Evaluation and Management of Iron Deficiency Anemia among Adults in KSA: A Systematic Review

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Abstract: Background: Iron deficiency anemia (IDA) is a significant public health concern in the Kingdom of Saudi Arabia (KSA). This systematic review aimed to evaluate strategies for diagnosing and managing IDA among adults in KSA.

Methods: A comprehensive search was conducted across multiple databases and grey literature sources to identify relevant studies. Eligible studies included randomized controlled trials, observational studies, and systematic reviews/meta-analyses reporting on the evaluation or management of IDA among adults in KSA. Data extraction and quality assessment were performed independently by two reviewers.

Results: The initial search yielded 207 studies, with 42 full-text articles reviewed. Only three studies met the inclusion criteria for this review. AlSulayyim et al. revealed wide variability in pediatric IDA management practices among physicians in Riyadh, emphasizing the need for intervention programs and national guidelines. AlAyoubi et al. found gender disparities in anemia prevalence among young adults in Riyadh, with females at higher risk. Owaidah et al. conducted a national epidemiological survey highlighting the prevalence of ID and IDA among young university students in Saudi Arabia, with a particular burden observed among females.

Conclusion: The reviewed studies underscored the complexity of IDA in KSA, with variability in clinical practices, gender disparities, and nutritional deficiencies playing significant roles. Multifaceted interventions, including standardized management guidelines and gender-specific strategies, are necessary to address

the burden of IDA effectively in the Kingdom. Further research is needed to explore additional factors contributing to IDA and evaluate the long-term efficacy of interventions in this population.

1. Introduction

W.H.O. estimates that 800 million women and children were afflicted by anemia globally in 2011 [1]. Anemia affected 38.2% of pregnant women and 29.4% of women of reproductive age, according to the same World Health Organization research. Children had the highest estimated prevalence of anemia at 42.6%, while non-pregnant women had the lowest at 29.0%, according to the survey. According to another research, about 2 billion individuals have anemia on a global scale [2]. According to the same research, almost 70% of newborn newborns in Arab nations have iron-deficiency anemia (IDA).

When the body does not absorb enough iron from food or when there is persistent, outside (non-resorptive) blood loss, the outcome is iron-deficiency anemia. Low iron reserves and a hemoglobin level two standard deviations below the age and sex-specific normal establish the diagnosis of Iron Deficiency Anemia. About 26% of Riyadh schoolgirls between the ages of 7 and 14 have IDA [3]. Premature delivery, low birth weight, stillbirth, and other complications are more likely in moms with maternal anemia. Iron deficiency anemia accounts for 20% of neonatal mortality and 10% of maternal mortality in underdeveloped nations [4]. There is a 30% reduction in maternal mortality for every 10 g/l rise in maternal hemoglobin level [5].

Because of its complex nature, anemia may function as both a cause and an effect of disease [6]. Many different variables, some of which are modifiable and others of which are more static, may have an effect on anemia. Among them may be dietary variables, gynecological/obstetric history, genetics, and socio-demographic factors including gender, age, and race [6]. Furthermore, anemia is often linked to long-term health issues and cancers, including malignancies, hypothyroidism, high blood pressure, chronic kidney disease, rheumatism, and heart failure [7]. Considerations for specific risk factors may include iron deficiency anemia, worm infestation, bleeding, a medical history that includes conditions like gastric ulcer and hemorrhoids, or the use of drugs like aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) [6].

The impact of iron-inhibiting and -enhancing foods on anemia and iron absorption and storage in the body is still debatable [8,9]. Iron-enhancing foods include meat and vitamin C. Iron-inhibiting foods include coffee and tea. Anemia has several different effects. In pregnant women, this disease may impact the physical or mental development of an embryo; in children, it can impact the growth of cognitive abilities and development; in adults, it can impair the capacity to physically exert oneself; and in the elderly, it can have a negative impact on quality of life in general [10–17]. It has the potential to kill both the mother and the baby in extreme cases [13-16].

It is presently difficult to get data about anemia in Saudi Arabia [18-21]. Results from a case-control study carried out by AlQuaiz et al. at all primary health care clinics of King Khalid University Hospital in Riyadh indicate that dietary habits, menorrhagia, and a history of ingesting NSAIDs or antacids are important risk factors for IDA among Saudi women of childbearing age. Anemia was also shown to be significantly linked with dietary and medication-taking habits in Saudi females of childbearing age, including a low meat or juice intake, as well as the use of antacids or NSAIDs [21].

