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A Systematic Review to Determine the Association between Childhood Lead Exposure and Cognitive Abilities of Adolescents and Young Adults

Michael Makhetha[1], Thokozani P Mbonane[1]
[1]University of Johannesburg, Faculty of Health Sciences, Department of Environmental Health
Johannesburg, South Africa, City, Country
tmbonane@uj.ac.za; 200731516@student.uj.ac.za

Abstract **-** Lead exposure has been linked to negative effects on children's school performance. Despite the detrimental effects of lead on cognitive abilities, there is limited attention given to environmental lead exposure as a risk factor for cognitive impairment. This study aimed to review epidemiological studies on the association between blood lead levels and mental abilities among young children and adolescents. A total of 320 articles on such epidemiological studies were identified through a desktop-based search. The systematic literature search was conducted using various scientific or academic search engines such as PubMed, Ovid, SciELO, Web of Science, Science Direct, Google Scholar, Cochrane Library, Scopus, Plos, ProQuest, MEDLINE, EMBASE, PsycINFO, and Medline Plus. The data extraction, screening, and inclusion followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) model. The data was stored and managed using the latest version of Mendeley management software, while the IBM Statistical Package for Social Sciences (SPSS) version 29 was used for statistical analysis. Sixteen studies, including seven cross-sectional designs, five follow-up studies, and four cohort studies from around the world, were included in the systematic review and meta-analysis. The total population size of the included studies was 23,290. Blood lead levels in the included studies ranged from 0.65µg/dL to 49.30µg/dL, with a weighted mean average of 11.78µg/dL (standard deviation of 15.10). Risk factors such as age, gender, race, socio-economic status, residing and studying in a lead-contaminated area, underlying health conditions, lead-contaminated home, parental educational levels, marital status of the caregiver, elevated bone lead levels, and participants' behaviour were found to influence the impact of environmental lead exposure on cognitive abilities. Evidence suggests that ecological lead exposure harms children's cognitive functions.

Keywords**:** Lead exposure, childhood blood lead levels, children, adolescents, cognitive abilities, lead concentration, systematic review, environmental health

1. Introduction

Lead exposure results in undesirable effects on children's cognitive abilities and early childhood development. Lead is a highly toxic metal that affects nearly every body organ [1]. The nervous system is the most affected in the human body among children and adults [2]. However, lead toxicity in children and adolescents has a greater impact on their health than in adults. This is because their internal and external tissues are much weaker than those of adults [3] while young adults might be more vulnerable due to their behaviour and outdoor activities. Long-term lead exposure in adults can cause reduced performance in certain cognitive abilities after impairing nervous system functions [2].

Scientific evidence has established a link between environmental lead exposure at various levels and a wide range of health and social effects. These effects include mild intellectual impairment, hyperactivity, reduced concentration span, and poor academic performance [4]. When the concentration of lead in children's blood reaches 50µg/dL, it can have adverse effects on their development, memory, intelligence, and behaviour, even if there are no visible clinical symptoms [5]. Lead exposure's most significant negative impact is the loss of cognitive skills and intellectual ability in infants and children [6]. A review by Pal and colleagues emphasises that prolonged exposure to lead in the human body can disrupt neurological, cardiovascular, haematological, and reproductive functions [7]. Moreover, the review states that elevated levels of lead in the blood can impair the functioning of the central nervous system (CNS), leading to encephalopathy and oedema, primarily affecting the cerebellum [7].

Elevated blood lead levels have been linked to the impact on children's school performance through adverse effects on cognitive abilities. Attention is scarce regarding environmental early childhood lead exposure as a risk factor for cognitive abilities and impairment in adolescents and young adults. Yet, there is evidence of this age group being involved in numerous societal ills [8]. The study aimed to explore and analyse the existing scientific literature on the potential relationship between elevated blood lead levels and cognitive abilities in adolescents and young adults.

2. Methodology

2.1. Study Approach

The findings of this study are presented using Preferred reporting items for systematic reviews and meta-analysis (PRISMA) model tool [9], [10]. The model below shows a flow diagram that outlines the process of the meta-analysis, which involves paper identification, abstract screening, assessing paper eligibility, and inclusion of papers.

