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A Review of the Effect of Outdoor Polycyclic Aromatic Hydrocarbons on Bladder Cancer

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Abstract

Context: Polycyclic aromatic hydrocarbons (PAHs) are pollutants that are among the most important risk factors for cancer, especially in individuals with underlying diseases. On the other hand, various types of cancers in the vital organs of the body, including the liver, lung, and bladder, and diseases related to the nervous system can be attributed to exposure to this polluting agent. Bladder cancer depends on numerous factors, such as inherited genetic predisposition and external exposure. Polycyclic aromatic hydrocarbons are by-products arising from the incomplete combustion of organic matter. They are found in all environments, such as hospitals, industries, and homes.

Objectives: The purpose of this review study was to investigate the epidemiological literature on the side effects of PAHs on bladder cancer and the risk factors related to cancer.

Methods: A total of 80 articles according to different databases, namely PubMed, Web of Science, Springer, Cochrane, and ScienceDirect, were retrieved. Then, 38 full-text articles were entered into the analysis process. Finally, 12 articles were selected for this study.

Results: The literature review showed that PAH exposure occurs in daily life through exposure to tobacco smoke, consumption of charcoal-smoked meats, and inhalation of air pollutants. The concentration of PAHs is related to the risk of developing bladder cancer during the lifetime of PAHs. Bladder tumors are directly related to exposure to carcinogens. While the exposure to risk factors increases, the risk of developing cancer increases. Risk factors affecting bladder cancer include smoking and occupational and dietary factors.

Conclusions: Polycyclic aromatic hydrocarbons are by-products of incomplete combustion of organic matter. They are found in all environments, such as hospitals, industries, and homes, and they can affect the urinary system, cause dysfunction, and eventually cause bladder cancer.

Keywords: Polycyclic Aromatic Hydrocarbons (PAHs), Risk Factors, Bladder Cancer, Urinary Tract

1. Context

Polycyclic aromatic hydrocarbons (PAHs) are organic chemicals that have multiple rings in their structure. They are produced from human processes and incomplete combustion of organic fuels. Among the most important sources of PAH emission are used cars in cities and individuals' exposure to tobacco smoke and cigarettes (1, 2). Polycyclic aromatic hydrocarbons have different effects. Bladder tumors are directly related to exposure to carcinogens. While the exposure to risk factors increases, the risk of developing cancer increases. Risk factors that affect bladder cancer include smoking and occupational and dietary factors (3, 4). The emission of this pollutant from various anthropogenic and natural sources increases its concentration in the outdoor air. Accordingly, the amount of this pollutant exceeds the permissible limit that can be inhaled by humans.

Among PAHs, 16 compounds are more prominent due to the lack of rapid biological decomposition by microorganisms and as a result of creating toxicity and

danger in the environment; therefore, they are considered the indicators of PAH compounds' pollution. On the other hand, various mechanisms of nature, such as the eruption of volcanoes, can also cause the release of these compounds into the air. Polycyclic aromatic hydrocarbons exist in both the particulate and gaseous phases. There is also a significant relationship between pollutant exposure and carcinogenesis in humans. Humans are exposed to atmospheric PAH mixtures because they are almost ubiquitous (1, 5). Exposure to PAHs causes health problems, such as pulmonary and cardiovascular problems (6, 7). Individuals are exposed to PAH through the inhalation of tobacco smoke, wood smoke, traffic emissions, and food consumption (8, 9). Polycyclic aromatic hydrocarbons are stored in fat, liver, and kidneys. There is a positive and significant relationship between PAH exposure and adverse effects on plants, birds, and mammals.

Urinary tract infections can have profound effects on the health of men and women. It is a very common disease. It can significantly affect the quality of life, leading to a significant economic burden on public health. Signs and symptoms of nonspecific urinary tract infections include fever without a source, which can interfere with rapid diagnosis (7, 10).

Bladder cancer (BC) is very common in men and women around the world. The incidence rate of bladder cancer has shown high numbers in many regions, especially in developing countries where the concentration of air pollutants is higher. There are several genetic polymorphisms for bladder cancer, including genetic effects, lifestyle, environment, occupational exposure, and tobacco (11). Additionally, there are other agents that cause bladder cancer, such as alcohol consumption, coffee consumption, low fruit and vegetable consumption, low selenium, and vitamin E consumption. Men smoke more than women, which is why they are more prone to bladder cancer (12).

