anti-inflammatory and anti-oxidant factors, such as high-density lipoprotein and apolipoprotein A-I mimetic peptide (D-4F).^[6] Exposure to PM can also develop TJ proteins disruption, and increase the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). These findings likely play an essential role in gut inflammation.^[26] Interestingly, evidence from *in vitro* studies indicated that air pollution exposure can increase gut

Table 2: Summary of some studies on air pollution and intestinal inflammation

Author, year	Country of origin	Study population, sample size and methodology	Type of pollutant	Concentration	Exposure time	Finding	Reference
Salim <i>et al.</i> , 2014	Canada	An experimental design, in IL-10 deficient mice, n=6	PM ₁₀	9 µg/g, g=Mouse weight	10, 14, and 20 weeks	PM ₁₀ exposure had important effects on the gut epithelium, gut barrier function, and TNF-α release, which may result in intestinal disease	[26]
Fitch <i>et al.</i> , 2020	United States	An experimental study, in 8 weeks old male, Apo E knockout mice	PM mixed diesel and gasoline engine emissions	300 µg/m ³ air	For 6 h/day, 7 days/week, for 50 days	Inhalation exposure to environmental pollutants increased ROS, rearranged TJ proteins, and developed intestinal inflammation	[25]
Mutlu <i>et al.</i> , 2011	United States	An experimental design, in male, C57BL/6 mice	Urban PM	200 µg for each mouse	48 h	PM exposure increased stress oxidative damage, TJ protein dysfunction, gut permeability, and gut inflammation in epithelial cells	[27]
Li <i>et al.</i> , 2015	United States	An experimental study, in Ldlr-null mice, at the age of 90 days and an average weight of 24.8±1.5 g, n=6/group	Atmospheric ultrafine particles	360 µg/m ³	5 h/day, 3 days/week for 10 weeks	Exposure to ultrafine particles increased HETEs, HODEs, and PGD ₂ , which may lead to inflammation in the small intestine	[28]
Mutlu <i>et al.</i> , 2018	United States	An experimental design, in male 8–12 weeks old mice, n=10	PM _{2.5}	135.4±6.4 µg/m ³	8 h/day for 5 days a week for 3 weeks	PM exposure altered the gut microbiota and increased inflammation in the GI tract which may lead to dysbiosis	[29]
Phillippi <i>et al.</i> , 2022	United States	An experimental study, in 4–6 weeks old male, C57BL/6 mice	DEPs	35 µg	30 days	DEP exposure increased TNF-α, altered gut flora diversity, and increased systemic inflammation	[30]
Zhao <i>et al.</i> , 2022	China	Prospective study, in 76 healthy seniors (age=60–69)	PM _{2.5}	57.11 µg/m ³	72 h	PM _{2.5} exposure decreased the level of IL-6 and changed the concentrations of proinflammatory and anti-inflammatory cytokines	[31]

ROS: Reactive oxygen species, TJ: Tight junction, SCFA: Short-chain fatty acid, PM: Particulate matter, TNF-α: Tumor necrosis factor, HETE: Hydroxy eicosatetraenoic acids, HODE: Hydroxy octadecadienoic acids, PGD₂: Prostaglandin D₂, GI: Gastrointestinal, IL: Interleukin, DEP: Diesel exhaust particle, Apo: Apolipoprotein

permeability. In this regard, exposure to $\geq 10 \mu\text{g PM}/\text{cm}^2$ for 4 h is related to higher activation of NF- κ B, and exposure to $\geq 5 \mu\text{g PM}/\text{cm}^2$ can increase ROS in Caco-2 epithelial cells. Besides, exposure to $5 \mu\text{g PM}/\text{cm}^2$ for 4 days can increase TNF- α . Last but not least, studies showed that exposure to $\geq 100 \mu\text{g}/\text{cm}^2$ for 1 week or exposure to $\geq 50 \mu\text{g}/\text{cm}^2$ for 2 weeks is associated with increased intestinal levels of the lipid peroxidation mediator 4-hydroxynonenal.^[33]

