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LITERATURE REVIEW Open Access

Systematic Review: Impact of Air Pollution on DNA Methylation

Tinjauan Sistematis : Dampak Polusi Udara pada Metilasi DNA

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ABSTRACT

Background: Quality of life is an important. It is influenced by exposure to chemicals in the body, such as air pollution, which can damage supporting life in the future.
Objective: The aim of writing this systematic review is to specify the impact of air pollution on DNA methylation.
Methods: The method in this study uses the Preferred Reporting Items for Systematic Review and Meta-analyses, this methode is carried out by searching for data in the form of articles or journals, which is carried out using the keywords "Air pollution" and "DNA methylation". Overall data from articles or jurnals based on searches using the keywords "Air pollution" and "DNA Methylation" (n=25), data from articles or journals focused on this research and articles or journals that can be accessed for free with the year publication year in the last 10 years (n=20), after which they are adjusted to the inclusion criteria of this study (n=15).
Result: In this study, the results of the systematic review were obtained that this long-term impact will affect a person's quality of life, apart from that, it can also cause serious complications such as repeated respiratory infections, which can lead to decreased lung function and a higher risk of death.
Conclusion: DNA is a logical tool for understanding the impact of air pollution on genome function and downstream activities that benefit health.

Keywords: Air pollution, DNA methylation, Humans, Impact, Life expectancy

ABSTRAK

Latar Belakang: *Kualitas hidup adalah hal yang penting dalam kehidupan. Kualitas hidup dipengaruhi oleh paparan bahan kimia dalam tubuh, seperti polusi udara, yang dapat memiliki dampak negatif terhadap kehidupan di masa depan.*
Tujuan: *Tujuan menulis tinjauan sistematis ini adalah untuk menentukan dampak polusi udara terhadap metilasi DNA.*
Metode: *Metode pada penelitian ini menggunakan metode* Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) *metode ini dilakukan dengan cara mencari data dalam bentuk artikel atau jurnal yang dilakukan dengan menggunakan kata kunci "Polusi udara" dan "Metilasi DNA". Data keseluruhan dari artikel atau jurnal berdasarkan pencarian menggunakan kata kunci "Polusi udara" dan "Metilasi DNA" (n=25), data artikel atau jurnal yang fokus pada penelitian ini dan artikel atau jurnal yang dapat diakses secara gratis dengan tahun publikasi dalam 10 tahun terakhir (n=20), setelah itu disesuaikan dengan kriteria inklusi penelitian ini (n=7).*

Hasil: *pada penelitian ini diperoleh hasil tinjauan sistematis, bahwa dampak jangka panjang ini akan mempengaruhi kualitas hidup seseorang, selain itu juga dapat menyebabkan komplikasi serius seperti infeksi pernapasan berulang, ini dapat menyebabkan fungsi paru yang menurun dan risiko kematian yang lebih tinggi.*
Kesimpulan: *DNA adalah alat logis untuk mencoba memahami dampak polusi udara terhadap fungsi genom dan aktivitas downstream yang menguntungkan kesehatan.*

Kata Kunci: *Dampak, Harapan hidup, Metilasi DNA, Manusia, Polusi udara*

INTRODUCTION

Contamination that occurs in the surrounding environment, both indoors and outdoors, by chemical, physical, or biological substances and anything that alters the natural characteristics of the atmosphere can be called air pollution (Nassikas *et al.*, 2024). In general, household combustion equipment, forest fires, industrial facilities, and motorized vehicles are sources of air pollution (World Health Organization, 2018). The primary public health concerns of pollutants include particulates, nitrogen dioxide, carbon monoxide, ozone, and sulfur dioxide (Kelly and Fussell, 2015). Pollution of the air originating from indoors and outdoors causes respiratory and other diseases and is a source of illness and even death. Data from the WHO indicates that almost the entire population, or 99% of people, inhales air pollution that exceeds WHO standards and contains high levels of pollutants. Low- and middle-income countries may also experience high exposure (World Health Organization, 2023). The effect of exposure to air pollution on public health ranges from increased hospitalizations and ER visits, disease attacks to increased risk of premature death (Kim *et al.*, 2018).

