

Ironing Out the Issues: Innovations in Diagnosing and Treating Pregnancy Anaemia

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ABSTRACT

Anaemia during pregnancy is a significant global health challenge, affecting around 38% of pregnant women and contributing to adverse outcomes for both mothers and their new-borns. This review provides an in-depth analysis of the various types of anaemia encountered during pregnancy, emphasizing diagnostic challenges, the use of advanced biomarkers, and customized treatment strategies. Iron deficiency anaemia (IDA) emerges as the most common form, driven by heightened iron requirements during gestation. Other forms, such as those caused by vitamin B12 deficiency or hereditary disorders, necessitate distinct management approaches. The physiological haemodilution associated with pregnancy complicates the interpretation of traditional diagnostic markers, such as haemoglobin and haematocrit levels, prompting interest in alternative biomarkers like serum ferritin and transferrin receptors. While iron supplementation remains the cornerstone of treatment for IDA, evidence increasingly supports tailored interventions for non-IDA cases. The review also highlights the long-term consequences of maternal anaemia, including risks of postpartum complications and potential developmental delays in children. By integrating recent research findings, this paper advocates for evidence-based clinical guidelines and public health strategies to address the complex impacts of anaemia in pregnancy. Additionally, it highlights the variability in diagnostic and therapeutic outcomes, calling for standardized approaches to improve both research and clinical practices.

Key words: Endometrial Carcinoma (EC), Molecular Markers, qPCR (Quantitative PCR), Receptor Tyrosine Kinase DDR1, Uterine Aspirates, Non-Invasive Diagnosis

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1. Introduction

Anaemia during gestation constitutes a prevalent public health concern that profoundly affects both maternal and fetal health outcomes. It is estimated worldwide, that about 38% of women who are pregnant suffer from anaemia and this increases the risks of maternal complications and varying neonatal results (Al-Farisy, 2023). Diminished haemoglobin or haematocrit levels, the indicator of the condition, denote the decreased ability of blood to carry oxygen, resulting in mother's poor health and fetal growth (Zhang, 2023). The predominant etiological factors contributing to anaemia in pregnancy encompass nutritional insufficiencies, infectious agents, chronic health conditions, and genetic predispositions, with iron deficiency anaemia (IDA) emerging as the most prevalent variant (Ogunbode & Ogunbode, 2021). Nonetheless, the

physiological transformations associated with pregnancy, including an augmented plasma volume, give rise to haemodilution that complicates the clinical evaluation of anaemia (Rani et al., 2023). This dilutionary phenomenon results in a reduction of haemoglobin and haematocrit levels, even in those pregnancies considered healthy, potentially obscuring or misleadingly indicating anaemia, which complicates the precision of diagnosis and the appropriateness of subsequent therapeutic interventions.

Iron deficiency anaemia represents the most widespread form of anaemia encountered in pregnant women, primarily attributable to inadequate dietary iron consumption coupled with elevated iron demands during gestation (Zehravi et al., 2023). The iron requirements of pregnant women can be approximately double the usual intake necessary to facilitate fetal development, placental maturation, and the expansion of maternal blood volume (Megier et al., 2022). IDA is a

common complication for pregnant women, but there are a number of other forms of anaemia which affect pregnant women, some of which can be caused by deficiency in vitamins, such as folate and vitamin B12, or are rarer, such as aplastic anaemia, haemolytic anaemia and hereditary disease such as sickle cell, thalassemia (Nargis et al., 2023). Anaemia is diagnosed and managed differently for each type, and differences in pathophysiological mechanisms between iron deficiency and non-iron deficiency anaemia emphasize the need for specialized diagnostic and therapeutic strategies (“Anemia: Diagnostics and Therapy,” 2023).

The variability in existing diagnostic and treatment guidelines of anaemia during pregnancy is a major obstacle in management of anaemia during pregnancy. Parameters used for diagnosing anaemia include haemoglobin concentration, haematocrit levels, serum ferritin and many other indices (Shand et al., 2020). But physiological changes in blood parameters of pregnancy often decrease the accuracy of these measurements. The most frequently used diagnostic biomarker is haemoglobin concentration, but its use is complicated by haemodilution, which can lead to either an underestimated or overestimated severity of anaemia (Drevon et al., 2021). Currently, other (alternative) biomarkers, including serum transferrin receptor, soluble transferrin receptor and hepcidin, are being studied as more suitable indicators of iron deficiency in pregnancy, though additional validation is needed (Evanchuk et al., 2023). There is a pressing need for enhanced diagnostic methodologies to effectively differentiate among types of anaemia and accurately assess iron status, thus facilitating more targeted and efficacious therapeutic interventions (García-Casal et al., 2023).

