INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

COMPARATIVE EFFECTIVENESS OF IRON SUPPLEMENTATION FORMS IN TREATING PREGNANCY-RELATED ANEMIA: A RANDOMIZED CONTROLLED TRIAL

Original Article

Kiran Jabbar[1], Areeba Farooqui[2]*, Maryam Asim Khan[2], Maham Maooz Ansari[2], Manahil Khan[3], Muhammad Naeem[4]

[1]Senior Registrar, Bahria University Health Sciences, Karachi, Pakistan.
[2]Fifth Year MBBS Student, Ziauddin Medical College, Ziauddin University, Karachi, Pakistan.
[3]Nutritionist, NUR International University, Fatima Memorial System, Lahore, Pakistan.
[4]Head of Department, Allied Health Sciences (HND), International Institute of Science, Arts and Technology (IISAT), Gujranwala, Pakistan.

Corresponding Author: Areeba Farooqui, Fifth Year MBBS Student, Ziauddin Medical College, Ziauddin University, Karachi, Pakistan, areebafarooqui366@gmail.com

Conflict of Interest: None

Grant Support & Financial Support: None

Acknowledgment: The authors express sincere gratitude to all participants and clinical staff involved in the study.

ABSTRACT

Background: Iron-deficiency anemia during pregnancy remains a global health concern with serious maternal and fetal implications. While oral iron salts are the standard treatment, they are often poorly tolerated, leading to reduced compliance. Iron polymaltose complex (IPC) offers a potentially better-tolerated alternative, though comparative data on efficacy and safety in pregnancy are limited.

Objective: To compare the efficacy and side effect profiles of oral iron salts and iron polymaltose complex in the treatment of pregnancy-related anemia.

Methods: This randomized controlled trial was conducted over eight months at two tertiary care hospitals in Lahore, Pakistan. A total of 200 pregnant women diagnosed with moderate iron-deficiency anemia were randomly assigned to receive either ferrous sulfate (200 mg daily) or iron polymaltose complex (100 mg daily) for 12 weeks. Hemoglobin and serum ferritin levels were measured at baseline, 6 weeks, and 12 weeks. Gastrointestinal side effects and medication adherence were also recorded. Data were analyzed using SPSS v26, with t-tests and chi-square tests applied as appropriate.

Results: Both groups showed significant increases in hemoglobin and serum ferritin over 12 weeks, with no statistically significant differences between them ($p > 0.05$). However, gastrointestinal side effects, particularly constipation and nausea, were more frequent in the iron salts group. Adherence was notably higher in the IPC group, with 79% completing over 90% of prescribed doses compared to 68% in the iron salts group.

Conclusion: Iron polymaltose complex is as effective as iron salts in correcting pregnancy-related anemia but offers superior tolerability and adherence. It presents a viable alternative for women who experience side effects from traditional iron therapy.

Keywords: Adherence, Anemia, Ferrous sulfate, Hemoglobin, Iron-deficiency anemia, Iron polymaltose complex, Pregnancy, Randomized controlled trial.

INTRODUCTION

Iron-deficiency anemia remains one of the most prevalent nutritional deficiencies among pregnant women worldwide, posing significant health risks to both mothers and their unborn children. The physiological demands of pregnancy, including increased plasma volume and red blood cell mass, make iron a critical micronutrient during this period (1). When these increased demands are not met, iron-deficiency anemia can develop, potentially resulting in fatigue, impaired immune function, increased risk of preterm delivery, low birth weight, and perinatal mortality. Despite global public health efforts to address maternal anemia, it continues to be a major concern in both developing and developed countries, suggesting the need to optimize both prevention and treatment strategies (2,3). Oral iron supplementation remains the cornerstone of anemia management in pregnancy due to its accessibility, cost-effectiveness, and safety profile. Among the most commonly prescribed formulations are iron salts, such as ferrous sulfate and ferrous fumarate, which are known for their high elemental iron content (4). However, these traditional iron salts are frequently associated with gastrointestinal side effects, including nausea, constipation, and abdominal discomfort, leading to poor adherence and suboptimal treatment outcomes. These limitations have prompted the exploration of alternative formulations that aim to enhance tolerability without compromising efficacy (5,6).

