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The Effect of Air Pollutants on Chronic Gastrointestinal Diseases: A Comprehensive Review

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ABSTRACT

Background: Today, chronic diseases have spread all over the world. The World Health Organization (WHO) mentions air pollution as the biggest environmental health hazard, attributing 7 million premature deaths every year to this pollution, which includes suspended particles and gases with concentrations that are detrimental to human health. Factors of interest in this field are micrometer diameter particles, tropospheric ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide. The purpose of this research is to increase public awareness of air pollution and its side effects on different parts of the digestive system.
Methods: A narrative review was done using several databases, including PubMed, Magiran, Web of Science, and Google Scholar. Relevant studies published from 1990-2021 were identified.
Results: Globally, ecological studies have demonstrated a relationship between short-term exposure to air pollution and several gastrointestinal diseases.
Conclusion: The results of these studies showed that pollutants have a direct effect on the increased prevalence and number of cases of chronic gastrointestinal diseases. The results of this research can inform policymakers in making comprehensive decisions to solve the problem, individuals who are exposed to pollutants, and the public in raising awareness and promoting the use of protective equipment.

1. Introduction

Health systems in the 21st century are facing the challenge of increasing burden caused by chronic diseases [1]. Non-communicable disease, as defined by the WHO in 1957, includes a reduction in the structure or function of the body that necessarily changes the patient's normal life and continues for a long time and is stable. Unhealthy and inappropriate lifestyles contribute to the occurrence of chronic diseases, which result in many deaths worldwide [2]. Developing countries are particularly vulnerable to health risks posed by chronic diseases, with mortality and disability rates surpassing those associated with infectious diseases in all but the poorest countries. According to the report of the WHO, by 2015 in the five largest developing countries, the economic burden due to stroke, cardiovascular diseases, and diabetes will be 1.25 trillion dollars. In the United States, half of the population suffers from chronic diseases, and this number is expected to rise in the coming years. Moreover, a large number of the population suffers from more than one type of chronic disease. According to studies, by 2025, more than one in four Americans will suffer from two or more types of chronic diseases, which will cover 75 % of health costs. It is estimated that chronic diseases cause 20 % of deaths in high-income countries, while 80 % of these deaths occur in middle-income and low-income countries, where