2. Objectives

The aim of this study was to investigate the effect of PAHs on the risk factors related to bladder cancer.

3. Methods

3.1. Eligibility Criteria and Search Strategy

This study is a review of English literature. For this purpose, keywords related to polycyclic aromatic hydrocarbons and bladder cancer were first prepared. The keywords used included ((("Urinary tract"[Title/Abstract]) AND (" PAHs"[Title/Abstract])) AND ("Bladder Cancer"[Title/Abstract])) AND ("Risk Factors"[Title/Abstract]) (Table 1). Finally, 549 articles were retrieved according to databases.

3.2. Study Selection

In the following, the search was conducted using these keywords in the search databases of scientific articles, including PubMed, Web of Science, Springer, Scopus, and Google Scholar. Moreover, time and language limitations were not considered in order to collect all the articles related to the topic. Accordingly, after combining keywords related to PAHs and bladder cancer, 93, 112, 65, 48, and 231 articles were obtained from PubMed, Scopus, Springer, Web of Science, and Google Scholar databases, respectively. After completing the search in each database, the articles were transferred to Endnote software for reference. In the software environment, after deleting the items that were entered repeatedly from different databases, first based on the title of the articles and then based on the items that were not specifically related to the topic, the articles were deleted. Then, the abstracts of the remaining articles were studied, and at this stage, the items that were not related to the subject were removed. In the next step, the complete file of all the articles that remained in the screening of the previous steps was prepared and carefully studied. Figure 1 shows the diagram related to the process of searching and filtering the articles found in this study. As can be seen in this figure, initially, 107 articles within January 1, 2000, to March 1, 2023, were found in the mentioned databases. Then, by removing duplicate items, 80 articles entered the stage of examining the title of the articles and removing irrelevant items based on the title of the article. In the following, 50 articles were selected to review the full file of the article. After reviewing 38 complete files of the articles, 12 articles were included in the study and were used to investigate the effect of PAHs on the risk factors related to bladder cancer.

3.3. Data Extraction

The information collected from all the studies included study aims, study setting, statistical analysis, main findings, and limitations. In studies containing health data, study design, study population, health metrics, and outcome assessment were also extracted.

4. Results

4.1. Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are a group of lipophilic organic compounds consisting of two or more fused aromatic rings, which enter the environment

Table 1. Search Terms and Query Results

Term	PubMed	ScienceDirect	Springer	Web of Science	Google Scholar	Unique results
Polycyclic aromatic hydrocarbons	44	26	17	20	61	168
Risk factors	15	17	13	10	47	102
Bladder cancer	8	12	4	4	32	60
Urinary tract	14	7	10	7	29	67
Exposure	12	50	21	7	62	152
Total	93	112	65	48	231	549