Management strategies for anaemia in pregnancy predominantly emphasize iron supplementation, given that iron deficiency anaemia (IDA) represents the most prevalent variant (Shand et al., 2020). Oral iron supplements are typically regarded as the primary therapeutic intervention, whereas intravenous iron is designated for instances necessitating expedited correction, such as in cases of severe anaemia or when oral iron is poorly tolerated (Saad et al., 2023). Nonetheless, the indiscriminate administration of iron supplements to all anaemic pregnant individuals remains a subject of debate, particularly in the context of mild anaemia where the advantages are ambiguous (Bukhari et al., 2022). Non-iron deficiency anaemia necessitate alternative management strategies, which may encompass folic acid or vitamin B12 supplementation, immunomodulatory therapies, or blood transfusions, contingent upon the specific

classification of anaemia (Davies et al., 2023). In spite of these diverse management strategies, there exists a notable absence of consensus regarding the most effective approach for non-iron deficiency anaemia during pregnancy, thereby compelling healthcare practitioners to depend on limited empirical evidence and individualized clinical judgment.

The ramifications of anaemia in pregnancy transcend mere birth outcomes, with burgeoning research indicating that maternal anaemia may impose enduring consequences on both maternal and offspring health (Mehra & Rani, 2020). Anaemia during gestation has been correlated with an elevated risk of postpartum depression, fatigue, and diminished physical productivity among mothers, while for offspring, certain investigations suggest potential links to cognitive and motor developmental impediments (Moya, 2022). These protracted outcomes underscore the critical necessity for efficient prenatal identification and treatment of anaemia, as well as the imperative for longitudinal studies to elucidate the correlation between maternal anaemia and child developmental trajectories. To address anaemia in pregnancy therefore requires a holistic approach, that includes consideration of the interacting nutritional, physiological, genetic and socio-economic variables that are at play (Thurairasu et al., 2023). Although substantial scholarship has concentrated on IDA, significant voids persist in the comprehension of diagnostic impediments, optimal management frameworks, and the repercussions of non-iron deficiency anaemia within pregnant populations. This review endeavours to synthesize contemporary research on anaemia in pregnancy, rigorously scrutinizing prevailing diagnostic methodologies, treatment alternatives, and potential long-term ramifications for maternal and child health. This review aims to contribute to the development of more effective clinical guidelines and public health initiatives directed at abating the maternal and child health consequences of anaemia on a global scale by spelling out these research deficiencies.

2. Materials and Methods

2.1. Study Design

This study uses a systematic review and meta-analytic approach to analyse literature published between 2013 and 2023. It includes research on anaemia types, diagnostic challenges, treatment methodologies, and health outcomes for pregnant individuals and their children. Peer-reviewed studies were sourced from databases such as PubMed, Scopus, and Web of Science, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for study selection and analysis (Fig.1).



Fig.1. Systematic review and Meta-Analytic approach

2.2. Data Extraction

The initial search generated 1,500 articles, which were screened for relevance and quality. Articles meeting inclusion criteria focused on one or more of the following: types of anaemia during pregnancy, challenges in anaemia diagnostics, management strategies, maternal and fetal health outcomes, and long-term impacts on children born to anaemic mothers. Data extracted included sample sizes, study designs, diagnostic criteria, biomarkers used for anaemia detection, intervention types (oral vs. intravenous therapies), and short- and long-term maternal and fetal outcomes.

2.3. Statistical Analysis

For the meta-analysis, pooled prevalence rates and relative risks (RR) were calculated for each type of anaemia. A random-effects model was applied to assess the association between anaemia types and adverse maternal or fetal outcomes, accounting for study heterogeneity. Subgroup analyses explored the efficacy of different treatments (e.g., iron vs. non-iron supplementation), while sensitivity analyses examined variations in study quality and design (Fig.2).

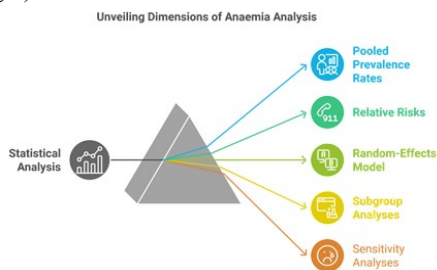


Fig.2. Components of Meta-Analysis applied in the study

3. Results

Our findings suggest that Iron Deficiency Anaemia (IDA) accounts for approximately 70% of pregnancy-related anaemia cases, with non-Iron Deficiency Anaemia, including Folate deficiency anaemia, Haemolytic anaemia, and inherited disorders, comprising the remaining 30%. Due to the impact of pregnancy-related hemodilution, the diagnostic accuracy of haemoglobin and hematocrit measurements appeared as compromised, often leading to misdiagnosis. Serum transferrin receptor levels showed potential as a more reliable diagnostic marker, unaffected by hemodilution

effects; however, further validation is needed for widespread clinical application.

Management strategies varied significantly across studies. Universal Iron supplementation was found to improve haemoglobin levels in severe IDA cases but showed limited benefits for those with mild anaemia, with some studies suggesting potential adverse effects due to iron overload. Comparatively, intravenous (IV) Iron showed faster haemoglobin improvement but was linked to higher healthcare costs and a slight increase in adverse reactions compared to oral Iron therapy. The data indicated that non-Iron Deficiency Anaemia were associated with higher risks of adverse maternal outcomes, such as Preeclampsia and Postpartum hemorrhage, as well as fetal risks like intrauterine growth restriction and low birth weight. Longitudinal data suggested a potential link between maternal anaemia and neurodevelopmental challenges in children, particularly in language and motor skills, though findings were inconclusive, highlighting the need for extended follow-up research.