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the world's largest population lives. Chronic diseases are one of the main causes of death and disability in Iran. With the change in society's age pyramid and the aging of the young population, as well as the expansion of industrial life and urbanization, the prevalence of these diseases will increase in the near future [3]. Gastrointestinal diseases have different types and are highly prevalent. They affect different parts of the digestive system, including the liver, small and large intestines, and the stomach. Gastrointestinal diseases are disorders and problems related to the digestive system that may involve one or more of these organs. Among the factors that cause digestive diseases is the entry of pollutants from air pollution into the human body. Air pollution occurs when a large number of particles or harmful substances such as gases, particles, and biomolecules enter the Earth's atmosphere. This pollution is the suspended particles and gases whose concentration has reached a level that harms humans and can exist both indoors and outdoors. Air pollutant measurement criteria include 2.5-micrometer particles, tropospheric ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide [4]. The Global Burden of Disease (GBD) study has identified particulate matter less than 2.5 micrometers in the air and tropospheric ozone as the primary indicators to quantify population exposure to air pollution, as they have consistently demonstrated a strong association with health outcomes [5, 6]. Tissues and organs such as the mouth, tongue, nose, throat, vocal cords, and a part of the esophagus are considered the most important routes for air pollutants to enter the body. Inflammatory bowel diseases, liver diseases, appendicitis, and digestive tract cancers are among the damages caused by air pollution [7, 8]. Additionally, exposure to air pollutants, such as particulate matter is associated with lung and cardiovascular diseases, as well as increased hospitalization and mortality rates. However, the effects of air pollution have not been extensively studied. Considering the industrialization of societies and the resulting air pollution caused by industries, it is essential to investigate the potential effects of air pollution on inflammatory bowel diseases. However, few studies have investigated the potential role of air pollution and its constituents in intestinal diseases. Cleaning the digestive system from pollution, for example, the intestine, which is exposed to air pollutants, occurs through the consumption of food and water and cleaning the mucus from the lungs. Gaseous pollutants are also not ineffective. The effects of air pollutants on the intestine can be in several forms. including direct effects on epithelial cells, systemic inflammation and immune system activation and modulation. There is limited epidemiological evidence to confirm the existence of a relationship between air pollution and intestinal diseases, so more studies should be done in this field to partially explain how environmental factors affect the epidemiology of inflammatory bowel diseases and the pathogenesis of the disease [9]. A positive relationship has been observed between air pollution and certain gastrointestinal, skeletal, and urinary diseases. For example, bone loss and fractures over time, peptic ulcer bleeding, and chronic kidney disease are the most common types of these diseases [7, 10, 11]. However, epidemiological evidence for many diseases remains inconclusive and scarce, often due to limited representation, small data sizes, and potential publication bias [12]. Ecological studies, on the other hand, have demonstrated a positive short-term exposure to air pollution and various digestive disorders, including inflammatory bowel disease, acute appendicitis, non-specific abdominal pain in young adults, and digestive disorders [11]. Recent studies have investigated the relationship between short-term increases in air pollution and increased risk of exacerbation in gastrointestinal diseases, including secondary upper gastrointestinal bleeding and its conversion to peptic ulcer disease, which is a significant source of global mortality. Peptic ulcer disease is a type of benign damage to the mucosa and submucosa of the digestive tract in the area of the stomach, duodenum, and sometimes the end part of the esophagus, which often involves the duodenum and stomach. Common symptoms include epigastric pain, loss of appetite, and weight loss. Secondary upper gastrointestinal bleeding, which can lead to peptic ulcer disease, is a serious medical condition associated with significant complications, high health care costs, and reduced quality of life. Patients suspected of secondary upper gastrointestinal bleeding require immediate medical attention. Nonsteroidal anti-inflammatory drugs and *Helicobacter pylori* are among the primary causes of stomach ulcers. However, it is worth noting that exposure to environmental air pollution also increases the risk of contracting this disease [13, 14]. Moreover, Notably, research conducted in various regions of Thailand has indicated that the presence of black carbon, organic carbon, and dust particles in the air poses a potential risk for colon cancer, particularly in relation to particles with a size of less than 2.5 micrometers [15]. The incidence of death due to stomach cancer in Asia is still the highest in the world. For instance, in Linzhou, China, stomach cancer is the second most common cancer in terms of incidence [16]. A multi-center European analysis showed that there is an association between particulate matter less than 2.5 micrometers in air and the incidence of stomach cancer. It is not known which components of suspended particles are related to gastric and upper gastrointestinal cancer, and some of them may not be strongly related to the mass of suspended particles [17]. The aim of this study was to investigate the potential effect of air pollutants on the increased risk of chronic diseases, focusing specifically on the gastrointestinal tract.

2. Materials and Methods

2.1 Evidence Acquisition

Table 1 explains the query results according to different databases including Google Scholar, Springer, Science Direct, PubMed, Web of Science, and search terms. The English language was used for a review of the epidemiological literature. All relevant studies published in 2000-2021 were identified. Four hundred and Sixty articles according to databases were retrieved.

2.2 Eligibility criteria

Medical Subject Heading (MeSH) used in this study was such as 'Air pollution', 'Chronic Diseases', 'carcinogenic', and 'gastrointestinal tract'. The range of 2000 to 2021 was limited in the review time efficiency of studies. Based on studies investigating the effect of air pollutants on increased risk of chronic diseases (gastrointestinal tract). Databases used for the search were Springer, Google Scholar, PubMed, Science Direct, and Web of Science. According to studies on the Investigating Effect of air pollutants on the increased risk of chronic diseases (gastrointestinal tract), including articles published in domestic and foreign journals and searches in PubMed database of 57 articles, Science Direct received 107 articles, 157 articles in the Google Scholar, Web of Sciences database 68 articles and springer database 69 articles search engine.

2.3 Study selection

According to the criteria mentioned above, after the initial screening, 460 research titles were obtained. 42 papers based on abstract and article text filtered. In the next stage, 32 studies were screened after review and 22 full-text articles entered into the analysis process. After removing 10 articles and then 9 articles in the secondary period, finally, 11 articles were included in the analysis process. Identify all relevant studies published from 2000-2021. Figure 1 shows how to prepare studies and the selection process articles based on the PRISMA flow diagram.

2.4 Extraction of the data

Data from selected publications were extracted and documented in an EXCEL spreadsheet.