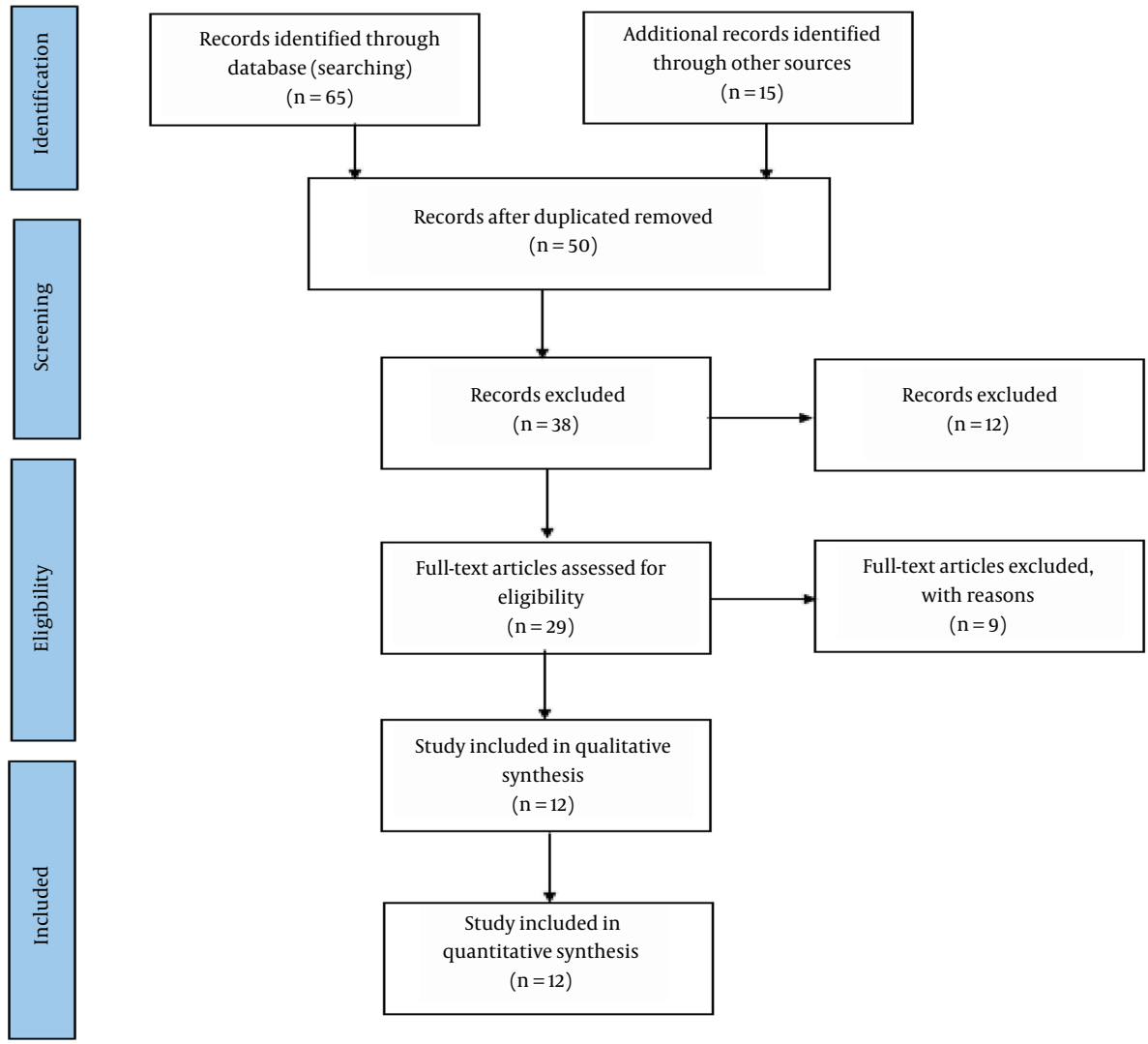

Figure 1. Representation of the search strategy based on PRISMA flow diagram

mainly through human activities. These compounds are a serious threat to the environment and human health. Their molecular structure is linear, clustered, or angular. Polycyclic aromatic hydrocarbons are carcinogenic and mutagenic. Polycyclic aromatic hydrocarbons are highly toxic and have a cumulative property. They have low vapor pressure and low solubility but high melting and boiling points. Exposure to PAHs can cause lung, bladder, and gastrointestinal cancers (13, 14).

Anthracene, consisting of three aromatic rings, makes up a few percent of coal tar. The separation of anthracene from coal tar is the most economical way of production. Anthracene is used as a paint precursor (15, 16). Benzofluoranthenes, such as benzo(y)fluoranthene and benzo(k)fluoranthene, are among the most commonly detected environmental polynuclear aromatic hydrocarbons, occurring in gasoline engine exhaust, urban air, cigarette smoke, soil, water, and broiled and smoked foods (17). Benzo (a) pyrene (BaP) is one of the aromatic hydrocarbons that have five benzene rings. The structure of this compound contains colorless isomers that are created as a result of the chemical connections of pyrene and phenylene. The studies and experiments conducted on animals have proven that this substance can cause diseases, including cancer, in a systemic way and in different organs (18).

Benz-anthracene (Bah A), recognized as a group 2A carcinogen by the World Cancer Research Center, is the first polycyclic aromatic hydrocarbon to undergo a purification process. From the past until now, numerous studies have been conducted on this compound to investigate various dimensions and aspects of cancers caused by PAHs. Although this substance is highly used for studies related to its carcinogenic properties, the presence of excessive amounts of it in oil-contaminated areas and coal manufacturing industries has reduced its popularity (19).