One such alternative is the iron polymaltose complex (IPC), a non-ionic iron preparation that has gained attention for its improved gastrointestinal tolerability. Unlike iron salts, IPC binds iron to a polymaltose carbohydrate complex, resulting in a gradual release and absorption that may reduce the incidence of adverse effects. Several studies have suggested that IPC is comparable in efficacy to iron salts while offering a more favorable side effect profile (7). However, findings across studies have been inconsistent, with some trials indicating lower bioavailability and others highlighting equal or better hematologic response with IPC. Furthermore, differences in study populations, dosing regimens, and outcome measures make direct comparisons challenging and limit the generalizability of results (8). Current clinical guidelines continue to favor iron salts as the first-line treatment, largely due to their established efficacy and lower cost. Yet, growing awareness of patient-centered care and the importance of treatment adherence underscore the need to reevaluate this preference, particularly in settings where gastrointestinal side effects pose a significant barrier to compliance (9,10). In this context, there is a clear need for well-designed randomized controlled trials directly comparing these formulations in pregnant populations, with careful attention to both hematologic outcomes and patient tolerability.

The existing body of research points to a critical gap: while numerous studies have independently evaluated different iron formulations, few have conducted direct head-to-head comparisons in pregnant women using rigorous randomized controlled methodologies (11,12). This lack of comparative evidence restricts clinicians' ability to make informed treatment decisions tailored to individual patient needs. Moreover, most comparative trials have been limited by small sample sizes, short follow-up periods, or insufficient reporting on adverse effects—factors that dilute the strength of their conclusions. To address this gap, the present study was designed as a randomized controlled trial aimed at comparing the effectiveness and safety of two widely used oral iron formulations—iron salts and iron polymaltose complex—in the management of pregnancy-related anemia. The primary objective is to assess and compare their efficacy in improving hematologic parameters, while the secondary objective focuses on evaluating and contrasting their respective side effect profiles. By generating robust, comparative evidence in a pregnant population, this research aims to inform clinical practice and support the development of more individualized, patient-friendly treatment strategies for maternal anemia.

METHODS

This randomized controlled trial was conducted over a duration of eight months at two tertiary care hospitals in Lahore, Pakistan both of which serve as high-volume public maternity centers catering to diverse socioeconomic populations. The study aimed to evaluate and compare the efficacy and side effect profiles of two commonly used oral iron preparations, iron salts and iron polymaltose complex, in the treatment of anemia during pregnancy. Participants were recruited from the antenatal outpatient departments of the study centers following a preliminary screening. Pregnant women aged 18–40 years with singleton pregnancies between 12 and 28 weeks of gestation and a diagnosis of iron-deficiency anemia (hemoglobin levels between 8.0 and 10.9 g/dL with serum ferritin <30 ng/mL) were deemed eligible. Exclusion criteria included multiple gestations, history of hemoglobinopathies (such as thalassemia), chronic systemic illnesses (including renal disease, hepatic dysfunction, or malabsorption syndromes), current iron supplementation or recent blood transfusion, known allergy to oral iron preparations, and any gastrointestinal disorder that might impair iron absorption or increase risk of adverse reactions. Women who were unable to provide informed consent or anticipated to be lost to follow-up were also excluded.

The calculated sample size was 200 participants (100 in each group), determined using OpenEpi software with a confidence level of 95%, power of 80%, and accounting for a 15% potential dropout rate. The sample size was based on detecting a minimum clinically significant difference of 1 g/dL in mean hemoglobin levels between the two groups, assuming a standard deviation of 1.5 g/dL from prior literature. Eligible participants who consented to the study were randomly assigned in a 1:1 ratio to either the iron salts group (Group A) or the iron polymaltose complex group (Group B). Randomization was carried out using a computer-generated sequence and sealed opaque envelopes to ensure allocation concealment. Both participants and investigators were blinded to group assignment by providing identical-appearing capsules in coded bottles.

Group A received ferrous sulfate 200 mg once daily, providing approximately 65 mg of elemental iron, while Group B received iron polymaltose complex 100 mg once daily, also providing 100 mg of elemental iron. The supplementation was continued for 12 weeks, during which participants were instructed to take the medication on an empty stomach with water, avoiding tea, milk, or calcium-rich foods for at least an hour before and after ingestion. Baseline investigations included complete blood count (CBC), serum ferritin, mean corpuscular volume (MCV), and reticulocyte count. These hematologic parameters were reassessed at 6 weeks and 12 weeks to evaluate the primary outcome—mean increase in hemoglobin level. Secondary outcomes included change in serum ferritin, patient-reported gastrointestinal side effects (nausea, vomiting, constipation, diarrhea, abdominal discomfort), and overall adherence to treatment. Side effects were recorded using a structured symptom checklist administered at follow-up visits (13). Adherence was assessed via pill count and patient self-report.

