Review Article

A Systematic Review on the Effects of Polycyclic Aromatic Hydrocarbons on Cardiometabolic Impairment

Abstract

Background: Various epidemiological studies have shown that exposure to environmental pollutants including polycyclic aromatic hydrocarbons (PAHs) might increase the risk of cardiovascular diseases (CVDs) and their risk factors. This study aims to systematically review the association of PAH exposure with metabolic impairment. **Methods:** Data were collected by searching for relevant studies in international databases using the following keywords: "polycyclic aromatic hydrocarbon" + "cardiovascular disease," PAH + CVD, polycyclic aromatic hydrocarbon and "air pollutant" + "CVD," and the desired data were extracted and included in the study according to the systematic review process. **Results:** From the 14 articles included in the present systematic review, eight articles were conducted on the relationship between PAH and CVDs, four articles were conducted to examine the association of PAH exposure with blood pressure (BP), and two articles investigated the link between PAH and obesity. **Conclusions:** Most studies included in this systematic review reported a significant positive association of PAH exposure with increased risk of CVDs and its major risk factors including elevated BP and obesity. These findings should be confirmed by longitudinal studies with long-term follow-up.

Keywords: *Blood pressure, cardiovascular disease, myocardial infarction, polycyclic aromatic hydrocarbon*

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Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_144_17

Quick Response Code:

Introduction

Nowadays, in spite of great advances in technology, as well as in the diagnosis and treatment modalities for various diseases, cardiovascular diseases (CVDs) are still the number one cause of death, accounting for a third of deaths worldwide.[1,2]

As shown in the literature, various factors such as malnutrition, stress, and exposure to environmental pollutants[3] could cause CVDs through atherosclerosis, angina pectoris, and myocardial infarction.[4] Epidemiological evidence indicates that exposure to certain substances in the air may cause increased risk of CVDs in human subjects.[5] Polycyclic aromatic hydrocarbons (PAHs) are of a major constituent of air pollutants, which is positively associated with cardiometabolic risk factors and atherosclerosis.[6-8]

PAHs are strong atmospheric pollutants that are mainly produced by incomplete combustion of organic materials and fossil fuels emitted from exhausts of motor vehicles, cigarette smoke, coal burning, household cooking, and industrial products, which has caused a mounting concern among the public.[9,10] PAH exposure might increase the rate of CVDs.[11] PAH exposure occurs differently by inhalation, ingestion, and dermal exposure.[9] The absorbed PAH enters into the body's metabolic process and finally, it is excreted through the urine.[12] However, some believe that PAH accumulates in adipose tissues and liver.[13]

It is documented that PAH exposure is associated with decreased cardiac autonomic function.[9] In addition, PAH exposures in certain occupational circumstances and CVD-caused mortality have been reported to be positively correlated.[14,15] Moreover, PAH exposure is shown to worsen atherosclerosis through inflammation.[16] However, still these effects of PAHs remain controversial. This systematic review aims to assess the relationship of PAH exposure with CVDs and their risk factors.

Methods

In this systematic review, we searched the databases of PubMed, Medline, ProQuest, and Google Scholar from 2000

How to cite this article: Poursafa P, Moosazadeh M, Abedini E, Hajizadeh Y, Mansourian M, Pourzamani H, *et al*. A systematic review on the effects of polycyclic aromatic hydrocarbons on cardiometabolic impairment. Int J Prev Med 2017;8:19.

to 2017. A number of major, sensitive keywords including "polycyclic aromatic hydrocarbon" AND "cardiovascular disease," PAH AND CVD, polycyclic aromatic hydrocarbon AND "air pollutant" AND "CVD" were used to retrieve relevant papers.