Table 1. Search terms and query results

Term	PubMed	Science Direct	Springer	Web of Science	Google Scholar	Unique results
Air pollution	17	32	19	20	58	148
Chronic Diseases	10	27	17	17	28	99
Carcinogenic	12	28	16	16	18	90
Gastrointestinal Tract	18	20	17	15	53	123
Total	57	107	69	68	157	460

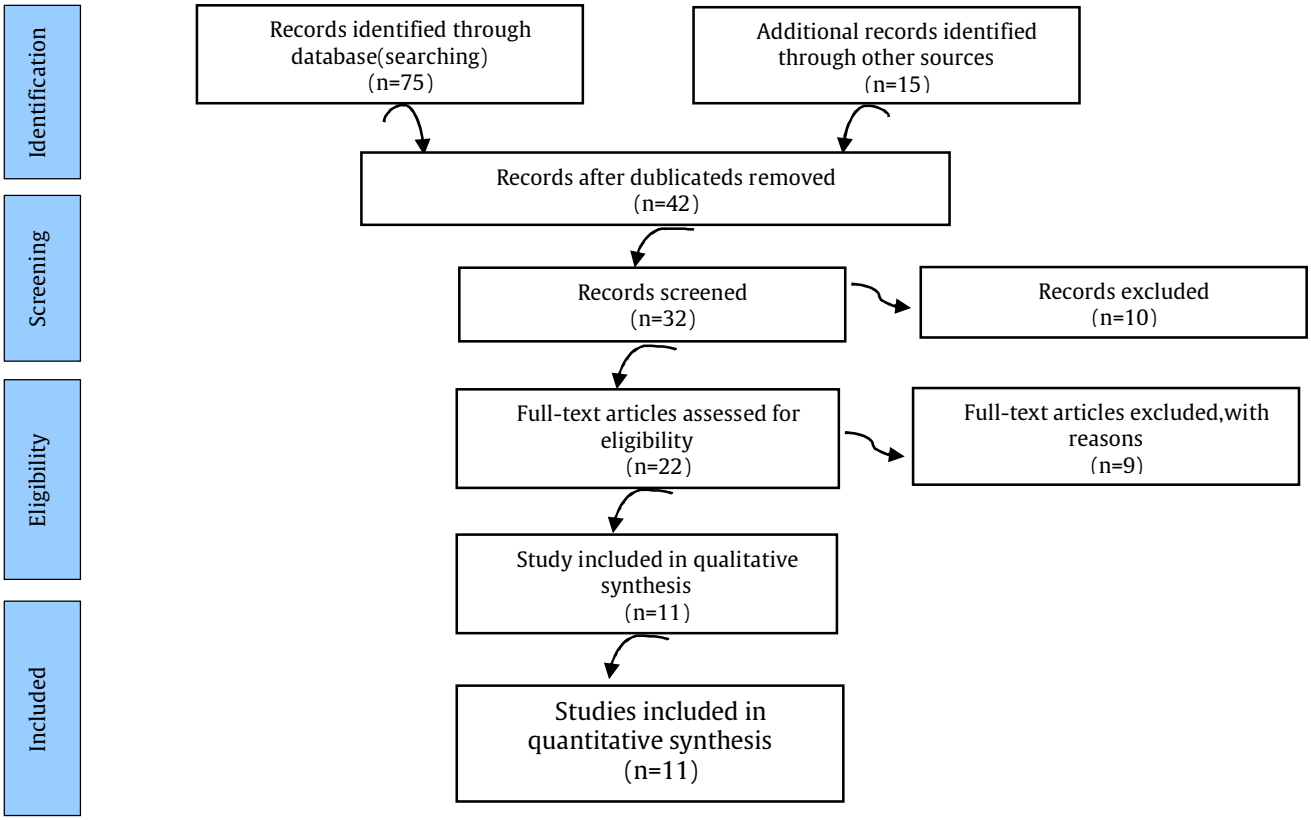

Figure 1. Representation of the search strategy based on PRISMA flow diagram

3. Results and Discussion

3.1 Chronic diseases and Gastrointestinal diseases:

Chronic diseases are long-term conditions that cause physical changes in the body and can disrupt its functioning. These diseases also have difficult treatments and require a long period of treatment and recovery. One of the characteristics of chronic diseases is that they may not have a definitive treatment, and patients may endure the symptoms and complications of the disease for the rest of their lives [18]. Chronic diseases include cancer, cardiovascular diseases, digestive diseases, stomach ulcers, chronic kidney failure, intestinal colitis, gastric gastritis, asthma and allergies, thalassemia, AIDS, and diabetes. Gastrointestinal diseases are one of the most common disorders in the world. The esophagus, stomach, large intestine, small intestine, liver, pancreas, and gall bladder make up the digestive system [19]. The first symptoms of digestive diseases include constipation, diarrhea, bloating, heartburn, nausea and vomiting, swallowing problems, abdominal pain, and weight gain or loss [20]. Gastrointestinal diseases include stomach cancer, small intestine cancer, colon cancer, liver cancer, esophageal cancer, irritable bowel syndrome, fatty liver, liver cirrhosis, hepatitis, gastric reflux, and peptic ulcer. Diseases related to the digestive system may involve any of these organs or a group of them. Many of the symptoms are similar in all digestive problems, which makes them difficult to distinguish [21]. Figure 2 presents the different parts of the human digestive system.