Air pollutants are likely associated with decreased expression of factors that play roles in gut barrier integrity and increased inflammatory mediators, such as IL-1 β , TNF- α , and toll-like receptor-4. For instance, PM exposure can increase ROS and rearrange TJ proteins.^[25] Long-term PM_{2.5} exposure can also increase gut permeability and intestinal inflammation due to the expression of genes involved in inflammation, like IL-6 and TNF- α . Moreover, PAH exposure is associated with the expression of IL-1 β , which can increase infiltration of mast cells, neutrophils, and macrophages.^[34]

It is claimed that air pollution can decrease the concentration of regulatory T-cells induced by *Clostridia*, Gram-Positive bacterial species belonging to the family of *Firmicutes*, which may result in asthma attacks. This may be due to the fact that there is an important communication between the lung and gut through the lymphatic and cardiovascular systems, which is called the gut-lung axis. Consequently, lung inflammation due to air pollution exposure can cause gut dysbiosis through the transportation of inflammatory cytokines and immune cells from the lung to the gut.^[3]

Short-chain fatty acids (SCFAs) are the main metabolites of gut microbiota that can suppress inflammation. Air pollution can decrease SCFA levels and increase systemic

inflammation through the interruption of the lung-gut axis and the development of gut microbiota dysbiosis.^[35]

Nonspecific abdominal pain is one of the important symptoms of IBS. Animal studies showed that the exposure of mice to air pollution can increase pain response. Additionally, previous studies in the youth age group (between the ages of 15 and 24 years) with the predominance of the woman indicated that the occurrence of nonspecific abdominal pain is likely correlated with air pollution, such as NO₂, SO₂, CO, and PM_{2.5}. According to these studies, releasing IL-8 from the small intestine and oxidative stress damage of colonic mucosa due to air pollution exposure may be the key factors in the prevalence of IBS symptoms.^[16]

Air pollution and gut microbiota

It is argued that gut microbiota may play significant roles in the pathophysiology of FGIDs. As a result, investigating the factors that alter the gut microbes' composition and function can help to comprehend disease pathogenesis.^[36]

The impact of air pollution on intestinal microbiota has been increasingly noticed in recent years.^[6] Table 3 illustrates a summary of some studies on air pollution and gut microbiota. The history of studies on the relationship between air pollution and human gut microbiome dates back to 1989. This study depended on bacterial species culturing, which indicated that occupational exposure to heavy metals was associated with increasing mercury-resistant *Enterobacteriaceae* in the gut microbiome.^[9] Moreover, other studies have shown that the gut microbiota can metabolize ingested particles into toxic metabolites. As a result, these metabolites are released into the circulation. For example, gut microbiota metabolizes the PAHs to metabolites that imitate the estrogen hormone

Table 3: Summary of some studies on air pollution and gut microbiota

Author, year	Country of origin	Study population, sample size, and methodology	Type of pollutant	Concentration	Exposure time	Finding	Reference
Zordão et al., 2023	Brazil	An experimental design, in 8 weeks old male and female, C57BL/6J mice	PM _{2.5}	600 $\mu\text{g}/\text{m}^3$	13 weeks for 24 h	Lower quantities of the <i>Bacteroidetes</i> phylum and higher quantities of the <i>Verrucomicrobia</i> were observed in PM-exposed mice	[37]
Dutta et al., 2022	United States	An experimental design, in male and female, Tg344-AD rats, (n=5-6)	Traffic-related air pollution	15.6 \pm 3.7 $\mu\text{g}/\text{m}^3$	14 months	Exposure to traffic-related air pollution was associated with an increase in the <i>Turicibacter</i> and <i>Ruminococcus gnavus</i> . The concentrations of <i>Desulfovibrionaceae</i> and <i>Lachnospiraceae</i> decreased in rats	[38]
Kish et al., 2013	Canada	An experimental study, in wild-type 129/SvEv mice	PM ₁₀	18 $\mu\text{g}/\text{g}/\text{day}$	14 days	PM exposure increased inflammatory cytokines, and altered the quantities of <i>Verrucomicrobia</i>	[39]
Li et al., 2017	United States	An experimental design, in Ldlr-null mice, (n=11-12)	Ultrafine particle	40 $\mu\text{g}/\text{mouse}/\text{day}$	3 days a week for 10 weeks	Exposure to ultrafine particles increased the number of <i>Verrucomicrobia</i> and decreased the number of <i>Actinobacteria</i> , <i>Cyanobacteria</i> , and <i>Firmicutes</i>	[40]
Mutlu et al., 2018	United States	An experimental design, in 8-12 weeks old male, C57BL/6 mice	PM _{2.5}	135.4 \pm 6.4 $\mu\text{g}/\text{m}^3$	8 h/day for 5 days a week for 3 weeks	Ambient particle exposure increased the <i>Bacteroidetes</i> and decreased the <i>Firmicutes</i> and <i>Staphylococcaceae</i> in exposed mice	[29]

