

PREVALENCE AND RISK FACTORS OF IRON DEFICIENCY ANEMIA IN PRIMARY CARE SETTING IN LOW INCOME COUNTRIES : A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: Children under the age of five are frequently affected by iron deficiency anemia. Iron deficiency affects children's psychomotor development and their cognitive ability.

Aims : This systematic review is to review the prevalence and risk factors of iron deficiency anemia in low income countries.

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, ScienceDirect and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Result: In the PubMed database, the results of our search brought up 828 articles, whereas the results of our search on SAGEPUB brought up 1683 articles, our search on SCIENCE DIRECT brought up 2880 articles. The results of the search conducted for the last year of 2014 yielded a total 273 articles for PubMed, 630 articles for SAGEPUB and 1319 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 3 of which came from PubMed, 1 of which came from SAGEPUB and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.

Conclusion: In summary, the global prevalence of iron insufficiency and iron deficiency anemia was noteworthy. To prevent complications, it is therefore necessary to regularly screen for and treat iron deficiency and iron deficiency anemia, especially in children who are considered high-risk.

Keyword: Iron deficiency anemia, low income country

INTRODUCTION

Globally, iron deficiency anemia (IDA) is the most prevalent kind of anemia. Nearly two billion individuals, or 25% of the world's population, are estimated by the World Health Organization (WHO) to be anemic, with over half of them having IDA. In addition, there is at least one patient with iron deficiency who is not anemic for every patient with IDA. As a result, over two billion people worldwide suffer from iron deficiency, either with or without anemia, and the majority of them live in nations with limited resources. Other dietary deficiencies (vitamin B12, folic acid, riboflavin), chronic illnesses, parasite infections such as malaria, hemoglobinopathies, and lead poisoning are other causes of anemia in low-income nations. In underdeveloped nations, anemia has a major role in maternal mortality and unfavorable pregnancy outcomes.¹

However, in affluent nations, IDA is also commonly found in specific high-risk populations, such as young children, teenage girls, women who are pregnant, and the elderly. The only common micronutrient deficit in affluent nations is iron insufficiency. At least 2.7% of toddlers in the United States between the ages of one and two are thought to have IDA. 2–25% of newborns aged 6–12 months were iron deficient, according to a review of 44 research done in 19 European nations. This incidence was greater in infants from socioeconomically disadvantaged backgrounds and in those who drank cow's milk throughout their first year of life. Iron deficiency was prevalent in children between the ages of 12 and 36 months, ranging from 3% to 48%, whereas IDA was prevalent in both age groups in Eastern Europe, reaching up to 50%, but not exceeding 5% in Western Europe. However, it is estimated that up to 40% of preschoolers in low- and middle-income nations are iron deficient and/or anemic. In affluent nations, several populations are more vulnerable to IDA: aboriginal people, recent immigrants, refugees, regular blood donors, endurance athletes, and vegetarians.^{1,2}

The final consequence of untreated iron deficiency is iron-related death (IDA), which is ranked ninth globally among the 26 modifiable risk factors for mortality that are part of the Global Burden of Disease project. Patients with IDA should receive treatment as soon as possible, even if they don't exhibit any symptoms, since they run the danger of developing organ ischemia and experiencing severe anemia until the underlying cause is addressed and the bone marrow's iron reserves are restored. Similarly, children who just have an iron shortage should receive treatment as sideropenia is linked to permanent neurocognitive deficits, diminished learning capacity, and altered motor function. It has also been demonstrated that individuals with iron deficiency are far more likely to experience febrile seizures, breath-holding episodes, and restless legs syndrome. Isolated iron insufficiency in female adolescents and young adults is linked to weariness and cold sensitivity, which can be alleviated with the right oral iron treatment.³

Although the frequency of anemia has somewhat declined globally over the last 20 years, conditions in Central and Western Africa are still alarming. In the United States, the frequency of iron insufficiency did not vary significantly in toddlers between 1976 and 2002 and remained high in several categories, such as Hispanic, younger, and overweight toddlers, despite a drop in the condition among newborns, Black, and impoverished children. Anemia (not only IDA) affects about 50% of younger children in poor nations, and as mentioned earlier, iron deficiency is thought to be the cause of around half of these cases. This percentage is lower in nations where the incidence of anemia is more than 40% (see below) and in nations where the burden of infectious illnesses is extremely high, as anemia is mostly caused by inflammation. In affluent nations and beyond the age of five, IDA is less prevalent in school-age children and resurfaces as a common issue in teenage girls experiencing strong menstrual flow, a growth spurt during puberty, eating poorly, and being older.³

