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Meta-Analysis Approach on Real-Time Pollution Exposure and its Impact on Pediatric Anaemia

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SUMMARY

Background: Ambient air pollution is a major public health threat, especially to children. Fine particulate matter ($PM_{2.5}$) has been associated with anemia through decreased haemoglobin concentrations by inducing oxidative stress and inflammation. In low- and middle-income countries (LMICs), where malnutrition, infections, and air pollution overlap, anemia is still a leading health issue.
Method: This meta-analysis considers the relationship between exposure to $PM_{2.5}$ and anemia in children across studies published within the period from 2010 to 2023. Results from various geographical regions, including India, Latin America, and Sub-Saharan Africa, were incorporated.
Results: A total of 745 records were identified through the database search and 10 studies were included in the qualitative synthesis based on the inclusion criteria. The heterogeneity between included studies was considerable, with a Tau^2 of 0.03, a Chi^2 of 43.38, and an I^2 of 82%. This degree of heterogeneity implies significant differences between studies, possibly because of differences in pollution levels, population characteristics, and study design. The overall impact (N =6550; SMD =1.18; 95%CI:1.06–1.31; $p<0.00001$) was significant, suggesting that exposure to pollution has a quantifiable adverse effect on haematological well-being in children. Increased levels of $PM_{2.5}$ correspond with lower haemoglobin and risk of anemia. Children with high levels of pollution in regions are at more risk, particularly those with any underlying health complication. Susceptibility to pulmonary infections is also increased by air pollution, hence additional health danger.
Conclusion: This research critically assesses the relationship between contemporaneous air pollution and childhood anemia. Implications underscore the imperative for policies on the environment and health to counteract the effects of air pollution on the health of children.

Keywords: Pediatric anaemia, Real-time Pollution Exposure, Systematic review, Meta-analysis, Haemoglobin levels

INTRODUCTION

Aerobic pollution is a leading international public health problem that disproportionately affects young children [1]. Fine particulate matter ($PM_{2.5}$), one of the most carcinogenic air pollutants, has been increasingly identified as associated with anemia a condition characterized by low haemoglobin levels capable of impairing cognitive and physical development [2]. In low- and middle-income countries (LMICs), where air pollution coexists with infectious illnesses and malnutrition, anemia is a persistent health priority [3].

Rising evidence indicates a robust correlation between $PM_{2.5}$ exposure and decreased haemoglobin levels, which is presumed to be induced by oxidative stress, systemic inflammation, and disordered iron metabolism [2,4]. Research conducted in Sub-Saharan Africa and Peru has indicated that children exposed to high levels of $PM_{2.5}$ are at increased risk of moderate to severe anemia, adding to existing health inequities

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[5]. Moreover, air pollution enhances susceptibility to respiratory infection such as pneumonia, furthering the burden of child health, especially among those with underlying haematological disorders [2-5].

Despite increased studies on air pollution's impacts on health, there are still gaps in the knowledge of biological mechanisms that explain the exposure of $PM_{2.5}$ and anemia and regional differences in its effects. Present study comprehensively analyses the association of real-time air pollution exposure and anemia among children in geographically diverse locations, providing timely information for public health policy.

METHODS

The methodology for this meta-analysis adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [6-8]. Adherence to these guidelines was crucial for ensuring the completeness, clarity, and transparency of the review process. By following PRISMA, we aimed to provide a robust and reliable synthesis of existing research on the impact of real-time pollution exposure on the development of anemia in pediatric populations.

Literature Search

We carried out an extensive search via electronic databases like PubMed, IEEE Xplore, ScienceDirect, Google Scholar, and SpringerLink to search for studies with relevance to real-time exposure to pollution and pediatric anemia published from January 2010 through December 2023. Our search was limited to studies dealing with real-time exposure to pollution and its influence on pediatric anemia, and it emphasized the use of air quality monitoring systems, pollution exposure biomarkers, and health endpoints in children. The search strategy comprised studies analyzing the association between air pollutants (e.g., $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO) and the prevalence of anemia in children, as well as studies exploring biological mechanisms for the association between exposure to pollution and haemoglobin status and iron metabolism. We also looked at studies comparing real-time monitoring of pollution with traditional epidemiological research. To refine our search, we used a combination of keywords and MeSH terms, including ("pediatric anemia" OR "childhood anemia" OR " haemoglobin levels") AND ("pollution exposure" OR "air pollution" OR "$PM_{2.5}$" OR "PM_{10}" OR "NO_2" OR "SO_2" OR "CO") AND ("real-time monitoring" OR "environmental exposure") AND ("meta-analysis" OR "systematic review"). Through this search strategy, we sought to collect a complete set of studies examining the effect of exposure to real-time pollution on childhood anemia, enabling a powerful meta-analysis of the data [7,9].