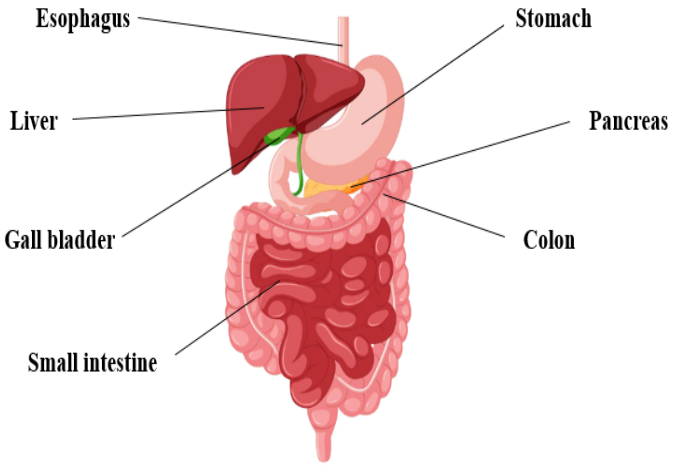

Figure 2. Different organs of the human digestive system

3.2 Air pollution:

Any substance in the air that may harm animals, humans, or vegetation is called an air pollutant. They have the potential to cause diseases, potentially endanger human health, and increase mortality rates [22]. Human health and the environment are at risk due to exposure to air pollutants. These pollutants include two categories primary pollutants (pollutants that originate from pollution sources and enter the atmosphere directly without change or reaction) and secondary pollutants (pollutants that interact with environmental factors such as humidity). Primary pollutants include carbon monoxide, nitrogen oxides, hydrocarbons, and dust, and secondary pollutants include ozone [23, 24]. Carbon monoxide (CO), sulfur dioxide (SO_2), ozone (O_3), volatile organic compounds (VOC_s), nitrogen oxides (NO_x), heavy metals, and suspended particles with a diameter of less than 2.5 microns ($PM_{2.5}$) and less than 10 microns (PM_{10}), vary in their chemical composition, ability to spread, and effects on humans [25]. One of the parameters that determines the impact of pollutants is their concentration. Some pollutants are harmful even at low concentrations, leading to adverse effects on living and non-living structures, reduced visibility, and increased blurring. Those types of pollution that may not have specific harmful effects can accumulate in the atmosphere over time and transform into pollutants with harmful effects. Perchloroethylene and Dichloromethane that cause serious health effects such as birth defects, reproductive harm, cancer, or others are called hazardous air pollutants (HAP_s) or toxic pollutants. Radioactivity is another type of air pollutant, which is both geogenic and anthropogenic. Radioactive minerals in the earth's crust and the interaction of cosmic radiation with atmospheric gases create radionuclides that form the terrestrial part, and radioactive emissions that originate from nuclear reactors, nuclear weapon explosions, and power plants form the radioactive anthropogenic part [26] In stagnant weather conditions, the concentration of air pollutants increases sharply. The historic smog event in London in December 1952, known as the Great Smog, resulted in a death toll of 4,000 to 12,000 people, more than three times the expected number, highlighting the connection between air pollution and human diseases [27, 28, 29]. Numerous studies have since been conducted on the relationship between air pollution and various health issues, including respiratory diseases, cancers, cardiovascular diseases, and gastrointestinal diseases [30]. Small amounts of uranium and thorium are also formed in residential buildings, which accumulate due to improper functioning of air conditioning and reach high concentrations that are even higher than the concentration of outdoor air pollutants. In this situation, the issue of indoor air pollution and sick building syndrome is raised. One of the causes of this syndrome is radioactive pollutants of human origin. Radioactivity, tobacco smoke, NO, CO, and SO_2 emitted from stoves, and harmful chemicals such as VOC_s emitted from household cleaners, air paints, and varnishes cause indoor pollution, which can greatly reduce the effects of these pollutions with proper air conditioning [26]. In general, the increase in deaths caused by air pollution is very evident in developed countries with a high rate of industrialization, and this increase in growth can be seen worldwide since 1990. Since the atmosphere of the air after the Industrial Revolution has a different chemical composition from the