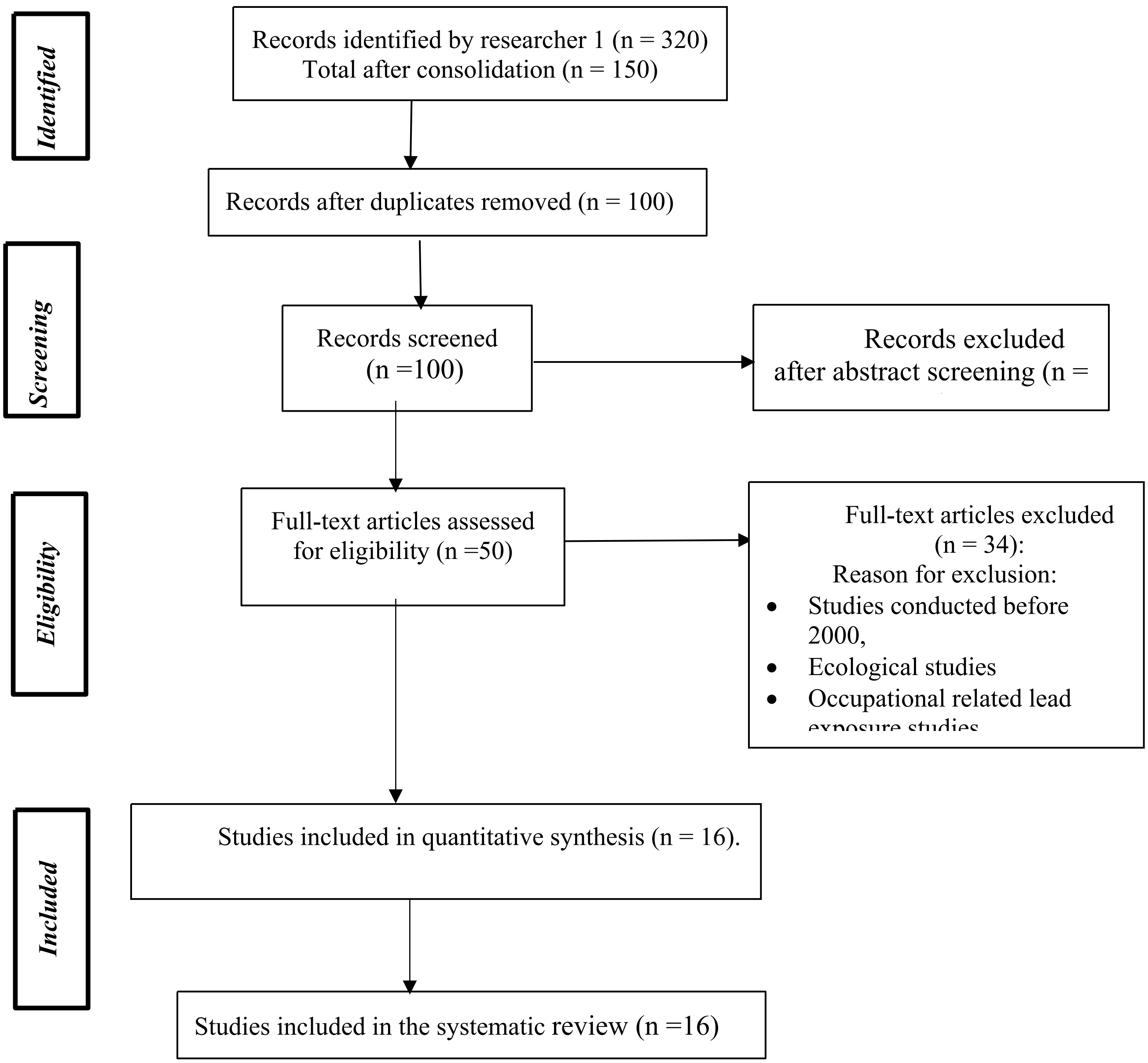

Fig 1. PRISMA flow diagram

2.2. Literature Search

A systematic literature search was conducted across multiple databases including PubMed, Ovid, SciELO, Web of Science, Science Direct, Google Scholar, Cochrane Library, Scopus, Plos, ProQuest, MEDLINE, EMBASE, PsycINFO, and Medline Plus. Additionally, a manual search of the reference lists of selected articles was performed to identify additional relevant publications. Grey literature, such as academic unpublished theses and dissertations, was also included. The study encompassed scientific data from January 2000 to June 2020. In this study, cognitive ability is defined as an individual's capacity to engage in various mental tasks that are closely associated with learning and problem-solving. The search incorporated the following terms interchangeably: blood lead levels, childhood lead exposure, short-term lead exposure, lead poisoning, cognitive ability, cognitive impairment, cognitive functioning, working memory index, learning difficulties, and intelligence quotient.

2.3. Inclusion and Exclusion Criteria

The study encompassed research conducted among adolescents (10-18 years old) and young adults (19-21 years old). Only observational studies investigating the correlation between environmental lead exposure and cognitive abilities were considered. Additionally, the review incorporated studies that utilized blood lead levels as a biomarker and concentrated on environmental exposure. The systematic review and meta-analysis excluded investigations focusing on individuals aged nine or younger, as well as those aged 22 or older. Furthermore, this study excluded research on occupational lead exposure, along with case studies, commentary papers, and previous reviews that were not incorporated in the analysis.

2.3. Data Screening, Extraction and Management

The principal reviewer (MMM) began by searching and retrieving articles based on titles and abstracts for the screening process. This process was supervised by the supervisor (TPM). Any questions or misunderstandings that arose during this process were escalated to senior personnel members in the department who were invited to oversee and resolve any unforeseen differences or queries due to their experience. MMM and TPM checked for duplicates independently. Afterwards, the principal reviewer extracted and downloaded the full-text articles identified during the screening process.