Routine screening for IDA should be conducted in pregnant women who are not experiencing any symptoms, according to the American Academy of Family Physicians, the United States Preventive Services Task Force, and the Centers for Disease Control and

Prevention. Screening for anemia and iron treatment should be implemented when IDA is established, according to the American College of Obstetricians and Gynecologists. In the first two trimesters of pregnancy, a hemoglobin level below 11 g/dL (110 g/L) is considered to be indicative of anemia; in the second trimester, a level below 10.5 g/dL (105 g/L) is acceptable. Fetal complications, including mortality, have been linked to maternal hemoglobin levels below 6 g/dL (60 g/L) [22]. The risk factors for iron deficiency anemia in children include a low birth weight, a history of preterm, lead exposure, prolonged exclusive nursing beyond the first four months of life, and the introduction of iron-fortified foods into a child's diet during weaning from whole milk and supplementary meals. Therefore, it is recommended that all children should be tested for hemoglobin and risk factors for iron deficiency at the age of one year [23].

Instead of being absorbed in the stomach, iron is most effectively taken in via the proximal jejunum and distal duodenum. Since acidic conditions are necessary for the release of ferric iron from meals, iron insufficiency may result from prolonged achlorhydria. After that, it is kept soluble and accessible for absorption in the more alkaline duodenum by being chelated with mucins and other compounds, such as sugars, amino acids, amides, and amino acids. Iron supplements must be taken at least two hours before or four hours after using antacids. Iron malabsorption and IDA may result from eating starch and clay, the latter of which is particularly prevalent in certain regions of the Middle East and Africa [24].

2. Methods

Review Question

The systematic review aimed to evaluate and provide recommendations for the evaluation and management of iron deficiency anemia (IDA) among adults in the Kingdom of Saudi Arabia (KSA). Specifically, it sought to identify the most effective strategies for diagnosing and treating IDA in this population, considering various interventions such as dietary modifications, iron supplementation, and other medical interventions.

Search Strategy

A comprehensive search was conducted across relevant databases including PubMed, MEDLINE, Embase, Scopus, and Cochrane Library. Additionally, grey literature sources such as conference proceedings and relevant organizational websites were searched. The search was limited to articles published in English and Arabic languages. The search strategy included keywords related to iron deficiency anemia, adults, evaluation, management, and Saudi Arabia. Types of Studies Included Randomized controlled trials (RCTs), observational studies (cohort studies, case-control studies), cross-sectional studies, and systematic reviews/meta-analyses were included in this review. Studies reporting on the evaluation or management of iron deficiency anemia among adults in KSA were considered for inclusion.

Participants

The review included studies involving adult participants (aged 18 years and above) residing in the Kingdom of Saudi Arabia who had been diagnosed with iron deficiency anemia.

Search Keywords

Keywords used in the search strategy included variations of the following terms: "iron deficiency anemia," "iron deficiency," "anemia," "adults," "evaluation," "management," "treatment," "diagnosis," "Saudi Arabia," and related Medical Subject Headings (MeSH) terms.

Study Selection Process

Two independent reviewers conducted the initial screening of titles and abstracts identified through the search strategy. Full-text articles of potentially relevant studies were then retrieved and assessed for eligibility based on predefined inclusion and exclusion criteria. Any discrepancies were resolved through discussion or consultation with a third reviewer if necessary.

Outcomes

The primary outcomes of interest included measures related to the effectiveness of interventions in managing iron deficiency anemia among adults in KSA, such as improvement in hemoglobin levels, iron status, and quality of life. Secondary outcomes might have included adverse effects of interventions and compliance rates.

Data Extraction and Coding

Two reviewers using a standardized data extraction form performed data extraction independently. Extracted data included study characteristics (e.g., study design, sample size), participant demographics, intervention details, outcome measures, and key findings. Any discrepancies were resolved through discussion or consultation with a third reviewer.

Data Management Data from included studies were managed using reference management software such as EndNote or Zotero. Duplicate records were identified and removed during the screening process. Extracted data were stored securely and accessible only to the review team to ensure confidentiality and data integrity throughout the review process.

3. Results

The initial search identified a total of 207 studies from PubMed, Embase, Cochrane Library, and CINAHL. There were some duplicates and 84 studies were screened based on their titles and abstracts. Of these, 42 full-text articles were reviewed, and only three studies were eligible for inclusion in this systematic review (Figure 1).