atmosphere before it, it can be said that air pollution has been created since humans changed the chemical composition of the atmosphere by burning fuel and is anthropogenic [26]. Factors such as the rapid expansion of megacities, the spread of pesticides and chemicals, the globalization of toxic industrial products, and the increased use of motor vehicles contribute to premature and unnatural deaths caused by air pollution [26, 31]. In 2015, air pollution caused the death of 6.4 million people, which is 17 % of all deaths in the world [32]. Of these deaths, 2.8 million were attributed to indoor air pollution, and the remaining 4.2 million to outdoor air pollution, while tobacco-reated deaths numbered 7 million, AIDS/HIV 1.2 million, tuberculosis 1.1 million, and malaria 0.7 million [33-35]. Meanwhile, it is predicted that air pollution can cause 6 to 9 million deaths annually by 2060 [36]. The increasing number of deaths related to air pollution has led to intensive studies on the effects of air pollutants on human health, with results showing a significant relationship between exposure to air pollutants and increased hospitalizations and mortality rates [37].

3.3 Sources of Air pollutants:

The sources of air pollutants are divided into two categories: natural and human-made sources. Human-made pollutants are composed of stationary sources, such as petrochemicals and chemical factories, which are fixed in one location, as well as mobile sources, including cars, airplanes, and trains, which are constantly in motion. Both of these sources play a significant role in air pollution [24]. The main sources of CO and $PM_{2.5}$ pollutants are the fuel combustion of motor vehicles, which is a mobile source. The usage of these mobile sources is lower during certain times of the day, such as midnight, resulting in a significant decrease in airborne CO levels [38]. Cars in areas with high gas station density and with a large presence in places such as compressed natural gas stations (CNG) and bus stations (BRT) cause more air pollution in these areas than in other places, which can be a good explanation for the existence of cases. Most stomach cancer is around these places [39]. Areas with high traffic load and little vegetation, in addition to CO and $PM_{2.5}$, also have high concentrations of NO_2 and dust, which shows that motor vehicles are the source of these four pollutants. In addition to cars, mines, and industries are also constant sources of NO_2 and dust [39]. Other sources of $PM_{2.5}$ include industrial facilities, residential fireplaces, and wood stoves [40]. PM10 also originates from geological materials and smoke emitted from moving motor vehicles [41]. Toxic air pollutants originate from car exhaust, factory activities, cigarette smoke, forest fires, and active volcanoes [24]. The effect of car exhaust smoke on GIT has been confirmed. Oil or diesel engines also emit aerosols that contain large amounts of PAH and BaP. The pollutants released from petrochemical industries include large amounts of standard pollutants, especially SO_2, NO_2, and PAH [42]. O_3 precursors are emitted from the combustion of fossil fuels, agricultural masses, and various industrial processes. Also, these pollutants are produced from the photochemical reactions of nitrogen oxides with compounds such as methane and volatile organic compounds (VOC_s) [43]. The main sources of heavy metal emissions such as lead, arsenic and antimony in the air are domestic heating, transportation and traffic [44]. polychlorinated biphenyls (PCB) are organic compounds that are also called persistent organic pollutants and are present in paints and lubricants and can enter the atmosphere through primary and secondary sources. Many plant specimens are the main sources of pollen, and the existence of a relationship between pollen and some pollutants from the main sources of air causes problems caused by pollen, such as allergies. Sources of air pollutants are shown in Figure 3.