Worldwide, IDA still has a significant impact on a lot of children and women who are fertile. Since approaches to enhance iron intake in the general population may be harmful for those affected by iron overload, iron deficiency prevention in industrialized nations should target specific populations at risk. To elucidate the physiological processes and mechanisms behind the advantages and hazards of supplementary iron for children exposed to parasite illnesses, such as malaria, further study is necessary in a resource-constrained situation. It is important to address not just iron deficiency in low-income nations, but also deficits in other micronutrients and hematinic factors, infections, and lead poisoning. Improving social and economic policies that combat poverty will be necessary to achieve these goals. In order to better serve their patients, doctors of various specializations who treat patients with iron deficiency and IDA of various etiologies should educate themselves on the many causes of IDA as well as the numerous therapeutic oral and parenteral iron solutions that are available.⁴

METHODS

Protocol

The author of this study ensured that it complied with the standards by adhering to Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. This is done to guarantee the accuracy of the results that are derived from the investigation.

Criteria for Eligibility

In order to complete this literature evaluation, we looked at published research that discusses the prevalence and risk factors of iron deficiency anemia in low income countries. This is done to enhance the patient's therapy management and

to offer an explanation. This paper's primary goal is to demonstrate the applicability of the issues that have been noted overall.

To be eligible to participate in the study, researchers had to meet the following requirements: 1) English must be used to write the paper. The manuscript must fulfill both of these conditions in order to be considered for publication. 2) A few of the examined studies were released after 2013 but prior to the time frame considered relevant by this systematic review. Editorials, submissions without a DOI, already published review articles, and entries that are nearly exact replicas of journal papers that have already been published are a few examples of research that are prohibited.

Search Strategy

We used "iron deficiency anemia " and "low income country" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SAGEPUB databases by inputting the words: ("iron deficiency anaemia"[All Fields] OR "anemia, iron deficiency"[MeSH Terms] OR ("anemia"[All Fields] AND "iron deficiency"[All Fields]) OR "iron-deficiency anemia"[All Fields] OR ("iron"[All Fields] AND "deficiency"[All Fields] AND "anemia"[All Fields]) OR "iron deficiency anemia"[All Fields]) AND ("developing countries"[MeSH Terms] OR ("developing"[All Fields] AND "countries"[All Fields]) OR "developing countries"[All Fields] OR ("low"[All Fields] AND "income"[All Fields] AND "country"[All Fields]) OR "low income country"[All Fields]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