PM: Particulate matter

activity. Moreover, gut microbiota converts inorganic arsenic in contaminated soils, into toxic metabolites.^[41] Remarkably, Zhang *et al.* indicated that PAH exposure can alter the gut microbiota composition. Unlike the phyla *Bacteroidales*, *Bacteroidetes*, and *Bacteroidia*, the study suggested that PAH exposure was positively associated with the phyla *Actinobacteria*, *Firmicutes*, and *Proteobacteria*.^[42]

Ingested pollutants can compromise the gut barrier integrity due to affecting the gut microbiota. Ingested pollutants likely alter the composition of the intestinal microbiome. In other words, absorbed pollutants may reduce the abundance of beneficial microorganisms, such as *Lactobacillus* and *Bifidobacterium* that play vital roles in protecting the intestinal barrier and suppressing inflammation. Furthermore, consumed pollutants can boost the abundance of pro-inflammatory microorganisms and change microbial diversity.^[6] For instance, increasing bacterial species from the *Bacteroidaceae* family is related to higher O₃ levels. Besides, a higher population of *Coriobacteriaceae* is correlated with higher NO₂ concentrations. It is worth noting that traffic-related air-pollution exposure can reduce the abundance of *Bacteroidaceae* and increase the abundance of *Coriobacteriaceae*. Exposure to PM₁ and PM_{2.5} may also reduce the quantity of *Proteobacteria*, *Firmicutes*, and *Verrucomicrobia*. Finally, various air pollutants, like ozone, SO₂, NO₂, and PM can alter the number of *Phascolarctobacterium*, *Eggerthella*, and *Clostridium*.^[3]

These alterations in the gut microbiota reduce the concentration of butyrate, the vital fatty acid for gut mucosal cells and colonocytes. A diminished concentration of butyrate may lead to impairment of the gut barrier and mucosal inflammation. Besides, changes in microbiota composition can increase the production of branched-chain fatty acids, such as isobutyrate and isovalerate. Increasing isobutyrate and isovalerate concentrations originating from the degeneration of amino acids, can shift the intestinal environment from a carbohydrate to a protein fermentation, which in turn contributes to the alterations in gut microbiota composition.^[36,41]

These findings, such as intestinal inflammation, increased gut permeability, disruption of the gut epithelial barrier, and gut microbiome alteration have been suggested in both FD and IBS.