Chrysene is another aromatic compound with four rings. Based on continuous research and sampling, this compound is present in relatively high amounts in the inhaled ambient air of many regions. Additionally, much evidence has proven that the exposure of this pollutant to the sun's ultraviolet radiation causes photo-genotoxic effects in this substance. In this case, exposure to chrysene might cause mutations in genes and the occurrence of cancer-related disorders (20). Naphthalene, which is a solid, white, aromatic hydrocarbon, is made from two fused rings of benzene. This aromatic hydrocarbon, which is mostly used as an insecticide, can cause various disorders in vital organs, such as the liver, kidney, eyes, and intestines, and other abnormalities (21).

4.2. Origin of Production and Distribution of Polycyclic Aromatic Hydrocarbons

The release of PAHs in the environment is generally through natural sources and human activities. Sources that emit PAHs include fixed and mobile sources.

4.2.1. Fixed Sources

4.2.1.1. Domestic Sources

Internal sources of PAH production include heating, cooking, burning waste, wood, or other organic materials. Climate change (due to the use of home heating systems) can affect the release of PAHs. Internal sources of hydrocarbons can be very dangerous for residents (22-24). Numerous major countries around the world, such as China, India, Southeast Asia, parts of South America, and Africa, use wood burning for daily cooking. Another source of indoor PAH production is cigarette smoke. In smoker's homes, PAHs are more than in non-smoker's homes (25).

4.2.1.2. Industrial Sources

Industrial activities produce PAHs, such as tire and cement production, petrochemical industries, bituminous pitch and asphalt factories, wood protection, electricity generation, and waste incineration. The fuels of industry are gas, oil, and coal. Xu et al. examined PAH diffusion from a rubber factory. The total PAH emission of the rubber company was 42.3 g/day, with an emission factor (EF) of 4 mg/kg (26). Yang et al. reduced PAH particles and gas emissions by using air pollution control devices. Particle and gas removal efficiencies were 42.5% and 11.7% for PAH, respectively (27). Yang et al. reported that PAH EFs from industrial stacks were 3.5 mg/kg of raw material. They also noticed that EFs for benzopyrene ranged from 1.87 to 15.5 μg/g of raw material. Researchers have studied the release of hydrocarbons (28). The Italian Environmental Protection Agency has reported hydrocarbon emissions were more than 200 micrograms per gram in municipal and industrial waste incinerators. The highest PAH emissions from medical incinerators in the same city exceeded 871 μg/kg of waste (24, 29).

4.2.2. Mobile Sources

Mobile resources cause numerous PAH emissions. Mobile sources include vehicle exhaust fumes, including cars, airplanes, and other means of transportation. Various polycyclic hydrocarbons are released into the ambient air from mobile sources that use fossil fuels, including diesel, gasoline, and coal. The air-to-fuel ratio has a large effect on the emission of hydrocarbon polycarbonates. The lower the ratio, the lower the PAH emission (30). Vehicle exhausts have a significant role in the concentration of

aromatic hydrocarbons in urban areas. de Abrantes et al. stated that the use of low ethanol fuel could reduce PAH emissions (31). Yang et al. concluded that the diffusion rate of 4-stroke (4-Stk/FI) motorcycle fuel injection was 3.390 mg/km. The EF equivalent to the total BaP is 10.8 μg/km, which indicates that the amount of emissions discharged from the 2-Stk/Cb motorcycle contains cancer-causing compounds and agents (27).

4.2.3. Natural Sources

Natural sources of hydrocarbon emissions include accidental forest fires, volcanic eruptions, and decaying organic matter. Meteorological parameters, such as wind speed and direction, temperature, and relative humidity, are among the influencing factors on the release rate of PAHs. There are numerous PAHs in nature, including benzo (a) anthracene (BaA), benzo (a) pyrene (BaP), benzo (b) fluoranthene (BbF), chrysene, and naphthalene (6, 32). Internal sources of PAH production are shown in Figure 2.