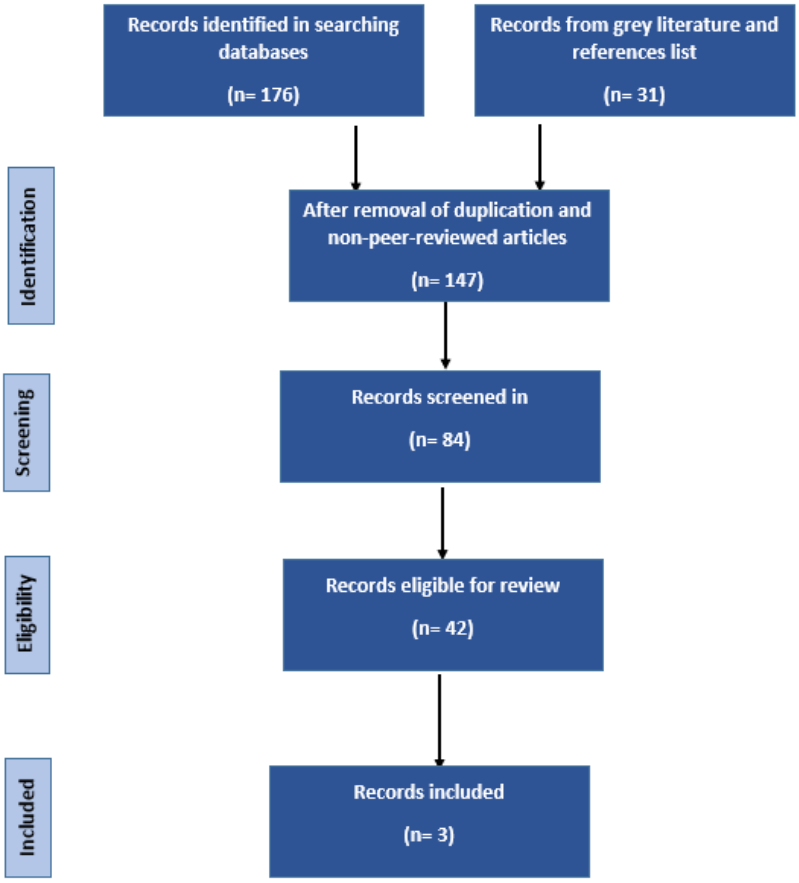

Figure 1: Flow chart of selection process

Many studies were found assessing prevalence of iron deficiency anemia among various populations in KSA. However, these studies were excluded as they do not meet the review criteria. Only three articles are found to meet the review criteria [25-27].

AlSulayyim et al. [25] focusing on pediatric Iron Deficiency Anemia (IDA) management, revealed significant variability in diagnostic and therapeutic practices among physicians in Riyadh. Out of 166 surveyed physicians, 147 were included, showing wide discrepancies in IDA diagnosis and therapy preferences. While ferrous sulfate was the preferred treatment for nutritional IDA, the total daily elemental iron doses varied widely. Professional qualification and workplace significantly influenced diagnostic and therapeutic approaches, with pediatric hematologists and those in tertiary care scoring higher. The study emphasized the urgent need for intervention programs and national guidelines to standardize pediatric IDA management [25].

AlAyoubi et al. [26] targeting young adults in Riyadh, anemia prevalence and risk factors were assessed. Among participants aged 18 to 28, a higher percentage of men were observed, with approximately one-third being overweight. Notably, gender emerged as the only significant factor associated with anemia, with females exhibiting a higher risk. Although factors like dietary lifestyle, menstruation, pregnancy, and NSAID intake were identified as potential risk factors, they did not attain statistical significance. This underscores the importance of addressing gender-specific factors in anemia prevention and management among young Saudi adults [25].

Owaidah et al. [27] a national epidemiological survey, highlighted the prevalence of ID and IDA among apparently healthy young university students in Saudi Arabia. Out of 981 surveyed students, 11% reported symptoms of anemia, with 34% diagnosed with IDA. Blood analysis confirmed high prevalence rates of ID and IDA, particularly among females. Additionally, thalassemia and sickle cell traits were detected in a small percentage of participants. These findings underscore the significant burden of ID and IDA among young Saudis and emphasize the necessity of addressing nutritional deficiencies on a national scale to mitigate the public health impact of anemia [25].

The methodologies employed in the three studies on anemia in Saudi Arabia vary in scope and approach. The first study, focusing on pediatric IDA management, utilized a cross-sectional design to assess diagnostic and therapeutic practices among physicians in a major healthcare facility in Riyadh. A validated questionnaire was employed, covering demographic data and patient case-scenarios related to IDA diagnosis and treatment. Robust regression analysis was utilized to identify factors associated with participants' overall scores. In contrast, the second study targeted young adults in Riyadh to assess anemia prevalence and risk factors. It employed a cross-sectional design at two universities, collecting data through interview questionnaires and clinical and laboratory evaluations. The third study, a national epidemiological survey, aimed to determine the prevalence of ID and IDA among apparently healthy young university students across four regions in Saudi Arabia. It utilized a survey questionnaire followed by blood sample collection and analysis. While all studies focused on anemia in Saudi Arabia, they differed in their target populations, settings, and methodologies employed, providing complementary perspectives on the issue.