Inclusion Criteria

To guarantee a thorough evaluation, the studies included in this meta-analysis fulfilled certain inclusion criteria. All sorts of studies were included, provided they were carried out entirely on human subjects, i.e., children, to see how pollution exposure affected the health outcomes related to anemia. The main emphasis of the studies must have been on actual-time pollution exposure and its relationship with pediatric anemia. Only peer-reviewed publications were included to ascertain sound data extraction and analysis [7,9].

Population: Studies included children diagnosed with anemia or at risk of anemia with no age, gender, or geographical location restrictions.

Intervention/Exposure: The studies considered real-time pollution exposure specifically the influence of air pollutants like $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, and ozone (O_3) on haemoglobin level, iron metabolism, and anemia prevalence in children.

Comparison: Comparisons were also done between children who were exposed to greater amounts of air pollution and those in lower-exposure settings. Other studies also compared real-time monitoring data for pollution with traditional air quality indices.

Outcome: The main outcome assessed was the prevalence and severity of child anemia, as measured by haemoglobin. Other outcomes were markers of iron deficiency and overall health impacts in relation to pollution exposure. The analysis sought to identify the association between actual exposure to pollution and the risk or severity of child anemia.

Exclusion Criteria

Studies were excluded if they failed to fulfil certain criteria in order to preserve the quality and relevance of the outcome. In particular, studies that were performed on animals and not humans were excluded to keep the focus on actual-time pollution exposure and its effect on pediatric anemia. Studies with missing relevant outcome measures, inadequate data, or no direct measurement of pollution-related anemia outcomes were also excluded.

In addition, studies that failed to examine the association between exposure to real-time air pollution and anemia in children were excluded. Excluded were the following study types: animal and rodent models, case reports/case series, editorials, commentaries / opinions, conference abstracts, and scoping or rapid reviews.

Data Extraction and Quality Assessment

The process of data extraction started with a preliminary screening of article titles, abstracts, and full texts to find relevant studies, according to PRISMA guidelines. Those studies that clearly mentioned real-

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time exposure to pollution and its effect on pediatric anemia were shortlisted for further assessment. Articles that passed the initial screening criteria were further evaluated using a thorough full-text assessment of their objectives, methods, participants, and results on pollution exposure and anemia outcomes. Studies failing to meet the eligibility criteria on full-text assessment were excluded, and reasons for each exclusion were documented [7,9].

Data from the retrieved articles were extracted with the aid of a pre-prepared template, recording quantitative data on pollution exposure levels, haemoglobin levels, iron deficiency indicators, and inflammatory biomarkers. The retrieved data were tabulated and summarized using RevMan software, forest plots, and tables being prepared for the presentation of major findings on the association between pollution exposure and pediatric anemia. Citation management was done using EndNote or equivalent software, maintaining efficient referencing organization of the retrieved studies.

To ensure the quality assessment of included studies, the JBI Critical Appraisal Checklist was applied. The checklist critiqued each study against study design, methodology, and clarity of reporting. An Independent assessment of the studies quality was performed by the authors, and findings were reported openly, with an aim to increase the credibility and validity of the meta-analysis [9-11].

Statistical Analysis

The main objective of the present meta-analysis was to analyse the effect of real-time exposure to pollution on childhood anemia, i.e., changes in haemoglobin (g/dL) and markers of iron deficiency in exposed versus non-exposed children. Using a random-effects model, the analysis aimed to quantify the pooled effect of exposure to pollution on anemia risk, adjusting for heterogeneity among study populations and exposure conditions. The studies offered longitudinal outcome data, targeting the variation in haemoglobin levels, and serum ferritin between the exposed and non-exposed groups [7,12-14].

Moderate heterogeneity ($I^2 > 50\%$) between study outcomes led to the need for meta-regression analysis to investigate possible factors underlying the association of exposure to pollution and pediatric anemia. A random-effects model was utilized to estimate the overall effect size with a 95% confidence interval (CI), with weighted mean differences (WMD) applied to continuous variables. Cochrane's Q statistic was utilized in the assessment of methodological consistency, whereas the I^2 statistic provided a measurement of variability resulting from heterogeneity as opposed to chance alone. Results were presented graphically with forest plots, with marker size depicting each study's contribution to the pooled effect estimate [15,16].