Selection criteria and quality assessment of the articles

At first, we prepared a list of titles and abstracts of articles available in the above-mentioned databases; then the articles were studied independently for selecting relevant titles. Duplicates were omitted through examining the titles, name of the author(s), year of publication, journal name, and issue number. After a careful study of the texts of the articles, relevant articles were selected and the rest were not included in this review. Then, the quality of relevant articles was assessed using the standard checklist of Strengthening the Reporting of Observational Studies in Epidemiology.[8] This checklist contains 43 diverse sections evaluating the various aspects of research methodology, including sampling methods, measurements, statistical analysis, and study objectives. In this checklist, by assigning one score to each section, papers could get a minimum score of 40 and a maximum score of 45. Finally, the articles that got scores higher than the minimum (40 points) were included in the review. The data of the selected articles were extracted in the form of name of the first author, study setting, year of publication, methodology, key findings, and outcomes.

Inclusion criteria

After achieving the required score during the quality assessment process, English-written articles examining the correlation between PAH and CVDs were included in this systematic review.

Exclusion criteria

Studies with scores lower than 40, based on the quality assessment checklist, as well as the studies that examined other pollutants were excluded from this review.

Results

At the first step of searching in the databases, 122 articles with relevant titles were obtained, from which 88 nonrelevant articles were then removed after careful examining of the titles. Further, twenty articles were also discarded due to being duplicated in the databases, leaving a total of 14 relevant articles for further review as they met the required inclusion criteria and obtained the necessary score based on the quality assessment checklist [Figure 1].

Of the 14 articles included in this review, eight articles assessed the relationship between PAH exposure and CVDs,[9-11,13,15-18] four examined this association with blood pressure (BP),[19-22] and two with obesity.[13,23] A summary of the main findings of these articles is shown in Table 1.

The information of the studies included in the review was as follows:

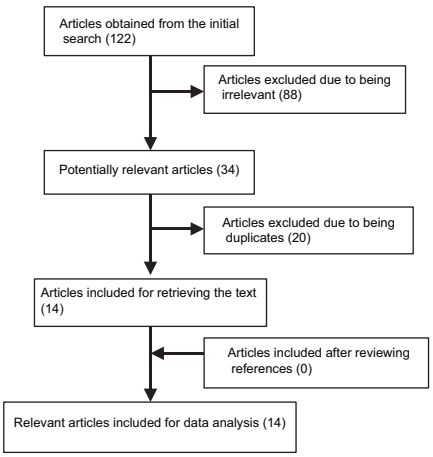

Figure 1: Flowchart of the database search, selection, and review process of articles

- Methods: Time-series studies were the most frequent study type among the selected articles,[11,16,18,19,24] followed by retrospective cohort,[10,13,15,23] cross-sectional,[9,20,21] quasi experimental,[17] and panel[22] studies
- Study population: The greatest number of participants was 15,447 individuals, as reported in one time-series study,[24] whereas the lowest number of participants was reported as 88 individuals in a panel study[22]
- Setting: Most of the studies[10-13,16-19,21,23,24] were performed in the United States, while others were conducted in different geographical regions around the world including Denmark, Finland, France, Germany, the Netherlands, Norway,[15] China,[9] Saudi Arabia,[20] and Belgium[22]
- Outcome: In most of the included studies, the outcome was reported as CVDs entitled, cardiovascular disease,[10,11,18] fatal ischemic heart disease,[15] heart rate variability,[9,17] inflammation, atherosclerosis,[16] and cardiometabolic heart rate.[13] However, the outcome was reported as BP with the titles of hypertension[19,21] and systolic and diastolic BP[20,22] in three of the studies, and as obesity[13,23] in one of them
- Key findings: Majority of the studies revealed significant positive association between PAH exposure and risk of CVDs.[9,10,13,17,18] However, the results in the study by Clark *et al*.[11] showed the opposite, as they claimed that no significant relationship existed between PAH exposure and risk of CVDs. Moreover, a positive association was reported between PAH exposure and hypertension,[16,19-22] as well as between PAH exposure and obesity[13,23] in some of the studies.