The results of the three studies shed light on the prevalence and management of anemia in Saudi Arabia but reveal varying perspectives and emphases. The first study highlighted significant variability in pediatric IDA diagnosis and therapy practices among physicians, underscoring the need for intervention programs and national guidelines. In contrast, the second study emphasized the gender disparity in anemia prevalence among young adults in Riyadh, with females exhibiting a higher risk. While potential risk factors like dietary habits and menstruation were noted, they were not statistically significant. The third study, a national epidemiological survey, revealed a high prevalence of ID and IDA among young Saudis, especially females, suggesting a substantial burden of nutritional deficiencies. Thalassemia and sickle cell traits were also detected in a small percentage of participants. Collectively, these results underscore the complex interplay of factors contributing to anemia in Saudi Arabia,

including clinical practices, gender disparities, and nutritional deficiencies, necessitating multifaceted interventions for effective prevention and management.

Table 1: Summary of characteristics of included studies

Authors	Year	Design	Setting	Main Findings	Implication
Hadi J. Al Sulayyim et al. [25]	2019	Cross-sectional study	Major public healthcare facility in Riyadh	Wide variability in pediatric IDA diagnosis and therapy practices; Urgent need for intervention	Development of national guidelines for standardized pediatric IDA management
Fakhr AlAyoubi et al. [26]	2019	Cross-sectional study	King Saud University and Alfaisal University	Gender as significant factor associated with anemia; Dietary lifestyle and other factors noted	Gender-specific interventions in anemia prevention and management
Tarek Owaidah et al. [27]	2020	Epidemiological survey	Nationwide	High prevalence of ID and IDA among young Saudis; Thalassemia and sickle cell traits detected	National strategies for addressing nutritional deficiencies in Saudi Arabia

4. Discussion

The prevalence of iron deficiency anemia is alarming, particularly in underdeveloped regions of the globe [28, 29]. The frequency of ID and IDA among young Saudi Arabian university students from four main areas is established in this research. In the early stages of ID, when iron reserves are exhausted, serum ferritin levels drop, resulting in simple ID. Several studies have attempted to quantify the scope of this public health crisis in Saudi Arabia; however, these studies have relied on data collected from a small sample size, have focused on men or females only, or have been limited to a particular geographic area. Evidence of IDA in Saudi Arabia varies widely, with estimates ranging from 10% to 60% [30, 31-33].

Diagnostic criteria and treatment strategies used by doctors for IDA have received very little attention in the scientific literature. Results from the study by [25] and another one from the United States by Powers et al. [44] showed that there was a great deal of variation among doctors when it came to diagnosing and treating IDAs, even though prior research had concentrated on IDA epidemiology [34–38], diagnosis [38–41], treatment [39,42], or prevention [38,43]. The [25] research, on the other hand, used a different strategy than Powers et al. Several less-than-ideal approaches to pediatric IDA diagnosis and treatment were uncovered by the study's total score, which was derived from participants' answers to several questions [25].

It is important to take into account the widely reported differences in the diagnostic criteria for IDA in studies [25]. In addition to the CBC, many patients seen at primary care clinics or sent to tertiary institutions have superfluous tests done on them [41]. The results of the research, which found that only 15.6% of participants in the study felt that no further tests were needed beyond the CBC, are in agreement with those of a study done in the US by Powers J et al. [44]. They also came up with a 15% figure.

When a patient tests anemic during the first screening, the American Academy of Pediatrics recommends further testing to rule out suspicious IDA, such as assessing TfR1 concentration, CHr or Ret-He, and/or SF with CRP [38]. Nonetheless, the AAP does not state that CHr or TfR1 are unable to distinguish between IDA and thalassemia or hemolytic anemia, respectively [45]. There is a lack of accessibility to these tests in many healthcare facilities, especially in nations with minimal resources. Hence, it may not be feasible to make a clinical choice on such examinations. To confirm a diagnosis of IDA, the majority of individuals in this research did not follow any particular protocols. No one used the AAP's method, according to the aforementioned American research of pediatric hematology/oncology doctors [44]. In order

to confirm IDA, Powers et al. suggested using a complete blood count (CBC), peripheral blood smear (PBS), reticulocyte count (RCC), serum iron (SeI), SF, and TIBC [46]. Nearly half of our individuals picked SF and TIBC, while more than half of the people in the Powers et al. trial went with such tests.