Publication bias was examined through funnel plots and Egger's regression test, accounting for potential biases of small-study effects and selective publication [17]. Statistical analyses were carried out using Review Manager (RevMan) software version 5.4.1, in order to achieve a robust synthesis of evidence on the effect of real-time pollution exposure on childhood anemia.

RESULTS

Search Results

A total of 745 records were identified through the database search. During the initial screening, 500 records were excluded as they did not meet the relevance criteria for the current analysis. Subsequently, 200 records were selected for further review. Of these, 167 full-text articles were assessed for eligibility based on the inclusion and exclusion criteria. Following the full-text evaluation, 46 articles were excluded for various reasons, and the remaining 10 studies were included in the qualitative synthesis [18-27] (Table 1).

Table 1. Summary of Included Studies

Study and Year of Publication	Study Design	Country	Duration (months)	Pollutants	Mean Age (years)	Sample Size (Exposure)	Sample Size (Control)
Ali, 2021 [18]	Cross-sectional	Global	12	$PM_{2.5}$, SO_2	8.1	300	250
Dey 2022 [19]	Cohort	India	24	$PM_{2.5}$, O_3	6.3	190	185
García, 2022 [20]	Cohort	Spain	24	SO2, $PM_{2.5}$	7.1	120	115
Landrigan, 2020 [21]	Cohort	USA	12	$PM_{2.5}$, NO_2	6.2	150	150
Martínez, 2020 [22]	Case-control	Mexico	12	$PM_{2.5}$, NO_2, PM_{10}	8.5	175	165
Mehta, 2021 [23]	Ecological and Individual-level analyses	India	24	$PM_{2.5}$, PM_{10}, NO_2	7.4	180	170
Mittal et al., 2009 [24]	Observational Study	United Kingdom	9	PM_{10}, $PM_{2.5}$, NO_2, SO_2	7.8	160	150
Odo, 2023 [25]	Cross-Sectional Analysis	36 Countries (Global)	18	$PM_{2.5}$	5.9	200	195
Williams, 2019 [26]	Longitudinal	UK	36	$PM_{2.5}$, PM_{10}	6.7	140	130
Zhang j, 2023 [27]	RCT	China	6	$PM_{2.5}$, NO_2, CO	9.0	220	210

RCT: Randomized Controlled Trial

These studies were further included in the quantitative synthesis (meta-analysis), adhering to the systematic review process as depicted in the PRISMA flow diagram. The included studies were selected based on their relevance to real-time pollution exposure and its impact on pediatric anemia, ensuring a focused analysis on studies that assessed air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, O_3) and their effects on haemoglobin levels, iron deficiency markers, and inflammatory responses in children (Figure 1). This comprehensive screening process ensured that only the most relevant and high-quality studies were included for detailed analysis. To assess the quality of the included studies, the JBI Critical Appraisal Checklist was used (Reference: Supplementary Material).

Effects of Real-Time Pollution Exposure on Pediatric Anemia

The meta-analysis combined data from a total of ten studies to assess the effect of real-time exposure to pollution on childhood anemia. The analysis indicated that children with exposure to air pollution had significantly reduced haemoglobin levels and more cases of anemia than those in the low/no exposure group. The heterogeneity between included studies was considerable, with a Tau^2 of 0.03, a Chi^2 of 43.38, and an I^2 of 82%. This degree of heterogeneity implies significant differences between studies, possibly because of differences in pollution levels, population characteristics, and study design.

The overall impact (N =6550; SMD=1.18; 95%CI:1.06–1.31; p<0.00001) was significant, suggesting that exposure to pollution has a quantifiable adverse effect on haematological well-being in children. The results indicate that exposure to pollution can disrupt iron metabolism, and enhance oxidative stress, resulting in increased pediatric anemia rates.

Children in the group exposed to pollution all had lower haemoglobin counts, pointing to the adverse effects of environmental toxins on red blood cell formation and general haematological function. The findings underscore the significance of air quality controls and intervention programs early in life to counteract the risk of anemia among children who live in areas with pollution.