In an indoor environment, exposure to PM2.5 from burning firewood for 1-2 hours per day (e.g., for cooking in a traditional kitchen) can reach concentrations of 100-1000 µg/m³, far exceeding the WHO's safe limit (25 µg/m³ for daily exposure) (Bruce, N *et al.*, 2015). Outdoors, the impact is lower due to better pollutant dispersion, but repeated exposure over several hours per week (e.g., cooking in an open yard) remains risky, especially in densely populated areas with limited ventilation (Bruce, N *et al.*, 2015). Sources of pollution are in the surrounding environment and hold areas. Ambient air pollution is outside air that enters the house which contains several substances in the air that have the potential to have a negative impact on health (Romieu, Moreno-Macias and London, 2010). The burning of household fuel causes air pollution. For example, cooking with firewood causes air pollution. The combined effects of outdoor and indoor air pollution exposure cause about 7 milion premature deaths each year, resulting in chronic obstructive pulmonary disease, lung cancer, and acute respiratory indections (Rider and Carlsten, 2019). Extended exposure to air pollution has been linked to several adverse health effects, including those that affect the methylation of human DNA. Research conducted by Laursen in Denmark revealed that cooking activities, especially baking and using candles, can actually have a negative impact on human DNA (Kurdyukov and Bullock, 2016). The results indicate that the process of cooking and burning wax produces certain varying sized particles and chemicals that may have different effects. The activity of both causes increased levels of proteins associated with respiratory tract inflammation. DNA damage during the cooking process was found due to exposure to emissions from cooking activities (Yadav *et al.*, 2021).

DNA methylation is the most extensively studied epigenetic regulator related to environmental exposure. Nomerous studies have identified how the environment influences DNA methylation, resulting in global and specific changes in DNA methylation (Poursafa *et al.*, 2022). Air pollutants cover various environmental exposures, including harmful particles of different sizes and compositions such as carbon monoxide, sulfur oxides, ozone, nitrogen oxides, diesel exhaust fumes, benzene, and other hazardous chemicals (Li *et al.*, 2016). Urban development and air pollution related to traffic are usually used to classify field exposures. The mixture of air pollutants is harmful to the epigenome. For example, research conducted by Carmona, et al. showed changes in DNA methylation levels in the Mitogen-Activated Protein Kinase (MAPK) pathway, which is associated with general air pollution exposure in humans (Munnia *et al.*, 2023). Research conducted by Bind et al. found that exposure to air pollutants can result in functional changes in blood protein expression measurements and changes in DNA methylation, which indicate susceptibility to these changes (Martin and Fry, 2018). This deviation in the form of DNA methylation is very dangerous because it can block proteins that attach to DNA so that the transcription or DNA reading process is hampered (Plusquin et al., 2017). The main objective of this research is to determine whether air pollutants (such as PM2.5, NO_2, and ozone) can cause epigenetic changes in human DNA. This study aims to map the types of pollutants that have the most significant impact on epigenetic alterations. It also explores the potential risks of increased incidence of diseases such as cancer, asthma, cardiovascular diseases, and neurodegenerative disorders. The benefits of this research include providing scientific data that can be used to strengthen emission regulations and air quality standards, promoting the implementation of environmentally friendly technologies in industrial and urban areas, and offering scientific evidence for policymakers to establish safe air quality limits.

METHODS

The research utilizes the systematic review method. Systematic review is a method for identify, evaluating, and interpreting all relevant research findings related to a specific research questions, topic, or phenomena of interest (Siswanto, no date). This systematic review study used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. This type of research is useful for summarizing the findings of various related studies (Hadi and Palupi, 2020).