More than half of the people who took part in the IDA treatment study (25 people) said that they rely more on their own experiences than on evidence when making therapeutic decisions. A dosage of iron between 3 and 6 mg/kg daily is recommended as an effective therapy for IDA in almost all published research [39, 40]. The vast majority of pediatric hematology oncology doctors recommend 6 mg/kg/day, yet this recommendation is unsupported by data. Low doses have been effective in several trials. When patients in a randomized experiment in Ghana were given 40 mg of iron (nearly 3 mg/kg/day) either all at once or spread out over three doses, the results were the same for both groups [42]. In a separate trial, 90 older adults were evaluated across three different iron dosages (15 mg, 50 mg, and 150 mg daily). Hb concentration and SF growth were comparable across all three groups at 60 days. The results show that even a little amount of iron taken orally may have the same beneficial effects as a larger dose. Also, fewer people dropped out and had fewer side effects in the groups given the lowest doses [47]. Previous research suggests supplementing with iron for three to six months [48-50], although the ideal length is still up for debate. For children aged 3 to 4 months, the Canadian Pediatric Surveillance Program recommends an oral iron dosage of 6 mg/kg/day [51]. Some research suggests that iron levels are replenished after two to three months of iron treatment [50].

When asked how long patients needed to keep taking oral iron until their hemoglobin, mean corpuscular volume (MCV), and ferritin levels returned to normal, participants' answers varied widely [25]. The research of Powers et al. [44] is similar to this. While 36% of respondents said that a patient's dosage should be based on their weight, 50.3% said that it should be based on their weight and 49.7% said it should be based on the number of pills, respectively, in the research [25]. Although there are several safe and efficient parenteral iron preparations available, only 14% of participants in this survey suggested using them for adults or children who did not respond to oral iron treatment. When compared to other oral iron treatments, ferrous sulfate was both the most effective and the most cost-effective of the 170 iron therapies used to treat and prevent IDA [52].At this time, it is the therapy that IDA patients seek out most often [46].

On the remaining two questions, participants' scores were very low [25]. Assuming the infant is "well compensated" and has no co-morbidities, only 33.3% got the question about the Hb number below which they would certainly suggest a blood transfusion right [25]. Some doctors advise transfusions irrespective of Hb levels since there is no universally accepted cutoff for blood transfusions; instead, they base their recommendations on patients' symptoms and overall health [53]. Additionally, only 32.7% of participants correctly identified the appropriate IV preparation for parenteral iron. According to relevant research, giving someone iron dextran intravenously may raise their hemoglobin levels in 7–14 days [54], while giving them iron saccharate (iron sucrose) or ferric gluconate can do the same after 7 days [55]. In clinical studies that looked for adverse events after giving ferric gluconate [57], iron dextran [58], and iron sucrose [56], the corresponding frequencies were reported as 36%, 35%, and 50% of the patients, respectively. Serious adverse events were not connected with the delivery of the iron sucrose, according to another research [59]. In addition, ferric gluconate and iron sucrose had superior bio-availability and fewer cases of the potentially fatal allergy compared to iron dextran [60]. Because of its many adverse events, including anaphylactic responses, iron dextran was prohibited for use in the United States [61, 62]. Nevertheless, maybe these low percentages of right responses are because when it comes to transfusions or IV iron preparation, most general practitioners, family doctors, and even some pediatricians refer their patients to

pediatric hematologists [25]. This agrees with the results from [25], which showed that hematologists and those working in tertiary care settings got higher ratings.

5. Conclusion

This systematic review identified three studies that provide valuable insights into the prevalence and management of anemia in Saudi Arabia. While many studies assessed the prevalence of iron deficiency anemia (IDA) among various populations in the Kingdom, only three met the inclusion criteria for our review. These studies addressed pediatric IDA management, anemia prevalence and risk factors among young adults, and a national epidemiological survey highlighting the prevalence of ID and IDA among university students. The methodologies employed varied, ranging from cross-sectional designs to national surveys, each offering unique perspectives on the issue. The results underscored significant variability in pediatric IDA diagnosis and therapy practices among physicians, emphasizing the need for intervention programs and national guidelines. Gender emerged as a significant factor associated with anemia prevalence among young adults, highlighting the importance of gender-specific interventions in anemia prevention and management. Additionally, the high prevalence of ID and IDA among young Saudis, especially females, emphasizes the necessity of addressing nutritional deficiencies on a national scale. Collectively, these findings underscore the complexity of factors contributing to anemia in Saudi Arabia and emphasize the need for multifaceted interventions for effective prevention and management.

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