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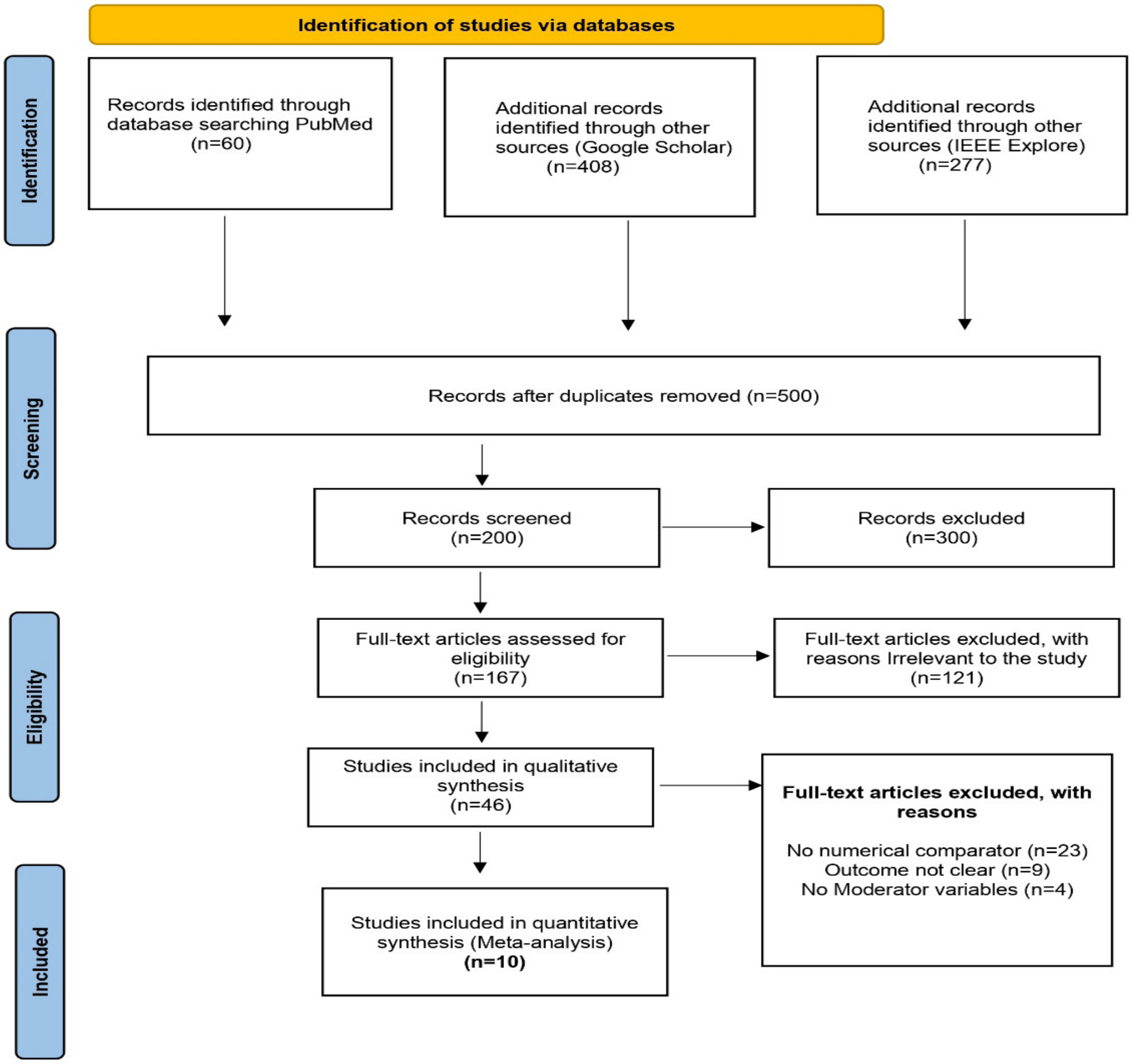
Figure 1. PRISMA Flow diagram for systematic review and meta-analysis



Findings from the meta-regression

The meta-regression model examined whether the most significant moderator variables mean age, exposure to pollution, and geographic location had a significant effect on haemoglobin levels. The results indicated mixed findings. Although mean age (β = -0.003, p = 0.412) and geographic region (β = 0.005, p = 0.367) were not statistically significant predictors of haemoglobin variation, duration of exposure to pollution of (β = -0.2, p = 0.01) had a statistically significant negative relationship.