The first step in this research is to identify scientific questions that will form the basis for developing a literature review. This question developed by considering the four stages of population, intervention, comparison, and outcome (PICO) and asking, “How does air pollution impact human DNA methylation?” Researchers have identified scientific questions by exploring data in the form of articles or journals using search methods in several sources using the keywords "impact of air pollution" and "DNA methylation". Inclusion criteria are human samples, quantitative, cross-sectional design, years between 2017-2024, international, and can be accessed. While the exclusion is abstract, not a research or research article, type of qualitative research. Determination of inclusion and exclusion criteria using PICO (population i.e human, intervention i.e cadmium exposure, and outcome i.e DNA methylation).DNA methylation and year of publication within the last 10 years in 2014-2024. An online search for articles/journals was carried out regarding relevant topics with the PICO keywords "impact of air pollution" and "DNA methylation" via Google Scholar. This search identified 35 articles/journals, then an assessment of compliance with the publication criteria specified in the title, abstract and full-text content was carried out, and 7 articles/journals were retrieved.

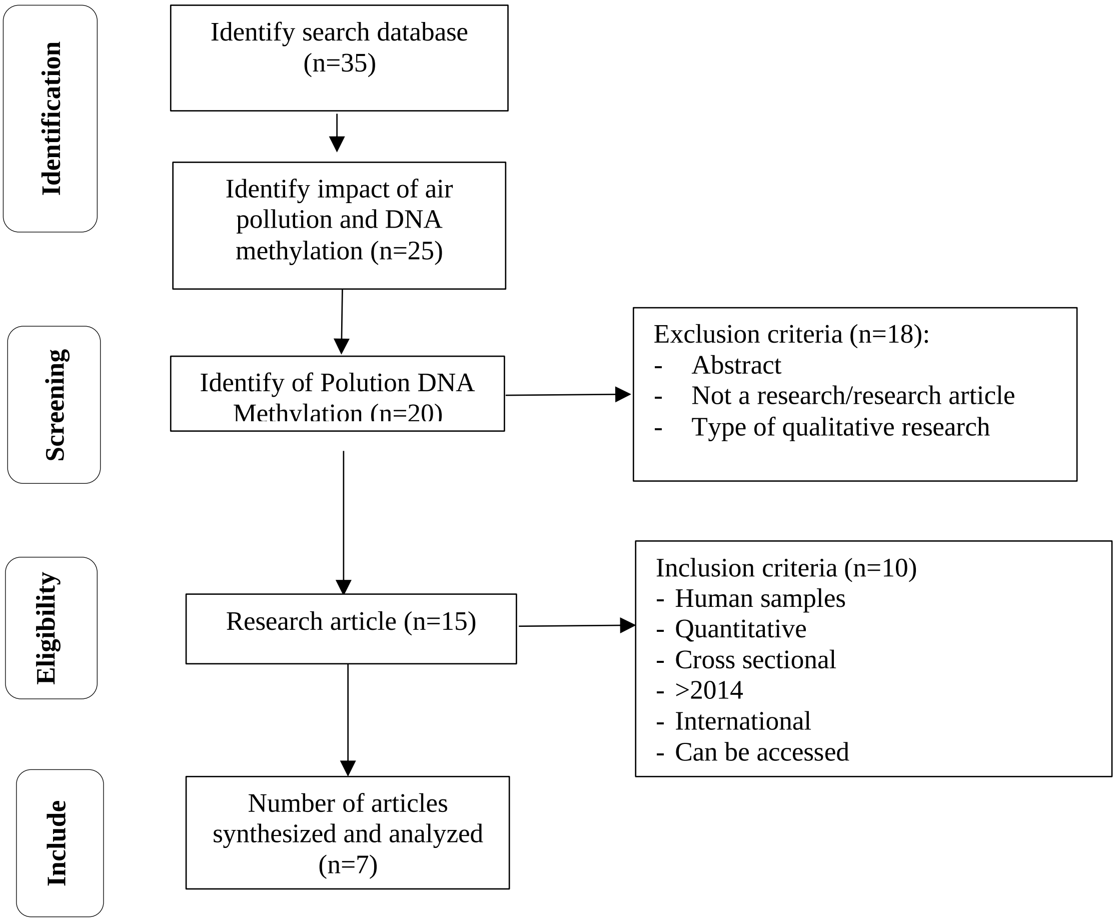

Figure 1. Framework Search Literature Review adapted from PRISMA

The diagram above-obtained data form articles/journals concerning the impact of air pollution and DNA methylation (n=25). The community to be tested was selected, namely humans (n=20). The data focused on study and research articles (n=15). The analysis of the article is obtained after conducting the stages of identification, screening and determination. From the analysis of these articles/journals, 7 articles/journals were obtained with inclusion criteria that were in accordance with this research. The following a table regarding the results of the articles used as research material.

RESULTS AND DISCUSSION

The following the result of impact of air pollution on DNA methylation, as shown in Table 1.

Tabel 1. The result of impact of air pollution on DNA methylation

No	Name of The Researcher	Title of The Research	Population	Methods	Outcome	Conclusion