4.3. Polycyclic Aromatic Hydrocarbons as Carcinogenic Agents

Based on published information from numerous studies, the risk of cancer in organs, such as the liver, lung, bladder, circulatory system, digestive system, and nervous system, is largely related to PAHs. Among the factors affecting the release rate of PAHs into the ambient air, we can mention the climatic conditions of the living area of individuals and the sources of emission of this pollutant (33). A number of the mentioned PAHs can cause numerous and sometimes irreparable genetic changes in human deoxyribonucleic acid (DNA) and have shown teratogenic properties in many cases. On this basis, exposure to these toxic and carcinogenic compounds can cause acute and chronic poisonings and various abnormalities, including kidney failure and pulmonary and blood disorders. On the other hand, most of the studies on the effect of PAHs on humans have been carried out in the outdoor environment and ambient air, and less attention has been paid to the indoor environment (34). This is despite the fact that, in general, individuals spend much time in their homes or closed work environments (33). Therefore, even during cooking, if the meat is cooked at a high temperature, there will be a possibility of producing polyaromatic hydrocarbons in it.

Polycyclic aromatic hydrocarbons are lipophilic and tend to precipitate in water. They have been observed in the air as a gas or attached to fine suspended particles. Although PAHs are relatively stable molecules, it is possible to gradually decompose them due to ultraviolet light radiation or the activity of some microorganisms. About 500 types of PAHs have been identified; however, due to the dangers caused by benzo (a) pyrene, most studies are focused on it (35). Polycyclic aromatic hydrocarbons usually enter the human body less through the skin. They often enter the body through eating and drinking and mostly through inhalation. What has caused more attention is the carcinogenic and mutagenic power of some aromatic hydrocarbons, especially benzo (a) pyrene. For this reason, standards have been developed to determine their permissible limits. The limits established for exposure to these cyclic aromatic compounds in occupational exposure for coal tar pitch volatile (CTPVs) substances are 0.2 mg/m^3 and 0.1 mg/m^3 for 8 hours (36).

4.4. Risk Factors for Bladder Cancer

Bladder cancer depends on many factors, such as inherited genetic predisposition and external exposure. They have different effects. Bladder tumors are directly related to exposure to carcinogens. While the exposure to risk factors increases, the risk of developing cancer increases. Risk factors that affect bladder cancer include smoking and occupational and dietary factors (Figure 3).

4.4.1. Smoking Factor

Smoking is one of the high-risk behaviors and an agent that threatens individuals with bladder cancer. The researchers stated that the relative risk of bladder cancer was significantly increased among smokers. In addition, individuals who use or are exposed to smoke have a greater potential of dying from bladder cancer compared to other individuals. Therefore, individuals who quit smoking are at lower risk than individuals who smoke. This study showed that individuals who have never smoked are at lower risk than individuals who quit smoking (37). There are many toxic, carcinogenic, and mutagenic substances in tobacco smoke. As a result, individuals who smoke are exposed to these toxic and mutagenic substances. The major toxins in cigarettes are hydrocarbon polyaromatics (38).

Based on many studies, a positive correlation has been observed between exposure to relatively high and continuous concentrations of tobacco smoke and bladder and urinary tract cancer. Some compounds, such as β-naphthylamine, which is an aromatic substance in tobacco smoke, cause oxidative stress and stop or reduce apoptosis. As a result of this event, the excessive accumulation of cells in one point of the bladder or urinary tract provides the basis for the formation of cancerous masses. These substances, similar to other body toxins, might be excreted through the kidneys; however, their high concentrations will eventually cause cancer (39).