Data were analyzed using SPSS version 26. Normality of distribution was confirmed using the Shapiro-Wilk test. Continuous variables such as hemoglobin levels and serum ferritin were expressed as mean ± standard deviation and compared between groups using the independent samples t-test. Within-group comparisons over time were analyzed using paired t-tests. Categorical variables such as incidence of side effects were compared using the Chi-square test. A p-value of <0.05 was considered statistically significant. Ethical approval for the study was obtained from the Institutional Review Board (IRB). All participants were fully informed about the study objectives, potential risks, and benefits, and provided written informed consent before enrollment. Data confidentiality was maintained throughout the study, and participants retained the right to withdraw at any time without affecting their standard antenatal care. The methodological rigor, standardized treatment protocols, and comprehensive follow-up in this trial were designed to ensure the reliability and generalizability of findings while safeguarding participant welfare and scientific integrity.

RESULTS

The study enrolled 200 pregnant women with iron-deficiency anemia, evenly randomized into two treatment groups receiving either oral iron salts or iron polymaltose complex. Baseline characteristics including mean maternal age, gestational age, parity, hemoglobin, and serum ferritin levels were statistically comparable between the groups, indicating homogeneity across cohorts and minimizing selection bias. Hemoglobin levels improved significantly in both groups over the 12-week treatment period. In the iron salts group, mean hemoglobin increased from 9.1 ± 0.5 g/dL at baseline to 11.5 ± 0.7 g/dL at 12 weeks. The IPC group demonstrated a similar improvement from 9.0 ± 0.5 g/dL to 11.3 ± 0.6 g/dL. Although the increase was slightly higher in the iron salts group, the difference between groups did not reach statistical significance at any time point ($p > 0.05$), suggesting comparable efficacy in hemoglobin correction. Ferritin levels also improved progressively in both cohorts. At baseline, serum ferritin was approximately 18.7 ± 3.2 ng/mL in the iron salts group and 18.9 ± 3.1 ng/mL in the IPC group. By week 12, levels rose to 31.2 ± 4.8 ng/mL and 32.1 ± 5.0 ng/mL respectively, again showing no significant intergroup differences ($p = 0.21$). These findings reinforce that both formulations are similarly effective in restoring iron stores during pregnancy.

Side effect profiles differed more noticeably between the groups. Constipation was the most frequently reported adverse event, affecting 30% of participants in the iron salts group compared to 17% in the IPC group ($p = 0.04$). Nausea and abdominal pain were also more prevalent in the iron salts group, although these differences did not achieve statistical significance. Diarrhea was the least commonly reported symptom in both groups. These results indicate a trend towards improved gastrointestinal tolerability with IPC. Medication adherence, an important secondary outcome, was notably better among IPC users. In the IPC group, 79% of participants adhered to more than 90% of prescribed doses compared to 68% in the iron salts group. Poor adherence (<70% doses) was more common in the iron salts cohort, reinforcing the impact of tolerability on compliance. Together, the findings demonstrate that both oral iron salts and iron polymaltose complex are effective in improving hematological parameters in pregnancy-related anemia. However, IPC may be better tolerated and associated with higher adherence rates, factors that could significantly influence real-world treatment success.

Table 1: Demographic Characteristic

Variable	Iron Salts Group (n=100)	IPC Group (n=100)	p-value
Mean Age (years)	26.8	27.1	0.45
Mean Gestational Age (weeks)	18.2	18.4	0.62
Parity (mean)	1.6	1.5	0.54
Baseline Hb (g/dL)	9.1	9.0	0.71
Baseline Ferritin (ng/mL)	18.7	18.9	0.80

Table 2: Hemoglobin Levels Over Time

Time Point	Iron Salts Group (mean ± SD)	IPC Group (mean ± SD)	p-value
Baseline	9.1 ± 0.5	9.0 ± 0.5	0.71
6 weeks	10.3 ± 0.6	10.1 ± 0.7	0.12
12 weeks	11.5 ± 0.7	11.3 ± 0.6	0.09