1.	Poursafa *et al.*, (2022)	DNA Methylation: A Potential Mediator between Air Pollution and Metabolic Syndrome	Population of different countries	This research is a causal-comparative.	The relationship between MetS dan air pollution has a significant impact. Epigenetic modifications, and it has been found that DNA methylation is one of the mechanisms of interaction between the environment and the genome. Changes in DNA methylation could potentially contribute to the development of metabolic diseases.	This study shows evidence supporting the possibility of mediating the effects of air pollution on metabolic syndrome through epigenetic regulation. Further research is required to investigate the causal relationship with DNA methylation and the biological mechanisms involved.
2.	Rasking *et al.*, (2022)	Lupus, DNA Methylation, and Air Pollution: A Malicious Triad	Independent Population	This research is an analytical epidemiology studies	There is a connection between inadequate epigenetic regulation and environmental impacts on the result of SLE. There is advancing evidence that DNA hypomethylation plays an essential role in the pathogenesis of SLE and has been studied mainly in naive CD4+ T-lymphocytes but has also been reported in B (CD19+) lymphocytes and CD14+ monocytes.	This research concludes that air pollution, a potentially significant risk factor, requires further evaluation. Homocysteine may function as a causal mediator in the connection between air pollution impacts and epigenetic changes, consequently, folate supplementation can decrease methylation caused by air pollution.
3.	Plusquin *et al.*, (2017)	DNA Methylation and Exposure to Ambient Air Pollution in Two Prospective Cohorts	Independent Population	This research is an European study of cohorts	DNA methylation has the ability to biologically mediate the effect of environmental exposures by affecting the epigenome and downstream processes. This study's main finding was that lowest DNA methylation levels in several functional regions on the genome, including CpG island's shores and shelves and gene bodies, were associated with exposure to higher ambient outdoor concentrations of NO_2 dan NO_x.	The conclusion of this study reveals that specific responses to low dose exposure can be used as a marker for low doses. Nevertheless, in the integrated analysis of both groups, air pollutant exposure was not associated with distinctions in DNA methylation at individual probes.
4.	Munnia *et al.*, (2023)	Traffic-Related Air Pollution and Ground-Level Ozone Associated Global DNA Hypomethylation	Nearby police population	This research is using a cross-sectional design.	A higher level of methylation was detected in the promoter region of this oncogene in heavy smokers, with intermediate levels in smokers who consume 1-9 cigarettes per day. Various epidemiological studies indicate DNA damage in	The role of air pollution in epigenetic changes and genotoxic effects, particularly the elevated target values, supports the need to develop public health strategies to reduce molecular alterations related to traffic-related air pollution.