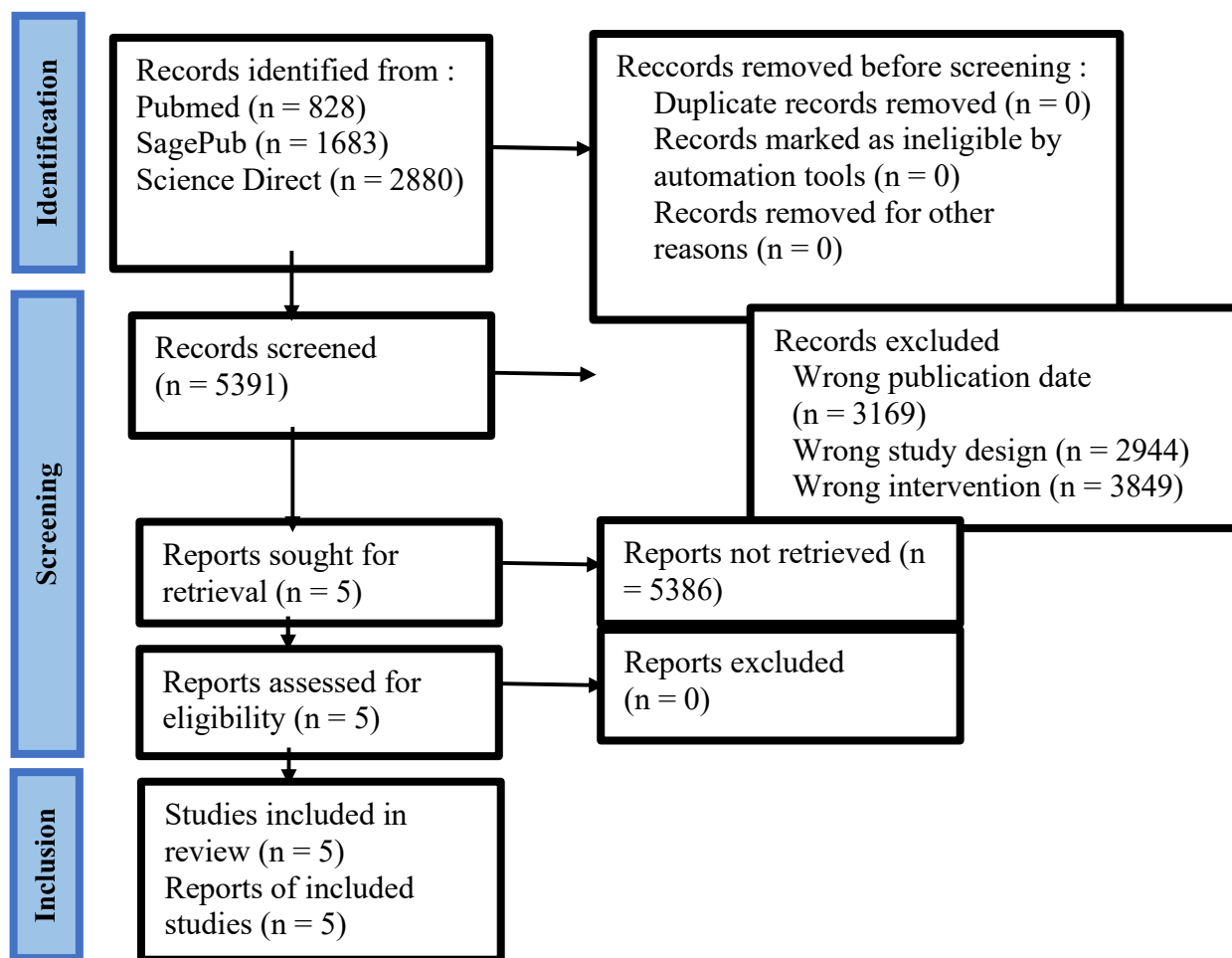


Figure 1. Prisma Flow Diagram

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. In order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 828 articles, whereas the results of our search on SAGEPUB brought up 1683 articles, our search on SCIENCE DIRECT brought up 2880 articles. The results of the search conducted for the last year of 2014 yielded a total 273 articles for PubMed, 630 articles for SAGEPUB and 1319 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 3 of which came from PubMed, 1 of which came from SAGEPUB and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.

Sahoo, et al⁵ (2023) showed that compared to comparable research carried out in other regions of the nation, the prevalence of anemia was lower. Despite the low rate of iron and folic acid coverage among recipients nationwide, our study demonstrated improved compliance and was linked to a notably higher level of hemoglobin among those who took iron folic acid (IFA).

Matias, et al⁶ (2018) showed that using micronutrient powder (MP) or lipid based nutrient supplements (LNSs) for home fortification, iron deficiency anemia (IDA) was decreased in 18-month-old Bangladeshi children. The use of LNSs throughout pregnancy and early infancy also decreased ID and anemia in children.

Byamugisha, et al⁷ (2022) showed that blister packaging has little influence on pregnant women's adherence to IFA. In contrast to the loose iron group, our results indicated that the blister packaged group saw a greater rise in hemoglobin.

Table 1. The literature include in this study

Author	Origin	Method	Sample	Result
Sahoo et al, 2023 ⁵	India	Cross sectional study	953 patients	37.3% of people were found to have anemia. 19.9% of people had mild anemia, 16.3% had moderate anemia, and 1% had severe anemia according to the World Health Organization's categorization. A statistically significant correlation was found between the amount of hemoglobin and the consumption of iron folic acid (IFA).
Matias et al, 2018 ⁶	Bangladesh	Cluster randomized study	4011 patients	Ferritin was higher and sTfR was lower in the LNS-LNS, IFA-LNS, and IFA-MNP arms compared to the IFA-Control arm; children in the LNS-LNS arms had lower odds of anemia (OR: 0.46; 95% CI: 0.25, 0.84), high sTfR (OR: 0.47; 95% CI: 0.29, 0.73), and ID (OR: 0.45; 95% CI: 0.28, 0.71)
Byamugisha et al, 2022 ⁷	Uganda	Randomised controlled study	478 patients	The blister and loose packaging arms had different mean hemoglobin levels at 4 weeks (11.9 + 1.1 g/dl and 11.8