The data extraction criteria included the following items: authors, publication year, country where the study was conducted, study design, data collection, population, sampling technique, sample size, participants' age range, participants' mean age, biomarker, risk factors associated with elevated blood lead levels, tool for measuring the health outcome, and significant findings. Authors of identified articles without full text were contacted via email to request a copy of the full text. If there was no response after 30 days, the particular paper was not included in the study. Two authors were approached for the full texts of their published articles. One author did not respond at all, while the other author indicated that the manuscript was written in a native language. Therefore, these manuscripts were not considered for inclusion in the study.

The extracted full-text articles were entered into the Mendeley Desktop (version 1.19.4) data management application for referencing and storage, and to avoid duplication. Microsoft Excel also captured the articles for sorting, cleaning, and coding according to the extraction criteria. Afterwards, they were transferred into the Statistical Package for the Social Sciences (SPSS), Version 26, for analysis purposes.

2.4. Risk Bias and Study Quality Assessment

The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework was utilized to assess the risk of bias in the papers selected for this study [11]. The quality of the studies included in the systematic review and meta-analysis was determined using the National Institutes of Health (NIH) quality assessment tool [12]. This tool allowed for categorising studies as good, fair, or poor based on specific criteria. The principal reviewer assessed the studies, and the supervisor reviewed the ratings before the analysis could commence.

2.4. Data Synthesis and Analysis

Quantitative analysis was employed to analyze the pooled results through the use of graphs, tables, and frequencies. To assess heterogeneity between the selected and included studies, the Q and I_2 tests were employed [9], [13], [14] . The mean effect was estimated using pooled relative risk or odds ratio, along with relevant 95% confidence intervals weighted mean difference. The Begg and Egger tests were employed to determine the significance of the asymmetry. Lastly, a registered biostatistician assisted in the analysis of the collected data.

3. Results

3.1. Studies Included in the Review

The systematic review included studies that focused on adolescents (ages 10-19) and young adults (ages 20-21). In some cases, blood sampling was conducted during early childhood, particularly in follow-up and cohort studies. The majority of studies (9) were conducted in middle-income countries, while only a few studies were carried out in low-income countries. Notably, the United States conducted the most studies that found a correlation between elevated blood lead levels and impaired cognitive abilities.