Air pollution and gastrointestinal motility

Changed GI motility is an important pathobiological mechanism of FGIDs. Fast or slow colonic motility can alter the composition of intestinal microbiota. Gut microbiota can also affect colonic motility through alteration of SCFAs and bile acid concentration in the colon.^[43] Animal studies have shown that air pollution can affect GI motility. In this regard, exposure to PM and gaseous pollutants, such as ozone, NO₂, and CO can cause disturbance in the contraction of the GI tract. Furthermore, constipation-predominant IBS can be accompanied by CH₄ exposure. Interestingly, long-term exposure to gaseous pollutants is associated with childhood IBS.^[8]

Consumption of biotics to prevent air pollution outcomes

Probiotics are a group of live microorganisms that, if administered in sufficient amounts, have beneficial effects on the host. The role of probiotics in the treatment of GI diseases, such as IBS, which can be accompanied by exposure to air pollution, has been suggested. In this regard, studies indicated that consumption of supplementations containing *Bifidobacterium* can decrease abdominal pain and increase the quality of life in patients with IBS. Unlike exposure to air pollution, which can have harmful effects on the intestinal microbiome, the consumption of biotics in diet can modulate the composition of the gut microbiota. Moreover, studies showed that biotics may play a significant role in oxidative stress. In fact, they can help to eliminate free radicals and peroxides. Besides, biotics may have immunomodulating and anti-inflammatory effects. Indeed, they can have an impact on T-cell differentiation and decrease pro-inflammatory cytokines, such as TNF- α and IL-6 in contrast to increasing anti-inflammatory factors, like IL-10.^[44]

CONCLUSION

The purpose of this narrative review was the investigation of available evidence regarding the possible impact of air pollution exposure on FGIDs. To the best of our knowledge, air pollution may play an important role in the pathophysiology of FGIDs due to its effect on gut microbiota and the intestinal immune system. Air pollutants can decrease beneficial microorganisms and increase pro-inflammatory factors in the intestine. Moreover, air pollution exposure can alter GI motility, which in turn contributes to the alterations of gut microbiota composition and diversity.

Air pollution is an important environmental issue and public health emergency. To tackle the air pollution problem, the government should encourage people to use public transportation. Another effective solution is using alternative energies, such as solar, wind, and hydropower. The consumption of biotics can be useful to prevent the negative effects of air pollution exposure on FGID patients.