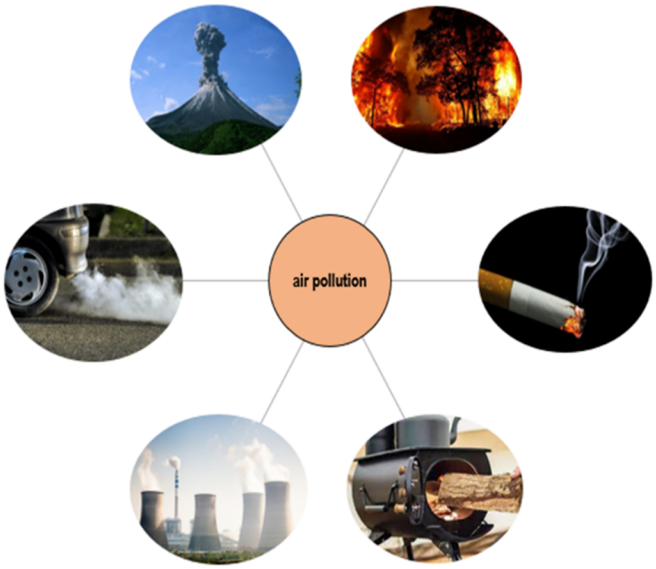

Figure 3. Sources of air pollutants

3.4 Digestive system:

Large and complex food molecules in the digestive system are converted into small and absorbable forms for the body, which is called digestion. Carbohydrates are large forms whose smaller forms are monosaccharides. Also, small forms of proteins are amino acids, lipids are glycerol, fatty acids, acylglycerols, and cholesterol. These small units can be easily absorbed after hydrolysis. The small hydrolyzed units are now absorbable and can pass through the intestinal mucosa, enter the lymph or blood, and be used by the body. The process of digestion is carried out in the digestive system. This system includes the mouth, pharynx, esophagus, duodenum, stomach, small intestine, large intestine, rectum, lymphatic tissue associated with the intestine, and microflora. Of course, the salivary glands, pancreas, and liver are involved in the process. Digestion and absorption participate in the digestive process [45, 46]. The general pattern of the gastrointestinal tract is the same from the esophagus to the large intestine. This pattern consists of an outer lining, a submucosa, a muscular layer with smooth

muscles in 2 layers, an outer longitudinal layer, and an inner circular layer containing blood vessels, lymphatics, and nerve complexes. Autonomy is located between these muscle layers. Tonsils of cecum and bursa also have a similar structure [45]. The gross microscopic anatomy of the intestine is the same throughout its length except for the epithelium, which varies greatly along the length of the intestine based on function. The epithelium is a part of this overall covering, which is made up of different tissues in each part of the digestive system. In the esophagus, it is made up of a scaly and cut coating, in the small intestine, it is made up of long folds and even in some parts, it is made up of highly specialized cells. The epithelium on the villi is located in a layer of columnar cells that cause mucus secretion by goblet cells, absorption of more nutrients by absorptive enterocytes, and hormone secretion by endocrine cells [45]. Figure 4 shows the effect of air pollutants on different parts of the digestive system.

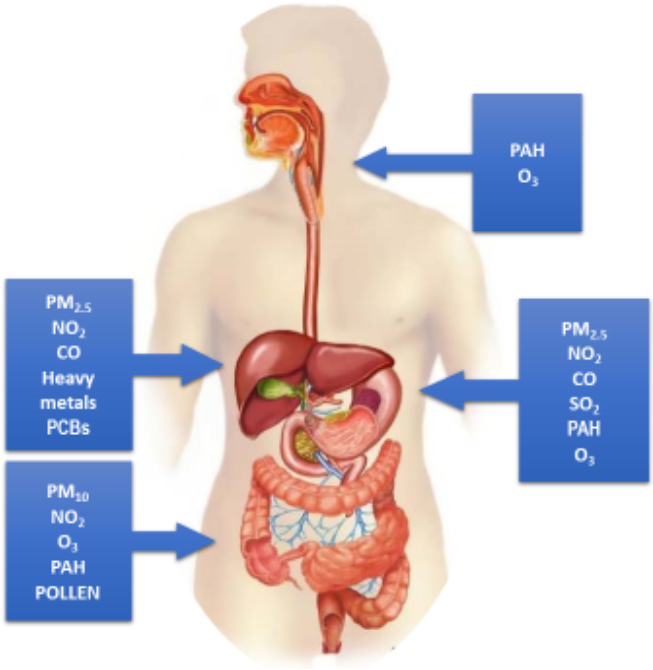

Figure 4. The effect of air pollutants on different parts of the digestive system