No	Name of The Researcher	Title of The Research	Population	Methods	Outcome	Conclusion
		and Bulky DNA Adduct Formation			smokers' respiratory tracts compared to white blood cells.	
5.	Yadav *et al.*, (2021)	Association of Air Pollution and Homocysteine with Global DNA Methylation: A population Based Study form North India	274 dan 270 individual from low and high pollution areas.	This research used a cross-sectional design	Consuming nutritional supplements and vitamin B can reduce the impact of air pollution on methylation levels. This can serve as a community-level method in natural environments to control metabolic disorders at the societal level.	Elevated homocysteine levels can improve the impact of air pollution on DNA methylation. B vitamins in low-pollution sites and folic acid in high-pollution sites may profoundly influence changes in DNA methylation levels.
6.	Rider and Carlsten, (2019)	Air Pollution and DNA Methylation: Effects of Exposure in Humans	Population in areas with high and low pollution in an area	This research is an epidemiological, population, and controlled crossover study designs	Impacts on DNA in the majority are often most noticeable after the more protracted direction, suggesting that transitions take time or must earn. However, data for interim resolution are still growing, and long-term outcomes are possible after the short-term peak. It remains unclear whether vulnerability to air pollution early in life accelerates the mark or whether disease passage reflects accumulated exposure.	DNA methylation is fixed and active, with enclosure patterns throughout life and the environment influencing DNA genes. Vulnerability to air pollution is associated with DNA changes throughout life, from gestation to old age.
7.	Martin and Fry, (2018)	Environmental Influences on the Epigenome: Exposure Associated DNA Methylation in Human Population	Population of various countries	This research is a causal-comparative.	The researchers have evaluated the stability of methylation over time. Although more and more researchers are interested in understanding the functional consequences by assessing gene expression, protein expression, or birth outcomes, this has yet to become a standard practice. Since methylation is an adaptive mechanism, it is unsurprising that methylation patterns change throughout a person's life depending on subsequent exposures.	The area of environmental epigenetics has extensively categorized the connection between openness and CpG methylation changes for different contaminants, nutrients, and social factors. Nevertheless, nowadays, there are four critical gaps in the scientific publication related to environmental factors and the epigenome: setting mixtures and exchanges of pollutants/nutrients, sex-specific reaction, tissue-specific reaction, and the strength and practical effects of CpG methylation.

Air pollution has a major impact on health such as respiratory tract disorders, heart disease, cancer, reproductive disorders and hypertension (Sood *et al.*, 2017). Air pollution has several types of substances, the most frequently found are Carbon Monoxide (CO), Nitrogen Oxide (NO_2), Sulfur Oxide (SOx), Photochemical Oxide and Particles (Surit *et al.*, 2023). The pollution caused can have an impact on the surrounding environment. This pollution is divided into two groups, namely indoor pollution and outdoor pollution. Indoor pollution occurs indoors such as homes, schools and offices. Outdoor pollution occurs outside the room, such as emissions from motor vehicles, industry, shipping, and natural processes experienced by living things (Government of Canada, 2015).

The impact of air pollution has long-term reactions (Fossati *et al.*, 2014; Nwanaji-Enwerem and Colicino, 2020). Long-term exposure to pollution can result in more serious respiratory problems, such as asthma which can become severe and difficult to control, in addition to chronic exposure that occurs can cause chronic bronchitis (Raju, Siddharthan and McCormack, 2020). Another long-term disease is chronic obstructive pulmonary disease (COPD), the emergence of endless injury to the respiratory tract and lungs indicates COPD (Lichtenfels *et al.*, 2018). In the long term, this impact will affect a person's quality of life, apart from that it can also cause serious complications such as repeated respiratory infections, this can lead to decreased lung function and a higher risk of death (McCartney *et al.*, 2018). Maintaining air quality and reducing exposure to air pollution is an important step in maintaining a person's quality of life (Fossati *et al.*, 2014).