The evidence that reveals the link between air pollution and FGIDs is very limited. As a result, this narrative review suggests future studies should be conducted on this subject, particularly investigating factors that can connect air pollution with FGIDs, such as diet, psychological stress, and enteric nervous system.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Robertson S, Miller MR. Ambient air pollution and thrombosis. *Part Fibre Toxicol* 2018;15:1.
- Mayer H. Air pollution in cities. *Atmos Environ* 1999;33:4029-37.
- Filardo S, Di Pietro M, Protano C, Antonucci A, Vitali M, Sessa R. Impact of air pollution on the composition and diversity of human gut microbiota in general and vulnerable populations: A systematic review. *Toxics* 2022;10:579.
- Zhu Y, Huang L, Li J, Ying Q, Zhang H, Liu X, *et al.* Sources of particulate matter in China: Insights from source apportionment studies published in 1987-2017. *Environ Int* 2018;115:343-57.
- Zhang L, Ou C, Magana-Arachchi D, Vithanage M, Vanka KS, Palanisami T, *et al.* Indoor particulate matter in urban households: Sources, pathways, characteristics, health effects, and exposure mitigation. *Int J Environ Res Public Health* 2021;18:11055.
- Feng J, Cavallero S, Hsiai T, Li R. Impact of air pollution on intestinal redox lipidome and microbiome. *Free Radic Biol Med* 2020;151:99-110.
- Fiordelisi A, Piscitelli P, Trimarco B, Coscioni E, Iaccarino G, Sorriento D. The mechanisms of air pollution and particulate matter in cardiovascular diseases. *Heart Fail Rev* 2017;22:337-47.
- Tan TK, Saps M, Lin CL, Wei CC. Is long-term ambient air pollutant exposure a risk factor for irritable bowel syndrome in children? A 12-year longitudinal cohort study. *J Neurogastroenterol Motil* 2019;25:241-9.
- Dujardin CE, Mars RA, Manemann SM, Kashyap PC, Clements NS, Hassett LC, *et al.* Impact of air quality on the gastrointestinal microbiome: A review. *Environ Res* 2020;186:109485.
- Drossman DA, Thompson WG, Talley NJ, Funch-Jensen P, Janssens J, Whitehead WE. Identification of sub-groups of functional gastrointestinal disorders. *Gastroenterol Int* 1990;3:159-72.
- Nafarin AR, Hegar B, Sjakti HA, Vandenplas Y. Gut microbiome pattern in adolescents with functional gastrointestinal disease. *Int J Pediatr Adolesc Med* 2019;6:12-5.
- Mukhtar K, Nawaz H, Abid S. Functional gastrointestinal disorders and gut-brain axis: What does the future hold? *World J Gastroenterol* 2019;25:552-66.
- Fikree A, Byrne P. Management of functional gastrointestinal disorders. *Clin Med (Lond)* 2021;21:44-52.
- Moser G. Functional gastrointestinal disorders. *Wien Med Wochenschr* 2006;156:435-40.
- Holtmann G, Shah A, Morrison M. Pathophysiology of functional gastrointestinal disorders: A holistic overview. *Dig Dis* 2017;35 Suppl 1:5-13.
- Marynowski M, Likońska A, Zatorski H, Fichna J. Role of environmental pollution in irritable bowel syndrome. *World J Gastroenterol* 2015;21:11371-8.
- Narayanan SP, Anderson B, Bharucha AE. Sex- and gender-related differences in common functional gastroenterologic disorders. *Mayo Clin Proc* 2021;96:1071-89.
- Burns G, Pryor J, Holtmann G, Walker MM, Talley NJ, Keely S. Immune activation in functional gastrointestinal disorders. *Gastroenterol Hepatol (N Y)* 2019;15:539-48.
- Koloski NA, Talley NJ, Boyce PM. The impact of functional gastrointestinal disorders on quality of life. *Am J Gastroenterol* 2000;95:67-71.
- Curciarello R, Canziani KE, Docena GH, Muglia CI. Contribution of non-immune cells to activation and modulation of the intestinal inflammation. *Front Immunol* 2019;10:647.
- Chen MK, Liu SZ, Zhang L. Immunoinflammation and functional gastrointestinal disorders. *Saudi J Gastroenterol* 2012;18:225-9.
- Thursby E, Juge N. Introduction to the human gut microbiota. *Biochem J* 2017;474:1823-36.
- Jandhyala SM, Talukdar R, Subramanyam C, Vuyyuru H, Sasikala M, Nageshwar Reddy D. Role of the normal gut microbiota. *World J Gastroenterol* 2015;21:8787-803.
- Mazmanian SK, Lee YK. Interplay between intestinal microbiota and host immune system. *J Bacteriol Virol* 2014;44:1-9.
- Fitch MN, Phillippi D, Zhang Y, Lucero J, Pandey RS, Liu J, *et al.* Effects of inhaled air pollution on markers of integrity, inflammation, and microbiota profiles of the intestines in apolipoprotein E knockout mice. *Environ Res* 2020;181:108913.
