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 cardiometabolic 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

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

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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. 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:

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
| 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[13] | 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-hydroxy-pyrene was significantly associated with heart attack (OR: 1.47, 95% CI: 1.05-2.06, P=0.027, PAR: 1.7%), and urinary 2-hydroxynaphthalene (2-naphthol) was associated with cancer (OR: 1.46, 95% CI: 1.12-1.90, P=0.008, PAR: 3.9%)    |
| Transande 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    |

Contd...
such as cigarette smoke, exhaust smokes, and cooking smoke 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 as well as people with diabetes, overweight, heart disease, and high systemic inflammation are under greater influence. A cross-sectional study showed a positive association between PAH exposure and hypertension (medium exposure, AOR=1.09, 95% CI: 0.88-1.36; high exposure, OR=1.40, 95% CI: 1.01-1.94) and high systemic inflammation are under greater influence. A cross-sectional study showed that PAH exposure is positively associated with the prevalence of self-reported CVDs. However, another study 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. Another study showed that the prevalence of hypertension increases with increasing age, living in high-traffic areas, and body mass index. 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 obesity and the expression of a number of obesity-related cardiometabolic health risk factors (P<0.05). 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. 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

| Author           | Study design        | Study participants | Place   | Implication          | Key findings                                                                 |
|------------------|---------------------|--------------------|---------|----------------------|-------------------------------------------------------------------------------|
| Liu et al., 2016 | 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 | Time-series study   | 3219 participants  | US      | CVD                  | There is no significant relationship between PAH exposure and CVD disease |
| Ranjbar et al., 2015 | 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 | Quasi-experimental study | 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 | Cross-sectional study | 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 | 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
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.

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**Conflicts of interest**

There are no conflicts of interest.

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