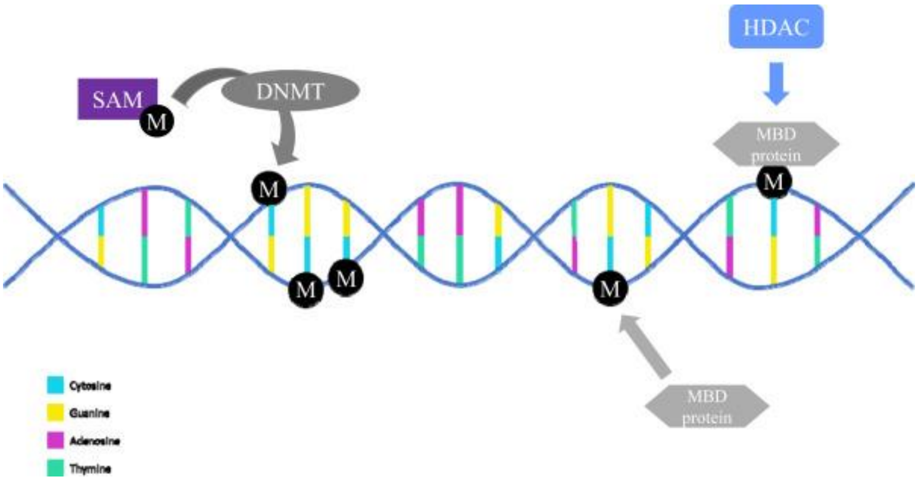

Figure 2. Epigenetic Mechanisms in Cancer

DNA methylation is the transfer of methyl groups to cytosine, which adds an additional layer of complexity to the genome (Gruzieva *et al.*, 2017). DNA methylation marks are recognized by cellular machinery and control transcription. Disruption of DNA methylation due to aging and exposure to environmental toxins can alter susceptibility to disease or trigger processes that lead to disease (Gruzieva *et al.*, 2017; Lee *et al.*, 2017). DNA methylation represents the extension of a methyl group to DNA, usually on the fifth carbon of cytosine, leading to the formation of 5-methylcytosine (5-mC). DNA methylation data from different analyses can use standard platforms and mirror transcription factor binding and gene manifestation (Wright *et al.*, 2010). Therefore, DNA methylation is a logical tool to try to understand the impact of air pollution on genome function and downstream activities that benefit health (Pidsley *et al.*, 2016).

A research shows that exposure to air pollution reduces DNA methylation in certain regions of the immune system and this is related to the regulation of related gene expression (Baccarelli *et al.*, 2009). They divided the methylation levels into ten quantiles according to the DNA methylation levels already present in each volunteer. We reviewed the air pollution and DNA methylation data, operating a correlation assessment system with air pollution. Average DNA methylation across these quantile draftees (Wright *et al.*, 2010). They saw a more powerful adverse association between F3 DNA and particle number in volunteers, increased methylation in F3 (higher decile) but a more powerful adverse association with IFNG in lower deciles (McCartney et al., 2018). In the 90th decile of ICAM1-DNAm there is a positive relationship between soot exposure and ICAM1-DNAm, while in the 10th to 60th decile there is a negative relationship. Such an approach could improve our capacity to reliably see differences in the impact of air pollution on DNA methylation (Leenen, Muller and Turner, 2016).

The effect of air pollution on DNA methylation will have long-term impact on life (Anandari, Farid Wadjdi and Harsono, 2024).