- Salim SY, Jovel J, Wine E, Kaplan GG, Vincent R, Thiesen A, *et al.* Exposure to ingested airborne pollutant particulate matter increases mucosal exposure to bacteria and induces early onset of inflammation in neonatal IL-10-deficient mice. *Inflamm Bowel Dis* 2014;20:1129-38.
- Mutlu EA, Engen PA, Soberanes S, Urlich D, Forsyth CB, Nigdelioglu R, *et al.* Particulate matter air pollution causes oxidant-mediated increase in gut permeability in mice. *Part Fibre Toxicol* 2011;8:19.
- Li R, Navab K, Hough G, Daher N, Zhang M, Mittelstein D, *et al.* Effect of exposure to atmospheric ultrafine particles on production of free fatty acids and lipid metabolites in the mouse small intestine. *Environ Health Perspect* 2015;123:34-41.
- Mutlu EA, Comba IY, Cho T, Engen PA, Yazıcı C, Soberanes S, *et al.* Inhalational exposure to particulate matter air pollution alters the composition of the gut microbiome. *Environ Pollut* 2018;240:817-30.
- Phillippi DT, Daniel S, Pusadkar V, Youngblood VL, Nguyen KN, Azad RK, *et al.* Inhaled diesel exhaust particles result in microbiome-related systemic inflammation and altered cardiovascular disease biomarkers in C57Bl/6 male mice. *Part Fibre Toxicol* 2022;19:10.
- Zhao L, Fang J, Tang S, Deng F, Liu X, Shen Y, *et al.* PM_{2.5} and serum metabolome and insulin resistance, potential mediation by the gut microbiome: A population-based panel study of older adults in China. *Environ Health Perspect* 2022;130:27007.
- Mutlu E, Engen P, Soberanes S, Urlich D, Gonzalez AR, Nigdelioglu R, *et al.* Exposure to ambient particulate matter causes oxidant-mediated increase in gut permeability in mice. *Gastroenterology* 2010;138:S273-4.
- Van Pee T, Nawrot TS, van Leeuwen R, Hogervorst J. Ambient particulate air pollution and the intestinal microbiome; a systematic review of epidemiological, *in vivo* and, *in vitro* studies. *Sci Total Environ* 2023;878:162769.
- Xie S, Zhang C, Zhao J, Li D, Chen J. Exposure to concentrated ambient PM (2.5) (CAPM) induces intestinal disturbance via inflammation and alternation of gut microbiome. *Environ Int* 2022;161:107138.
- Cheng TY, Chang CC, Luo CS, Chen KY, Yeh YK, Zheng JQ, *et al.* Targeting lung-gut axis for regulating pollution particle-mediated inflammation and metabolic disorders. *Cells* 2023;12:901.
- Salim SY, Kaplan GG, Madsen KL. Air pollution effects on the gut microbiota: A link between exposure and inflammatory disease. *Gut Microbes* 2014;5:215-9.
- Zordão OP, Campolim CM, Yariwake VY, Castro G, Ferreira CK, Santos A, *et al.* Maternal exposure to air pollution alters energy balance transiently according to gender and changes gut microbiota. *Front Endocrinol (Lausanne)* 2023;14:1069243.
- Dutta M, Weigel KM, Patten KT, Valenzuela AE, Wallis C, Bein KJ, *et al.* Chronic exposure to ambient traffic-related air pollution (TRAP) alters gut microbial abundance and bile acid metabolism in a transgenic rat model of Alzheimer's disease. *Toxicol Rep* 2022;9:432-44.
- Kish L, Hotte N, Kaplan GG, Vincent R, Tso R, Gänzle M, *et al.* Environmental particulate matter induces murine intestinal inflammatory responses and alters the gut microbiome. *PLoS One* 2013;8:e62220.
- Li R, Yang J, Saffari A, Baek K, Jacobs J, Pisegna J, *et al.* Ambient ultrafine particle digestion alters gut microbiota in association with increased atherogenic lipid metabolites. *Sci Rep.* 2017 Feb;7:42906.
- Anwar H, Iftikhar A, Muzaffar H, Almatroudi A, Allemailem KS, Navaid S, *et al.* Biodiversity of gut microbiota: Impact of various host and environmental factors. *Biomed Res Int* 2021;2021:5575245.
- Zhang W, Sun Z, Zhang Q, Sun Z, Su Y, Song J, *et al.* Preliminary evidence for an influence of exposure to polycyclic aromatic hydrocarbons on the composition of the gut microbiota and neurodevelopment in three-year-old healthy children. *BMC Pediatr* 2021;21:86.
- Shin A, Preidis GA, Shulman R, Kashyap PC. The gut microbiome in adult and pediatric functional gastrointestinal disorders. *Clin Gastroenterol Hepatol* 2019;17:256-74.
- Keulers L, Dehghani A, Knippels L, Garssen J, Papadopoulou N, Folkerts G, *et al.* Probiotics, prebiotics, and synbiotics to prevent or combat air pollution consequences: The gut-lung axis. *Environ Pollut* 2022;302:119066.