3.5 The relationship between air pollution and chronic gastrointestinal diseases:

Air pollutants can enter the human body either through the digestive system or the respiratory system. The digestive system eliminates pollutants by ingesting contaminated food and water and cleaning the particles from the lungs [39]. When pollutants enter the body through the lungs, they are absorbed into the blood. Primary detoxification in humans is done by the liver, and this organ plays an important role in fighting pollutants. Pollutants can cause problems including systemic inflammation, oxidative stress, and indirect damage to the liver [47]. Air pollution has been identified as the most effective cause of stomach cancer. Stomach cancer is associated with the rapid growth of gastric mucosal epithelial cells and causes many deaths every year [39]. Particulate matters (PMs) such as $PM_{2.5}$ affect the stomach and increase the risk of stomach cancer. In places with a high density of gas stations tend to have elevated levels of suspended particles in the air resulting in a direct correlation between suspended particle concentrations and the incidence of stomach cancer. Certain occupations, such as mining, involving exposure to substantial amounts of dust, also increase susceptibility to this cancer [48]. Furthermore, Sulfur in $PM_{2.5}$ also plays a significant role in the risk of stomach cancer [11]. A study conducted in 2019 investigated the relationship between $PM_{2.5}$ and mortality from stomach and colon cancer. Long-term exposure to $PM_{2.5}$ may have been associated with colorectal cancer (CRC). Polycyclic aromatic hydrocarbons (PAHs) and reactive oxygen species (ROS) caused by first transition metals associated with PMs can damage DNA and may cause cancer in the long term by causing continuous inflammation. Finally, it was found that a large number of deaths due to stomach and colon cancer were recorded in high concentrations of this agent, and this incidence was higher in men aged 2 to 65 than in women of the same age [49]. However, this pattern was reversed for indoor air pollution where women were more susceptible to stomach cancer than men. This discrepancy can be attributed to the extended periods housewives spend cooking at home, resulting in increased exposure to indoor air pollution and cooking fumes [16]. Accumulation of fat in the liver, causing inflammation and leading to non-alcoholic fatty liver disease (NAFLD), can eventually turn into liver cancer. Given that the prevalence of NAFLD has been steadily rising since 1980, with approximately a quarter of the world's population affected, it represents a significant public health concerns in the world. NAFLD is mainly caused by an unhealthy diet and lifestyle, and alcohol and tobacco consumption also cause and aggravate this disease. PMs, heavy metals, poly chlorinated compounds and nitrogen dioxide (NO_2) are all pollutants associated with the development of NAFLD. Individuals at higher risk of developing NAFLD due to environmental pollution include those who consume alcohol, smoke, are obese, or follow a high-fat diet [47]. The increase in the incidence of stomach ulcers in the cold seasons of the year when pollutants such as sulfur dioxide (SO_2), NO_2, CO, ozone (O_3), and $PM_{2.5}$ are high is significantly higher than in the hot seasons of the year [13]. Also, NO_2 affects the stomach of elderly patients, especially those over 65 years old, leading to bleeding ulcers [14]. Ozone is a highly oxidative gas pollutant that has adverse consequences on human health, especially microbiomes. In addition to the negative effects it has on the liver, this gas also disrupts the oral microbiome [50, 51]. The intestinal microbiome along with its metabolites such as short-chain fatty acids (SCFAs) can deal with O_3 entering the body, which indicates the importance of the role of microbiomes in relation to O_3 and its effects [51]. Air pollution causes intestinal inflammation

by increasing intestinal permeability and changing the intestinal microbiome. The 2 main pollutants that cause this inflammation are NO_2 and O_3 [11]. CO and PMs are also two important air pollutants that increase in concentration in areas with low vegetation cover and high traffic load. These two pollutants, with O_3 and NO_2, affect the gut microbiome and liver function and cause more liver enzymes (GPT and GOT) to be produced in the body [39, 51]. Cigarette smoke inhalation is one of the leading causes of preventable deaths worldwide. Smoking and smoke inhalation cause and accelerate the development of NAFLD and advanced fibrosis. Additionally, exposure to toxic wastes increases the risk of autoimmune liver disease [40]. Smoking can cause various adverse effects on organs that have no direct contact with the smoke, such as the liver. Among the adverse effects that cigarette smoke causes on the liver are: direct toxic effects, immune effects, and carcinogenic effects [52]. Smoking alters enzymatic and inflammatory pathways in liver physiology. By directly affecting liver cells, tobacco smoke accumulates the key enzymes involved in liver fatty acid synthesis, namely triglyceride, CoA carboxylase (ACC), and fatty acid synthase (FAS), and thus causes fat accumulation in liver cells [40, 52]. In addition, the chemicals created by smoking have cytotoxic potential through the induction of oxidative stress, which activates stellate cells and causes liver fibrosis. Hypoxia is an indirect toxic effect of smoking that occurs when carboxyl levels increase and red blood cells decrease their carrying capacity. Hypoxia induces the production of erythropoietin, which absorbs iron from the gut and increases catabolic iron. Consequently, excess iron accumulates in macrophages and liver cells, leading to increased absorption and catabolic. This iron accumulation in macrophages and group cells, ultimately induces oxidative stress [52]. Pollutants can indirectly affect the intestine by disrupting the body's immune system, thereby increasing the risk of viral infections. Pollutants such as NO_2 reduce immunity and cause inflammation in the mucosa of the digestive tract and eventually infection. Moreover, high doses of PM_{10} also destroy intestinal epithelial cells, which ultimately causes intestinal inflammation [53]. Countries like Japan, which experience high levels of pollution from flower pollen, have observed a rise in the incidence of pancreatic, colon, and stomach cancers, with colon cancer consistently exhibiting a higher prevalence than stomach cancer [54]. Stomach cancer exhibits a significant correlation with heavy metals such as lead, arsenic, and antimony. Men face a higher risk of developing stomach cancer compared to women, potentially attributable to physiological differences. Occupational exposure to asbestos in men or the protective effect of estrogen in women may contribute to these disparities [55-58]. Carbon aerosols and polycyclic aromatic hydrocarbons (PAH) caused by incomplete combustion of diesel and oil engines also play a role in gastrointestinal cancers, including the esophagus, colon, and rectum, and also cause nausea and vomiting [42]. Investigating the concentrations of $PM_{2.5}$ and CO in urban areas during the months of pregnancy of mothers shows the effect of these variables on the fetus.