During incubation, exposure to air pollution in utero significantly altered DNA methylation in a concentration-dependent way, with the consequences of disclosure detectable up to 6 months later in placental and cord blood samples collected at birth (Rasking *et al.*, 2022). In youth and adolescence, the connection between air pollution, DNA methylation, and health to prenatal exposure and birth products, and effects may continue into youth. The effect of direction in early life and possible distinctions rely on the type of pollution and the developmental stage of vulnerability (Hansel *et al.*, 2008). This means that changes induced by exposure to air pollution during gestation may persist into youth (Pope *et al.*, 2006). Ongoing DNA changes are one mechanism that maintains the effects of exposure during pregnancy into childhood. In adulthood exposure to air pollution reduces DNA methylation in some areas of the immune system, and this is associated with the regulation of related gene expression (Joubert *et al.*, 2012). This study is in line with previous research demonstrating that exposure to air pollution, particularly fine particulate matter such as $PM_{2.5}$ and gases like NO_2, contributes to changes in DNA methylation patterns. Several earlier studies also found that air pollution can cause both global hypomethylation and gene-specific hypermethylation involved in the regulation of inflammation and immune function. This is consistent with the findings of the present study, which show a correlation between pollutant exposure levels and methylation changes in genes relevant to respiratory and cardiovascular health.

However, this study also shows differences compared to previous research in terms of the range of pollutants analyzed and the populations studied. While some earlier studies focused more on short-term exposure, this study emphasizes the effects of long-term and cumulative exposure. Additionally, this study includes DNA methylation analysis across a more diverse age group, including vulnerable populations such as children and the elderly, thereby providing a more comprehensive picture of the impact of pollution on the epigenome. Another difference lies in the DNA methylation measurement methods used. This study adopts the epigenome-wide association study (EWAS) technique, which is more comprehensive compared to gene-specific approaches used in some earlier studies. This allows for the identification of new methylation sites potentially affected by air pollution and opens opportunities for a deeper understanding of the molecular mechanisms underlying pollution's effects on health. To mitigate the epigenetic impact of air pollution on DNA methylation, comprehensive strategies are essential. Strengthening air quality regulations and enforcing stricter emission standards can effectively reduce pollutant exposure. The adoption of clean and low-emission technologies in industrial, transportation, and energy sectors is critical for sustainable pollution control. Public education campaigns play a vital role in raising awareness about pollution-related health risks and promoting preventive behaviors. Advancements in epigenetic biomarker development may enable early detection of DNA methylation changes, facilitating timely interventions.

Nutritional and lifestyle modifications, including diets rich in antioxidants and DNA-repair nutrients, have potential to alleviate epigenetic damage. Finally, continued research into epigenetic therapies offers promising avenues to reverse or mitigate pollution-induced methylation alterations. Collectively, these solutions could reduce the long-term health burden associated with air pollution. DNA methylation is a key mechanism that links environmental factors, such as air pollution, to tangible biological changes in the body (Plusquin et al., 2017). These changes not only affect exposed individuals but also have the potential to be passed down transgenerationally (Plusquin et al., 2017). Therefore, understanding the impact of DNA methylation is crucial for disease prevention, the development of epigenetic-based therapies, and the formulation of public health policies that are more responsive to environmental pollution (Plusquin et al., 2017).

CONCLUSION

The conclusion of the literature review as stated in the aim, is to determine the impact of air pollution on DNA methylation. The literature review results show that air pollution hurts DNA methylation, causing several diseases, such as respiratory problems, and has long-lasting effects on a person. Therefore, as much as possible, avoid pollutants on the road by using a mask so that your quality of life is better maintained. Despite significant advances in understanding the impact of air pollution on DNA methylation, several areas warrant further investigation. Future studies should expand the range of environmental pollutants analyzed, including ozone (O_3), carbon monoxide (CO), heavy metals, and volatile organic compounds (VOCs), to capture a more comprehensive profile of epigenetic alterations induced by diverse air pollutants. Longitudinal cohort studies are essential to establish the temporal relationship and causality between exposure to air pollution and persistent DNA methylation changes. Employing advanced epidemiological methods such as Mendelian randomization could further strengthen causal inferences.

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Conflict of Interest and Funding Disclosure

There is none.

Author Contributions

MIIM: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, validation, writing-original draft, editing. ART: conceptualization, data curation, formal analysis, obtaining funding, resources, supervision, validation, writing reviews & editing. SZ: writing reviews & editing. JJ: writing reviews & editing.

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