				+ 1.3 g/dl, respectively; p = 0.02), but by week 8, they were similar (12.1 + 1.2 and 12.0 + 1.3, respectively; p = 0.23). Over the course of eight weeks, the hemoglobin level in the blister packaging arm was greater than that in the loose packaging arm (blister package 0.6 ± 1.0; loose packaging 0.2 ± 1.1; difference: 0.4 g/dL (95% CI: 0.24-0.51 g/dL); p = 0.001). There were no significant negative outcomes.
Siamisang et al, 2023⁸	Botswana	Cross sectional study	250 patients	Anemia was seen in 42.8% of this group. Of those, 145 (58%) were men. 56.1%, 39.2%, and 4.7% of the anemic individuals had mild, moderate, and severe anemia, respectively. In 61 (57%) of the patients, microcytic anemia associated with iron deficiency was found. The only reliable indicator of anemia was age. Compared to younger children, children 24 months of age and older had a 50% decreased risk of anemia (odds ratio (OR) 0.52; 95% Confidence Interval (95% CI) 0.30 to 0.89)
Elmugabil et al, 2023⁹	Sudan	Cross sectional study	208 patients	During the index pregnancy, 45 (21.6%) women did not take iron-folic acid. Four women (1.9%) had severe anemia, out of the eighty-eight (42.3%) who had anemia. Age, parity, history of miscarriage, interpregnancy interval, education, and degree of prenatal care were found to be unrelated to anemia in the univariate analysis. Compared to women without anemia, a greater proportion of anemic women did not take iron-folic acid during the index pregnancy (29/80 [33.0%] vs. 16/120 [13.3%], respectively, p =.001). The multivariate analysis revealed a correlation between anemia and not taking iron-folic acid (adjusted odds ratio = 3.19, 95% confidence range = 1.60–6.63).

Siamisang, et al⁸ (2023) showed that anemia is a severe health issue that has to be addressed quickly in Botswana, requiring better screening methods.

Elmugabil, et al⁹ (2023) showed that in this investigation, anemia was identified as a significant health issue for the expectant mothers. None of the anemic women had any conclusive proof that their anemia is the result of not taking iron

or folic acid; in fact, several anemic women did take iron or folic acid. In this region of Sudan, taking iron-folic acid might perhaps prevent anemia.

DISCUSSION

This systematic review involved a total of 5900 data of patients with iron deficiency anemia in country with low income. Approximately two billion individuals worldwide suffer from iron deficiency and iron-deficiency anemia (IDA), with the majority living in low- and middle-income nations. Other dietary deficiencies, hemoglobinopathies, chronic illnesses, parasite infections including malaria, and lead poisoning are among the additional causes of anemia in these countries. In countries with limited resources, maternal anemia is linked to low birth weight, more perinatal deaths, and worse labor productivity. It is difficult to maintain a proper iron balance in these conditions since meals high in iron and having good bioavailability are usually derived from animals and are either expensive or scarce. In addition to seldom consuming meat, poor vitamin C intake and diets high in iron absorption inhibitors are significant risk factors for iron deficiency anemia (IDA) in low-income nations. Although it has been demonstrated to significantly lower the risk of iron deficiency and IDA in infants and early children in developing nations, in-home iron fortification of complementary foods with micronutrient powders is linked to adverse changes in gut flora and the induction of intestinal inflammation, which may result in diarrhea and hospitalization. The only common micronutrient shortfall in modern nations is iron insufficiency.⁹

Study by Sahoo, et al showed that anemia is one of the major global public health issues. Adolescents have the greatest rate of anemia prevalence. Particularly disadvantaged are tribal populations, since several studies show that anemia affects tribal teenagers at a significant rate. Using spectrophotometry, a cross-sectional study was conducted in three primarily tribal regions of Odisha to determine the incidence of anemia among adolescents who had attended residential schools. The 953 participants had an average age of 13.07 ± 1.48 years. Compared to comparable research carried out in other regions of the nation, the prevalence of anemia was lower.

Matias, et al in their study with 4011 pregnant women showed that using MNP or LNSs for home fortification, IDA was decreased in 18-month-old Bangladeshi children. Pregnancy-related anemia and ID in children were also decreased by the use of LNSs. These results apply to comparable population-targeting approaches. LNS-LNS: LNSs (including 20 mg Fe) for women throughout pregnancy and the first six months after giving birth, and LNSs (including 9 mg Fe) for children between the ages of six and twenty-four months (LNS-C); 2) IFA-LNS: iron (60 mg) and folic acid (IFA) for women every day throughout pregnancy and every other day for the first three months after giving birth, and LNS-C for children; 3) IFA-MNP: IFA for women, and MNP (including 10 mg Fe) for children every day between six and twenty-four months; and 4) IFA-Control: no child supplement and IFA for women. To detect anemia, ID, and IDA, hemoglobin, serum ferritin, and soluble transferrin receptor (sTfR) were measured in a subsample of children at 18 months of age. Mixed-effects modeling was used to evaluate the data.