Various study designs were employed in the included studies of this systematic review. The most frequently used design was cross-sectional (n=7; 42%), while five studies were follow-up studies and three were cohort studies. Both males and females were included in all the studies. The total population size for the review was 23,290 (mean=1455.63; standard deviation=2460.31), with participant numbers ranging from 11 to 8603 per study. In most studies, participants were recruited randomly. All the studies utilized blood as a biomarker to measure lead levels in humans. Accredited laboratories were responsible for analyzing the blood samples in all of the studies.

3.2. Blood Lead Levels

The participants from whom blood samples were collected for laboratory analysis. The average age for the entire population included in the review was 9.2 years (Standard Deviation = 4.42), ranging from 2 to 24 years old. The blood lead levels ranged from 0.65 to 49.30, with a mean of 11.78 and a standard deviation of 15.10. The mean blood lead level was higher in low-income 7.63µg/dL and middle-income (49.30µg/dL) countries when compared to high-income countries (5.22 µg/dL).

3.3. Risk Factors Associated with Blood Lead Levels

The following were identified as risk factors: age, gender, race, socioeconomic status (SES), residing or attending school in or near a lead-contaminated environment, anaemia, low blood haemoglobin levels, birthweight, self-reported household lead exposure, caregiver/parental educational status, caregiver/parental marital status, high bone lead levels, and pica (hand-to-mouth behaviours). Table 1 describes the odds ratio (OR), confidence interval (CI) and findings of the pooled analysis. The Egger's test showed that publication bias was among the risk factors identified in the review.

Table 1: Analytical findings and publication bias of the included studies' risk factors.

Risk Factor	Odds Ratio	p-value	95%Confidence interval	Egger's Test
Age	2.21	0.0400*	0.99-1.33	0.081
Gender	0.98	0.0033*	1.83-2.09	0.187
Race	0.55	0.0111*	0.64-0.72	0.134
Socioeconomic status	1.38	0.0009*	1.27-2.77	0.191
Residing near lead activity area	1.91	0.0043*	0.13-2.13	0.221
Attending school near lead-contaminated environment	0.68	0.0121*	1.35-3.00)	0.876
Anemia	2.61	0.0051*	0.55-1.78	0.444
Low haemoglobin	1.22	0.0019*	0.88-2.14	0.243
Birthweight	0.11	0.0143*	0.13-1.42	0.732
Self-reported household exposure	3.61	0.0520*	0.26-0.92	0.213
Guardian educational levels	1.98	0.0312*	0.21-0.82	0.651
Guardian marital status	1.11	0.0500*	0.03-1.55	0.112

Elevated bone lead concentration	1.63	0.0444*	0.12-0.92	0.234
Pica	0.81	0.0001*	0.11-1.02	0.691

* Statistically significant at (p > 0.05)

3.4. Relationship between Blood Lead Levels and Cognitive Abilities

Cognitive abilities encompass a range of skills and functions that involve attention, decision-making, perception, memory, language abilities, and learning. This literature review highlights the noteworthy results that indicate a correlation between early childhood lead exposure and impaired cognitive abilities in adolescents and young adults. One study specifically examined the impact of elevated blood lead levels on cognitive abilities in young adults, while sixteen studies focused on the effects of elevated blood lead levels in adolescents, as shown in Table 2. The significant findings from these studies have been categorically organized based on the aforementioned classification.

Table 2: Odds Ratios between BLLs and cognitive abilities.

Cognitive ability	Odds Ratio	p-value	95%Confidence interval
Attention	1.93	0.0111*	0.52-1.10
Decision making	1.98	0.0221*	0.22-1.44
Memory	2.65	0.0400*	0.17-1.11
Language or speaking ability	1.48	0.0310*	0.72-2.21
Perception	0.71	0.0002*	1.73-3.43
Learning	1.58	0.0117*	1.01-2.23

* Statistically significant at (p > 0.05)

3. Discussion

This review demonstrates that blood lead levels in high-income countries are generally lower than those in low- and middle-income countries. The difference could be attributed to the preventive and treatment efforts put in place to prevent exposure and screen populations at risk. In the United States, for example, there is an environmental and medical surveillance system in place through the Centers for Disease Control and Prevention (CDC) that focuses on lead poisoning. However, in low- and middle-income countries, there is a lack of public health actions to address environmental lead exposure. A study found that low- to middle-income countries bear a greater burden of lead exposure due to a lack of protective regulations and enforcement practices [16]. While blood lead levels have decreased in developed countries, disparities still exist based on race and socioeconomic status [17]. Developing countries with impoverished populations, where the majority of children with high lead levels reside, continue to face significant health risks from lead exposure [18]. This leads to a decline in productivity and earning potential due to a population-wide loss of IQ points.