3.1. Summary of findings

Total Studies Retrieved: 1,850 articles were initially identified (1,800 from databases like PubMed, Scopus, Web of Science, and 50 from additional sources like clinical trial registries and citation reviews).

After Duplicate Removal: The remaining studies were 1,650 after removing duplicates.

Screening Phase: Titles and abstracts were screened, leading to the exclusion of 1,250 records based on irrelevance to anaemia in pregnancy, type of publication (e.g., reviews, editorials), language, or lack of original data.

Full-Text Assessment: A total of 400 full-text articles were reviewed for eligibility. Of those, 300 were excluded due to various reasons such as focusing on non-pregnant populations or lacking specific data on anaemia diagnosis and outcomes.

Final Inclusion: A total of 100 studies were included in the qualitative synthesis, with 85 providing sufficient data to be incorporated into the quantitative synthesis (Meta-Analysis).

The **PRISMA** diagram reflected a standard, rigorous selection process for a systematic review and provides a clear overview of how the final study sample was derived. This setup helped to ensure that the included studies were of high relevance and quality for the comprehensive systematic review on anaemia in pregnancy (Fig.3).

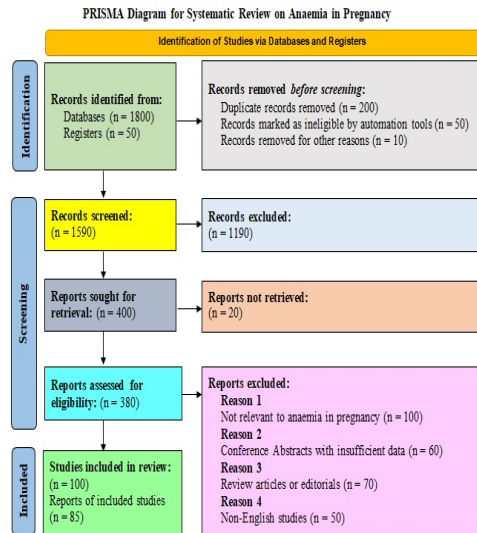


Fig.3. PRISMA Diagram for Systematic Review on Anaemia in Pregnancy

4. Discussion

The findings emphasize the necessity for enhanced diagnostic protocols regarding anaemia during gestation. The impact of haemodilution on conventional haemoglobin-centric diagnostic methods complicates the precise evaluation of anaemia, indicating that an exclusive dependence on haemoglobin concentrations may result in either insufficient or excessive treatment. Levels of transferrin receptor have surfaced as a potentially effective alternative biomarker; nevertheless, extensive validation studies are imperative prior to clinical implementation. Moreover, the heterogeneity in management strategies indicates a deficiency in consensus regarding the treatment of anaemia in pregnancy, especially in relation to the suitability of universal iron supplementation. This therapeutic strategy may prove advantageous for cases of severe anaemia but appears inadequate for non-iron deficiency anaemia or mild anaemia, where the risks of iron overload or ineffectiveness pose significant concerns.

The inconsistency in outcomes associated with non-iron deficiency anaemia reveals a significant research void. These variants of anaemia frequently involve distinct pathophysiological processes that require individualized treatment approaches. The elevated incidence of complications linked to non-iron deficiency anaemia accentuates the pressing need for focused management strategies, as existing treatment protocols, predominantly formulated for iron deficiency anaemia (IDA), may not adequately mitigate the associated risks in these populations. Ultimately, the evidence indicating potential developmental adversities in offspring of anaemic mothers necessitates further longitudinal investigations to ascertain the comprehensive

ramifications of anaemia on child health, thereby reinforcing the imperative for proactive intervention strategies within prenatal and early childhood healthcare.

5. Conclusion

This review underscored the intricacies involved in the diagnosis and management of anaemia during the gestational period, wherein physiological alterations and the heterogeneous nature of anaemia types necessitate the development of enhanced, evidence-based methodologies. The prevailing dependence on haemoglobin and haematocrit metrics inadequately considers the phenomenon of pregnancy-induced haemodilution, thereby rendering alternative diagnostic indicators such as serum transferrin receptor concentrations as promising alternatives. Management protocols must undergo further refinement to cater to the distinct types of anaemia, advocating for a transition towards targeted supplementation to mitigate the risks of iron overload and to maximize therapeutic efficacy. It is imperative to address non-iron deficiency anaemia during pregnancy due to their substantial ramifications for both maternal and fetal health. Furthermore, the potential long-term neurodevelopmental consequences for offspring underscore the critical significance of early and accurate diagnosis and intervention, in conjunction with longitudinal studies aimed at elucidating the enduring effects of anaemia. Ultimately, the resolution of these deficiencies necessitates a collaborative, multidisciplinary framework that spans both healthcare and policy domains to enhance maternal and child health on a global scale.

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