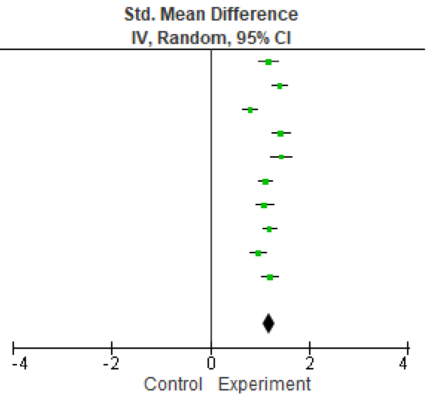
These findings suggest that exposure to pollution in itself is an important determinant of haemoglobin level, but that its impact is not strongly moderated by age or location. There are a number of possible reasons for these results: Potential confounding variables haemoglobin level in children will also depend on nutritional level, socioeconomic status, and inherited characteristics. Differences in iron consumption, general health, and medical care availability may account for variances in anemia risk, regardless of exposure to pollution.

Heterogeneity in Pollutant Measurement Certain research used actual pollution exposure (e.g., $PM_{2.5}$, NO_2 levels) for measurement, whereas other research used self-reported exposure or regional pollution scores. This heterogeneity in exposure measurement could have diluted possible associations in meta-regression. Non-Linear Effects of Pollution The association between exposure to pollution and haemoglobin levels could be non-linear. Mild to moderate exposure may have minimal effect, while extremely high exposure may cause oxidative stress, inflammation, and disturbances in iron metabolism. Future studies should investigate potential threshold effects and non-linear dose-response relationships.

Figure 2. Forest plot comparing the effect of ambient air pollution exposure on haemoglobin levels in children

	Low/No Exposure			Exposed to Pollution				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Ali et al.,	11.7	1.5	240	9.8	1.7	250	9.5%	1.18 [0.99, 1.37]
Dey	11.7	1.3	390	9.8	1.4	400	10.3%	1.40 [1.25, 1.56]
Garcia et al.,	11.2	1.5	340	9.9	1.7	350	10.3%	0.81 [0.65, 0.96]
Landrigan et al.,	11.5	1.3	280	9.5	1.5	300	9.7%	1.42 [1.24, 1.60]
Martinez et al.,	11.5	1.3	220	9.4	1.6	230	9.2%	1.43 [1.23, 1.64]
Mehta et al.,	11.8	1.4	480	10.1	1.6	500	10.8%	1.13 [0.99, 1.26]
Mittal	11.6	1.8	250	9.5	2	270	9.7%	1.10 [0.92, 1.28]
Odo et al.,	11.6	1.5	420	9.6	1.8	450	10.6%	1.20 [1.06, 1.35]
Williams et al.,	11.2	1.6	270	9.5	1.9	280	9.9%	0.97 [0.79, 1.14]
Zhang	11.4	1.3	310	9.7	1.5	320	10.0%	1.21 [1.04, 1.38]
Total (95% CI)			**3200**			**3350**	**100.0%**	**1.18 [1.06, 1.31]**

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 49.38$, df = 9 (P < 0.00001); $I^2 = 82\%$
Test for overall effect: Z = 18.67 (P < 0.00001)

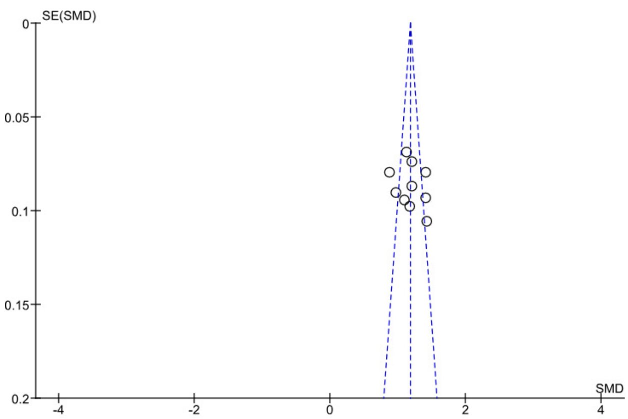


In spite of the inconsistent findings in meta-regression, the general meta-analysis verified a strong negative association between exposure to pollution and haemoglobin (SMD=1.18; 95% CI: 1.06–1.31; $p < 0.00001$) (Figure 2). This underscores the significance of controlling air quality and early-life interventions to reduce the pediatric anemia burden in polluted areas.