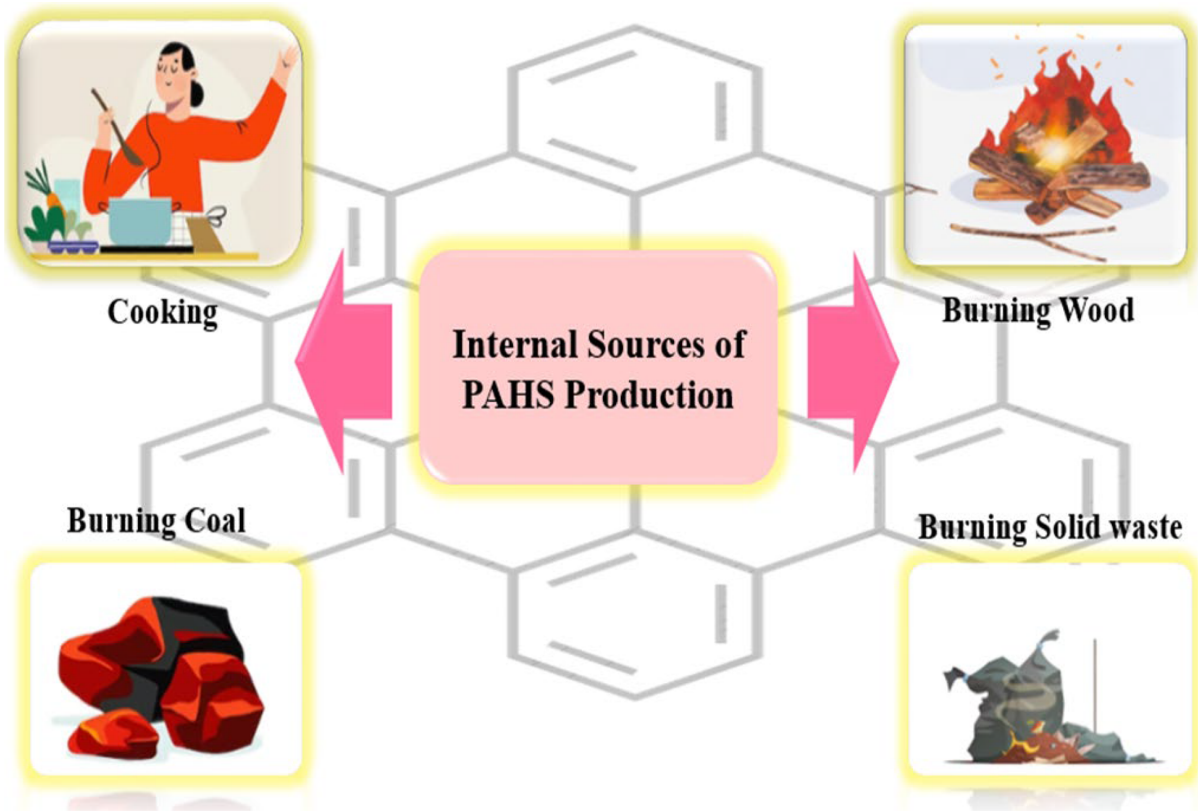

Figure 2. Internal sources of polycyclic aromatic hydrocarbons (PAH) production

4.4.2. Occupational Factor

Exposure to occupations related to coke, coal, construction paints, furnaces, and textile manufacturing industries can increase the rate of bladder cancer. Polycyclic aromatic hydrocarbons are produced in industrial processes, such as dyeing, rubber manufacturing, and burning fuel (40). Burning coal, wood, gas, tobacco, or waste produces hydrocarbons. These compounds are abundant in fossil fuels. They enter the body through the skin or by respiration. These toxic substances, which are also capable of causing cancer, are broken down by the kidneys in the body and then removed from the body by the urinary system. About 20% of bladder cancers are due to exposure to industrial occupations, such as paints, metals, and petroleum products (41). A study by Samanic et al. showed that individuals who worked as machine operators in the printing industry were more likely to develop bladder cancer. Nevertheless, no association was noticed between farmers and bladder cancer (42). Risk factors that affect bladder cancer are depicted in Figure 3.

4.5. Bladder Cancer Associated with Exposure to Polycyclic Aromatic Hydrocarbons

The substances that are left in nature, whether they are of natural origin or those that are created during human activities, also have effects on the environment and human societies; if they enter or have an adverse effect on the environment as pollutants and in the event of side effects, such as affecting the functioning of the glands and the occurrence of cancer in the human body, they are considered carcinogens. Polycyclic aromatic hydrocarbons are among the most important environmental carcinogens that have natural and human origins. Polycyclic aromatic hydrocarbons are absorbed in the body in three ways: Breathing (lungs and air sacs), contact (skin), and digestion (in the liver and kidney) (43). The speed of PAHs entering the body is influenced by the presence of compounds that a person is exposed to at the same time. The absorption of PAHs from ingestion is usually slow and occurs mostly through inhalation (44). Therefore, numerous epidemiological studies have shown that there is a high risk of bladder cancer in individuals exposed to PAH caused by cigarette smoke; therefore,