Discussion

In this systematic review, we assessed the relationship of PAH exposure with cardiometabolic impairment. The findings showed that PAH exposure and risk of CVD were significantly positively correlated. PAH-rich sources

Table 1: Summary of studies included in the systematic review

Author	Study design	Study participants	Place	Implication	Key findings
Alshaarawy *et al*., 2016[10]	Retrospective cohort 2001-2010	3550 males and 3751 females	US	Cardiovascular disease	PAH exposure was positively associated with CVD (β=0.12; 95% CI: 0.03-0.20)
Xu *et al*., 2010[18]	Time-series study	13,156 people	US	Cardiovascular disease	PAH was significantly associated with self-reported CVD. Patients within the middle and highest tertiles had higher self-reported CVD (the second tertile: AOR=1.29, 95% CI: 0.97-1.72; the third tertile: AOR=1.45, 95% CI: 1.01-2.07; *P* for trend=0.04)
Burstyn *et al*., 2005[15]	Retrospective cohort 1953-2000	12,367 male asphalt workers	Denmark, Finland, France, Germany, Israel, The Netherlands, and Norway	Fatal ischemic heart disease	There is a positive relationship between benzo-(a) pyrene exposures of 273 ng/m^3 or higher, for which the relative risk was 1.64 (95% CI 1.13-2.38)
Feng *et al*. 2014[9]	Cross-sectional	1978 adult residents	Wuhan, China	HRV	Elevated total concentration of all PAH metabolites (ΣOH-PAHs) was associated with decreased LF and LF/HF (*P* for trend=0.005 and <0.0001, respectively)
Shiue, 2015[19]	Time-series study	5560 adults	US	Hypertension	Urinary 4-hydroxyphenanthrene was associated with hypertension (OR: 1.33, 95% CI: 1.00-1.76, *P*=0.048, PAR: 5.1%), urinary 1-hydroxypyrene was significantly associated with heart attack (OR: 1.47, 95% CI: 1.05-2.06, *P*=0.027, PAR: 1.7%), and urinary 2-hydroxynapthalene (2-naphthol) was associated with cancer (OR: 1.46, 95% CI: 1.12-1.90, *P*=0.008, PAR: 3.9%)
Trasande *et al*., 2015[20]	Cross-sectional	184 adolescent males	Jeddah, Saudi Arabia	Systolic and diastolic BP	Systolic (0.47 SD units, *P*=0.006) and diastolic (0.53 SD units, *P*<0.001) BP *Z*-scores were highest at the maximum PAH, with a 4.36-fold increase in prehypertension (*P*=0.001)
Rundle *et al*., 2012[23]	Retrospective cohort 1998-2006	African-American and Hispanic children aged 5 (*n*=422) and 7 (*n*=341) years	Bronx or northern Manhattan, New York	Childhood obesity	Children of mothers in the highest exposure tertile had a 0.39-unit higher body mass index *Z*-score (95% CI: 0.08-0.70) and a relative risk of 1.79 (95% CI: 1.09-2.96) for obesity at the age of 5 years, and they had a 0.30-unit higher body mass index *Z*-score (95% CI: 0.01-0.59), a 1.93-unit higher percentage of body fat (95% CI: 0.33-3.54), and a relative risk of 2.26 (95% CI: 1.28-4.00) for obesity at the age of 7 years. The data indicate that prenatal exposure to PAHs is associated with obesity in childhood
Everett *et al*., 2010[16]	Time-series study	999 participants	US	Inflammation and atherosclerosis	OH-PAHs were classified as low, medium, and high. Low OH-PAH was 2-hydroxyphenanthrene ≤48 ng/g creatinine and 9-hydroxyfluorene ≤160 ng/g creatinine. High OH-PAH was 2-hydroxyphenanthrene >148 ng/g creatinine or 9-hydroxyfluorene >749 ng/g creatinine

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Table 1: Contd...