Table 2. Investigating the sources of pollutants and their effects on the chronic gastrointestinal system

Pollutant	Sources	Effect on the Member	What Effect Does It Have?	References
$PM_{2.5}$	Fuel combustion of motor vehicles Home fireplaces Wood stoves	liver Stomach Colorectal	Causing stomach and colorectal cancer	[38-40, 49]
PM_{10}	exhaust smoke Geological factors	intestine	Destruction of intestinal epithelial cells Intestinal inflammation and infection Diarrhea in children	[41, 53]
NO_2	Fuel combustion of motor vehicles mines Petrochemical Industries	liver Stomach intestine	Rebleeding Gastric ulcer Intestinal inflammation causing gastrointestinal infection Decreased immunity	[11, 39, 42, 47, 53]
SO_2	Petrochemical Industries	Stomach	Causing Gastric ulcer	[13, 26, 42]
CO	Fuel combustion of motor vehicle exhaust smoke	Liver Stomach	Effect on gut microbiome Causing Gastric ulcer Increased secretion of liver enzymes GOT and GPT	[26, 38, 39, 51]
O_3	Wildfire Burning of agricultural residues Fuel combustion of motor vehicles	Stomach intestine Mouth	Causing Gastric ulcer Disrupting the oral microbiome Changing the gut microbiome and causing intestinal inflammation	[11, 39, 43, 51]
Heavy Metals	exhaust smoke Traffic Home heating	Stomach liver	Accumulation of fat in the liver Cause inflammation of the liver liver cancer	[47]
PCBs	Pigmentation Softeners	liver	Cause inflammation of the liver Development of NAFLD	[47, 59]
PAH	Petrochemical Industries petrol and Diesel engine	Esophagus Stomach rectum	DNA damage causing inflammation and various types of cancer Nausea	[42, 49]
Pollen	Plants that produce a lot of pollen The relationship between pollen and some pollutants	Colorectal Pancreas	Causing pancreatic, colon, and stomach cancers	[60]

The results of the biochemical indicators in newborns indicated that increased average concentrations of CO and $PM_{2.5}$ causes more production of liver enzymes and ultimately decreases the weight and height of the newborn [39]. Children from families with a member addicted to substances exhibit signs of oxidative stress, confirming the detrimental effect of passive smoking on the liver [52]. The use of a biogas stoves has also been assiciated with diarrhea in children, who experience a 31 % higher incidence of diarrhea compared to children not exposed to biogas stove usage [57]. Symptoms of diarrhea and fever in children under 3 years old who used high-polluting fuel such as wood and agricultural waste at home instead of low-polluting fuel such as gas and oil have also been common [58]. Air pollution, carrying viruses such as rotaviruses, noroviruses, and other pathogens on PM_{10} particles, can contaminate the living environment through dust. Inhalation or ingestion of these contaminants can lead to intestinal infections and diarrhea in children, and even facilitate the transmission of these diseases to others through the children's feces [53]. Table 2 illustrates the sources of pollutants and their effects on the organs of the digestive system.

4. Conclusion

In this study, the effect of increased risk of gastrointestinal tract disorders due to exposure to various air pollutants, including carbon monoxide, nitrogen oxides, sulfur dioxide, hydrocarbons, dust, and secondary pollutants was estimated. The findings indicated that the combined presence of these pollutants in indoor and ambient air had a synergistic impact on human health.

Authors' Contributions

Mohammad Javad Mohammadi: formal analysis; supervising the project. Maryam Baratifar, Parisa Asban: Writing-review and Editing; search strategy and drafting; supervising the project; editing the manuscript; investigation; resources. Fatemeh Kiani, Maryam Hormati, Raziyeh Kazemi Bareh Bichast: Conceptualization; methodology.

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Conflicts of Interest

The authors declare that they have no conflict of interests.

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Ethical considerations

Ethical approval of the present study was obtained from the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences. According to the national guidelines, individual consent was not required for this type of study. (Ethics Code: IR.AJUMS.REC.1401.139).

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