Byamugisha, et al showed in their study with randomized controlled trial in 474 patients, that blister packaging has little influence on pregnant women's adherence to IFA. In contrast to the loose iron group, our results indicated that the blister packaged group saw a greater rise in hemoglobin. Participants in the control and intervention groups totaled 474 and 478, respectively. At the 4th week (40.6 and 39.0%, $p = 0.624$) and 8th week (51.9 and 46.8%, $p = 0.119$), both groups' adherence to IFA consumption was comparable.

Siamisang, et al did study about the prevalence and risk factors of anemia in Botswana. The trial had 250 patients in total. Anemia was seen in 42.8% of this group. Of those, 145 (58%) were men. 56.1%, 39.2%, and 4.7% of the anemic individuals had mild, moderate, and severe anemia, respectively. In 61 (57%) of the patients, microcytic anemia associated with iron deficiency was found. The only reliable indicator of anemia was age. Compared to younger children, children 24 months of age and older had a 50% decreased incidence of anemia (odds ratio (OR) 0.52; 95% Confidence Interval (95% CI) 0.30 to 0.89). The results of this study show that anemia poses a significant health risk to Botswana's juvenile population.

Lastly in this study is the research by Elmugabil, et al with cross sectional study in 208 patients showed in this investigation, anemia was identified as a significant health issue for the expectant mothers. Among the 208 women who were recruited in the study, the median (interquartile range) age and parity were 2 (1-4) and 25 (21.0-30.0), respectively. During the index pregnancy, 45 (21.6%) women did not take iron-folic acid. Four women (1.9%) had severe anemia, out of the eighty-eight (42.3%) who had anemia. Age, parity, history of miscarriage, interpregnancy interval, education, and degree of prenatal care were found to be unrelated to anemia in the univariate analysis. Compared to women without anemia, a greater proportion of anemic women did not take iron-folic acid during the index pregnancy (29/80 [33.0%] vs. 16/120 [13.3%], respectively, $p = .001$).

CONCLUSION

In summary, the global prevalence of iron insufficiency and iron deficiency anemia was noteworthy, especially in the global south. To prevent complications, it is therefore necessary to regularly screen for and treat iron deficiency and iron deficiency anemia, especially in children who are considered high-risk.

REFERENCE

- [1] Pasricha SR, Drakesmith H, Black J, Hipgrave D. Epub 2013 Jan 25. Control of iron deficiency anemia in low- and middle-income countries. *Blood*. 2013;2607–17.
- [2] Bailey RL, West Jr KP, Black RE. The epidemiology of global micronutrient deficiencies. *Ann Nutr Metab*. 2015;22–33.
- [3] Vos T, Allen C, Arora M, Barber RM, Brown A, Carter A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*. 2016 Oct 8;388(10053):1545–602.
- [4] Mantadakis E, Chatzimichael E, Zikidou P. Iron deficiency anemia in children residing in high and low-income countries: Risk factors, prevention, diagnosis and therapy. Vol. 12, *Mediterranean Journal of Hematology and Infectious Diseases*. Universita Cattolica del Sacro Cuore; 2020.
- [5] Sahoo J, Mohanty S, Gupta S, Panigrahi SK, Mohanty S, Prasad D, et al. Prevalence and Risk Factors of Iron Deficiency Anemia among the Tribal Residential Adolescent School Students of Odisha: A Cross-Sectional Study. *Indian Journal of Community Medicine*. 2023;48(4):562–6.
- [6] Matias SL, Mridha MK, Young RT, Khan MSA, Siddiqui Z, Ullah MB, et al. Prenatal and Postnatal Supplementation with Lipid-Based Nutrient Supplements Reduces Anemia and Iron Deficiency in 18-Month-Old Bangladeshi Children: A Cluster-Randomized Effectiveness Trial. *J Nutr*. 2018;11671–1176.
- [7] Byamugisha J, Adero N, Kiwanuka TS, Nalwadda CK. The effect of blister packaging Iron and Folate on adherence to medication and hemoglobin levels among pregnant women at National Referral Hospital antenatal clinics in a low to middle income country: a Randomised Controlled Trial (The IFAd Trial). *BMC Pregnancy Childbirth*. 2022;179.
- [8] Siamisang AB, Gezmu AM, Slone JS. Prevalence and Associated Risk Factors of Anemia Among Hospitalized Children in a Tertiary Level Hospital in Botswana. *Glob Pediatr Health*. 2023;
- [9] Elmugabil A, Adam I. Prevalence and Associated Risk Factors for Anemia in Pregnant Women in White Nile State, Sudan: A Cross-Sectional Study. *SAGE Open Nurs*. 2023 Jan 1;9.