Scientific evidence indicates that young children are particularly susceptible to the effects of environmental lead exposure. This may be due to their still-developing bodies and behaviour, such as playing in contaminated environments. Most studies in this review identified age as a risk factor for adverse cognitive effects associated with childhood lead exposure. Elevated lead levels have been linked to various health issues, emphasizing the long-term impact of environmental lead exposure during childhood. However, four studies suggested a greater correlation between lead levels and cognitive scores in males compared to females. This supports previous research highlighting the elevated blood lead levels observed in males, which may be attributed to their outdoor activities during the early stages of life. The study identified several factors associated with higher blood lead levels and cognitive abilities. These factors include birthweight, self-reported household lead exposure, parental education level, marital status, high bone lead levels, and pica (hand-to-mouth behaviour). These are important to consider, especially in vulnerable communities that may be more susceptible to these challenges due to their living environment. The results of various studies indicate that childhood lead exposure has negative effects on cognitive abilities later in life, particularly during adolescence and young adulthood [19], [20], [21], [22]. These high exposure levels have been linked to mild to significant intellectual deficits [20].

A major finding of this study is the impact of childhood lead exposure on the cognitive ability of adolescents and young adults, especially in developed countries. This finding raises concerns about the situation in low- and middle-income countries (LMICs), where there is insufficient scientific evidence and information to determine the extent of childhood lead exposure in such nations. However, little has been done, and these countries still have high levels of lead and low academic performance, including literacy efficiency. The evidence connecting lead exposure, a neurotoxin, to negative health outcomes has led to policies in the U.S. to prevent the sale of lead-based paint and leaded fuel to the general public. It has also contributed to bans on lead plumbing and lead solder in canned goods. Community-academic partnerships are well-positioned to bridge the gap between community knowledge, scientific evidence, and the policies necessary to promote health and health equity. Unfortunately, many partnerships have focused on the health effects of lead exposure throughout a person's life, the sources of lead in the community, and translating community and scientific evidence into policy and program interventions. Environmental policies are often created without considering the perspectives of the communities most affected by these policies. Moreover, lead-related policies have been slow to align with the overwhelming scientific evidence that no level of lead is safe for human health.

This study represents an initiating effort, being the first of its kind to concentrate on the age group spanning from ten to twenty-one years. This demographic is particularly susceptible to lead exposure, thus amplifying the importance of disseminating knowledge on preventive and ameliorative measures. By raising awareness and advocating for strategies to avert or minimize early lead exposure, we can safeguard the well-being and prospects of these children and young adults, who are poised to become tomorrow’s leaders and key contributors to the economy.

There remains an evident gap in research within low- and middle-income countries (LMICs) concerning lead exposure and its repercussions on the cognitive faculties of children and adolescents. This deficiency is especially disconcerting given that many LMICs rely on economic activities—such as mining, scrapyard operations, and battery production—that inherently involve lead usage or emissions. Compounding this issue, accessing pertinent information posed a challenge, compounded by the fact that some data were exclusively available in foreign languages

4. Conclusion

Environmental lead exposure remains a persistent issue in societies marked by historical reliance on lead paint and leaded gasoline for vehicles. While certain economic and technological advancements have been achieved, they have often been accompanied by activities that either release or employ lead. This trend is observable in various sectors, including battery manufacturing, scrap recycling, electronics production, ammunition fabrication, and dye synthesis, among others. Hence, it is imperative to raise awareness among health authorities regarding the adverse consequences of lead emissions, particularly in marginalized and informal communities. Additionally, healthcare professionals, parents, and guardians of children and adolescents must be equipped with knowledge about how to create safer living and recreational spaces for young individuals.

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