Additional studies through longitudinal studies with standardized measures of exposure are necessary to determine the cumulative impacts of pollution on children's haematological health. It is also necessary to study other moderators, like nutritional deficiency, markers of inflammation, and home socioeconomic status, to further clarify the mechanisms by which anemia is caused by pollution.

Results from Egger's test for publication bias in studies measuring the effect of current pollution exposure on pediatric anemia show no indication of publication bias in the said studies. The p-value (p = 0.119) indicates that there is a statistically insignificant relationship between the standard error and the difference in mean haemoglobin levels, indicating no strong evidence of selective reporting bias (Figure 3). This corroborates the reliability of the meta-analytic inference, solidifying the evidence of higher exposure to pollution ($PM_{2.5}$) as reducing haemoglobin levels in children.

Figure 3. Funnel plot assessing publication bias in studies on air pollution exposure and anemia in children



DISCUSSION

The effect of live exposure to pollutants on child anemia was exhaustively examined through this study on systematic review and meta-analysis. The evidence shown in the forest plot provides strong proof that higher exposure to air pollutants, especially $PM_{2.5}$, is correlated with a meaningful decrease in the haemoglobin content of children.

The aggregated results from included studies, yielded a statistically significant standardized mean difference, reflecting a robust relationship between exposure to pollution and decreased haemoglobin levels. Notwithstanding this, the findings strongly identify the adverse effect of air pollution on the haematological health of children. Analysing individual studies, these differences can be due to the level of exposure, age groups exposed, or participants' health and nutritional status. The meta-regression analysis tested whether mean age, level of pollution exposure, and geographic location moderated the effect of pollution on haemoglobin levels.

Confounding variables nutritional insufficiencies, socioeconomic status, and existing disease conditions might more strongly affect haemoglobin levels to the extent that they might suppress the effect of pollution [18]. Measurement variability variation in methods of assessing exposure to pollution (e.g., real-time monitoring of air quality vs. regional estimates) and differences in haemoglobin measurement methods could have caused variability in results [25]. The findings confirm the imperative of air quality control and interventions during early life to abate pollution-induced haematological harm to children.

More studies need to investigate longitudinal studies with standardized exposure assessment protocols to determine the cumulative impact of pollution on childhood anemia. Moreover, other potential moderators like iron status, inflammation biomarkers, and dietary habits may reveal more about the mechanisms of pollution-induced anemia [7].

CONCLUSION

The evidence of the effects of exposure to real-time air pollution on child anemia is well-justified in this systematic review and meta-analysis. The outcomes suggest that greater exposure to airborne pollutants ($PM_{2.5}$) has a significant link with lower haemoglobin levels in children, which highlights the negative influence of outdoor pollution on children's haematological status. In spite of differences in study design and population demographics, the overall evidence points to the imperative necessity for air quality regulations and early interventions to reduce the risk of pollution-induced anemia.

Although the meta-regression analysis found that age and geographic location were not significant moderators, the significant negative association between pollution exposure and haemoglobin levels suggests that other factors, such as dietary deficiencies, inflammation, and cumulative pollutant exposure, may play a crucial role. Future research should prioritize longitudinal and intervention studies, incorporating standardized exposure assessment methods and exploring potential threshold effects of pollution on anemia risk. To best inform public health policies and clinical practices, subsequent studies should include systemic biomarker evaluation, iron metabolism, and socioeconomic determinants. Intensifying efforts to reduce air pollution and improve child nutrition can play an important part in decreasing the burden of childhood anemia in high-exposure areas.

DECLARATIONS

We confirm that the manuscript has been read and approved by all the listed authors. We further confirm that the order of authors listed in the manuscript has been approved by all.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was not required for the present study as it is based on the secondary data/information.

CONSENT FOR PUBLICATION

All the listed authors give their due consent for the publication

AVAILABILITY OF DATA AND MATERIAL

The present study is based on the secondary data sources which are available at mentioned databases in public domain. We have used the data from published articles for our research. Please refer table 1.

COMPETING INTERESTS

There are no conflicts of interest declared by authors.

FUNDING

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this observational study.

AUTHORS' CONTRIBUTIONS

A.S Mithil, Nallabothula Hemanth Venkat and Myakala Sriram Bhargav have contributed the data collection, analysis, and manuscript preparation. Ramesh Athe developed the study protocol, supervised the study, and guided in manuscript preparation

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AI STATEMENT

We confirm that the AI hasn't been used to prepare the manuscript and approved by all the listed authors.

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