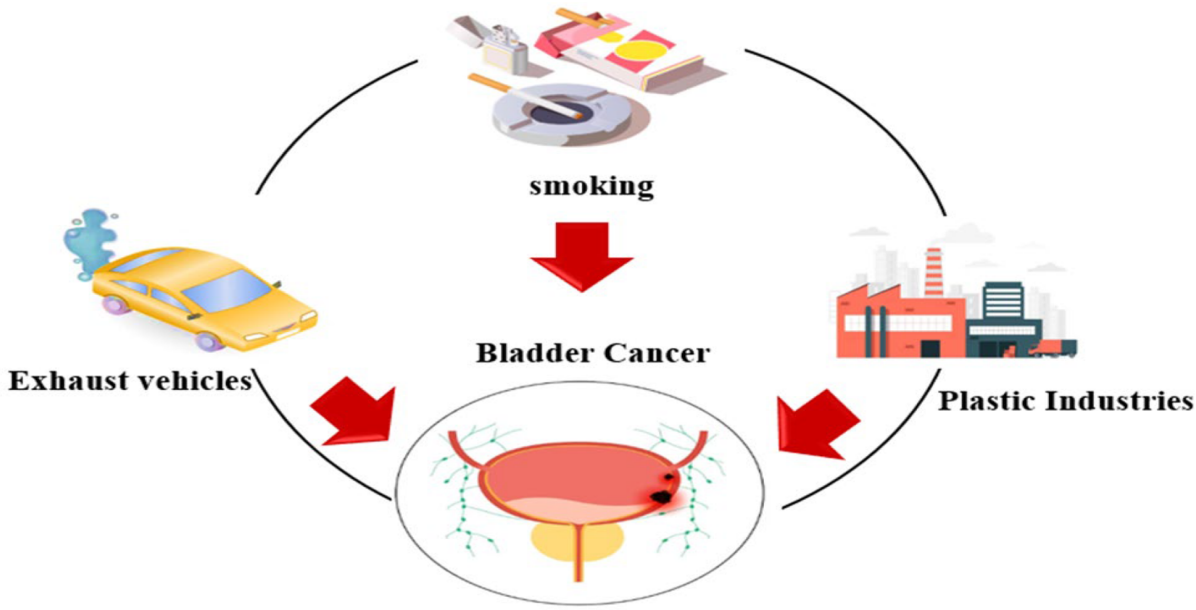

Figure 3. Risk factors affecting bladder cancer

the number of cigarettes smoked in a day and the years of smoking determine the risk of bladder cancer. Urine stays in the bladder for a long time; consequently, there is ample time for carcinogens to affect the bladder. The duration of PAH contact with the bladder is high; as a result, it increases the risk of cancer.

Men smoke more than women and are more exposed to industrial pollutants, which is why men are more likely than women to develop bladder cancer. Aromatic amines (aryl amines) are used in various industrial and agricultural activities (45). These compounds (aromatic amines with 2-naphthylamine and 4-aminobiphenyl) are converted into compounds in body tissues, some of which are less dangerous and some of which are more harmful than the original PAHs. Animal studies show that PAHs do not tend to stay in various tissues for a long time, and most of these compounds are removed from the body after a few days through feces and urine. The type and severity of the effects that PAHs have on human health depend on several factors, including the received dose, duration of exposure, health status of the person, underlying diseases, and route of exposure (46).

5. Conclusions

Polycyclic aromatic hydrocarbons are highly toxic and have a cumulative property. They are mainly emitted from natural resources and human activities. Sources that release PAHs include fixed sources and mobile publications. There are many toxic, carcinogenic, and mutagenic substances in tobacco smoke. As a result, individuals who smoke are exposed to these toxic and mutagenic substances. The major toxins in cigarettes are hydrocarbon poly aromatics. Polycyclic aromatic hydrocarbons are produced in industrial processes, such as dyeing, rubber manufacturing, and burning fuel. Foods containing vitamins and antioxidants have anti-cancer properties. Because these substances are eventually excreted in the urine, they are thought to prevent bladder cancer. The results of this study showed that long-term exposure to PAHs, especially in high concentrations, causes the bioaccumulation of these tumor-causing compounds in fat tissues and causes cancerous tumors over time.

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Footnotes

Authors' Contribution: M. B., P. A., F. KN, M. J-M, and M. F. were the principal investigators of the study and drafted

the manuscript. P-A, MJ-M, and A-F were the advisors of the study. A. S., M. T., and B. F. performed the statistical analysis. All the authors contributed to the design and data analysis and assisted in the preparation of the final version of the manuscript. All the authors read and approved the final version of the manuscript.

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