Author	Study design	Study participants	Place	Implication	Key findings
Liu *et al*., 2016[24]	Time-series study	15,447 children	US	Asthma	Remarkable association between urinary 2-phenanthrene and diagnosed asthma in boys (OR: 2.353, 95% CI: 1.156-4.792; *P*=0.021) aged 13-19 years. Positive association was observed between ever wheeze and 4-phenanthrene among girls aged 13-19 years (OR: 4.086, 95% CI: 1.326-12.584, *P*=0.043)
Clark *et al*., 2012[11]	Time-series study	3219 participants	US	CVD	There is no significant relationship between PAH exposure and CVD disease
Ranjbar *et al*., 2015[13]	Retrospective cohort 2001-2008	4765 adult participants	US	Cardiometabolic health risk	PAH is related to obesity and the expression of a number of obesity-related cardiometabolic health risk factors (*P*<0.05)
Yang *et al*., 2016[17]	Quasi-experimental	489 coke-oven workers	US	HRV	PAH exposure was associated with plasma cytokines, and higher cytokines were associated with decreased HRV (*P*<0.05)
Bangia *et al*., 2015[21]	Cross-sectional	11,218 participants	Texas	Hypertension	A positive association between PAHs and hypertension (medium exposure, AOR=1.09, 95% CI: 0.88-1.36; high exposure, OR=1.40, 95% CI: 1.01-1.94)
Jacobs *et al*., 2012[22]	Panel study	88 nonsmoking persons	Antwerp, Belgium	Systolic and diastolic BP	Each PAHs' increase of 20.8 μg/m ≥in 24-h mean outdoor PM (2.5) was associated with an increase in pulse pressure of 4.0 mmHg (95% CI: 1.8-6.2), in persons taking antihypertensive medication (*n*=57), but not in persons not using antihypertensive medication (*n*=31) (*P* for interaction: 0.02)

PAHs=Polycyclic aromatic hydrocarbons, CVDs=Cardiovascular diseases, OR=Odds ratio, AOR=Adjusted OR, CI=Confidence interval, HF=High frequency, LF=Low frequency, OR=Odds ratio, BP=Blood pressure, SD=Standard deviation, HRV=Heart rate variability, PM=Particulate matter

such as cigarette smoke,[15] exhaust smokes, and cooking smoke[25-27] are known as risk factors influencing the human cardiovascular system. According to studies conducted in this area, people with cardiometabolic risk factors are more vulnerable in PAH-contaminated environments; here, the elderly[28] as well as people with diabetes,[29] overweight,[30] heart disease,[31] and high systemic inflammation[32] are under greater influence. A cross-sectional study[18] showed that PAH exposure is positively associated with the prevalence of self-reported CVDs. However, another study[11] demonstrated no significant connection between PAH exposure and CVDs through inflammation; however, this study did not discuss the possible underlying reasons to adequately support their findings.

Furthermore, the results showed that PAH exposure is significantly correlated with elevated BP. Accordingly, it was reported that systolic and diastolic BP is higher in students in schools close to oil refineries and those who are exposed to large amounts of this substance, as compared to those in schools outside this area.[20] Another study showed that the prevalence of hypertension increases with increasing age, living in high-traffic areas, and body mass index.[21] Likewise, studies conducted on people with elevated cholesterol, history of myocardial infarction, or diabetes, as well as those with physical disabilities, showed an increased prevalence of hypertension as a result of PAH exposure. A positive relationship is also documented between PAH exposure and BP level.[22] Experimental studies have indicated that exposure to PAH-containing organic compounds might lead to elevated arterial BP.[33]

It is also documented that a significant relationship exists between PAH exposure and obesity. In this regard, it is found that prenatal PAH exposure can demonstrate its effects as obesity at the age of 5, as well as higher BMI, obesity, and fat mass at the age of 7.[23] The effects observed on the body size of children prenatally exposed to PAH can be detected through accumulation of fat mass in their bodies, and not by their differences with fat-free mass. Women smoking cigarettes during pregnancy expose their fetuses to high concentrations of PAH, which is in

turn correlated with weight gain in childhood, during adolescence and then, at young ages.[34,35]

Conclusions

The findings of this systematic review support a significant positive association of PAH exposure with increased risk of CVDs and their major risk factors, notably elevated BP and obesity. Longitudinal studies with long-term follow-up are necessary in this field.

Financial support and sponsorship

This study was conducted as part of the project number 193042, funded by Isfahan University of Medical Sciences,Isfahan,Iran. The current review was conducted without financial support.

Conflicts of interest

There are no conflicts of interest.

Received: 06 Nov 16 **Accepted:** 14 Mar 17
Published: 06 Apr 17

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