Table 3: Ferritin Levels Over Time

Time Point	Iron Salts Group (mean ± SD)	IPC Group (mean ± SD)	p-value
Baseline	18.7 ± 3.2	18.9 ± 3.1	0.80
6 weeks	24.5 ± 4.1	25.1 ± 3.9	0.38
12 weeks	31.2 ± 4.8	32.1 ± 5.0	0.21

Table 4: Side Effects Comparison

Side Effect	Iron Salts Group (n%)	IPC Group (n%)	p-value
Nausea	22 (22%)	14 (14%)	0.11
Constipation	30 (30%)	17 (17%)	0.04
Abdominal Pain	18 (18%)	11 (11%)	0.18
Diarrhea	10 (10%)	9 (9%)	0.81

Table 5: Adherence Rate

Adherence Category	Iron Salts Group	IPC Group
>90% doses	68	79
70–90% doses	21	15
<70% doses	11	6

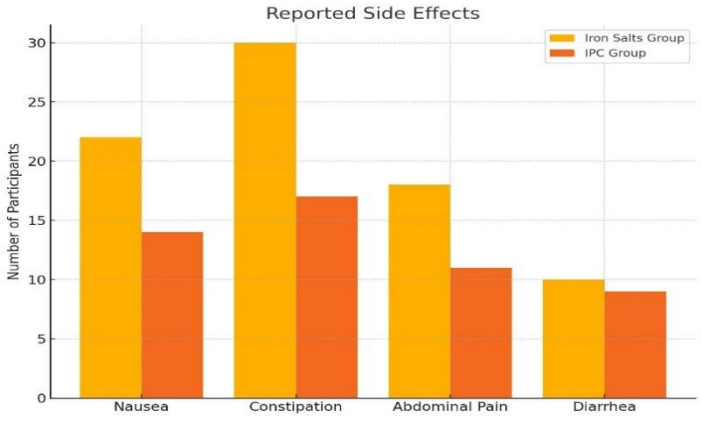

Figure 1Reported Side Effects

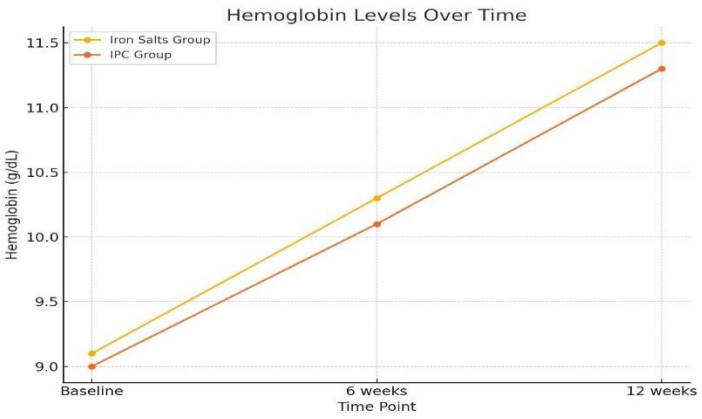

Figure 2 Hemoglobin Levels Over Time

DISCUSSION

The present study aimed to compare the efficacy and side effect profiles of oral iron salts and iron polymaltose complex (IPC) in the treatment of anemia among pregnant women. Findings indicated that while both treatment groups experienced significant improvements in hematologic parameters, IPC was associated with superior gastrointestinal tolerability and higher adherence, aligning with prior research on this subject. The increase in hemoglobin and serum ferritin observed in both groups was statistically comparable, reinforcing existing evidence that IPC and iron salts provide similar therapeutic efficacy in correcting iron-deficiency anemia during pregnancy. A randomized controlled trial reported that IPC, ferrous ascorbate, and ferrous sulfate were equally effective in raising hemoglobin levels, with only minor variation at later stages of therapy (14,15). These results support the current findings, suggesting that both iron formulations can serve as viable options for anemia correction in antenatal care. However, a key differentiator between the two treatments lies in tolerability. The present study observed a lower incidence of gastrointestinal side effects in the IPC group, a finding mirrored by several previous investigations (16). Such as a study demonstrated that IPC resulted in significantly fewer gastrointestinal complaints compared to ferrous sulfate, and this improved safety profile was directly associated with better patient compliance (17). A similar conclusion was reached by a study emphasized the role of reduced adverse effects in improving adherence to IPC therapy (18).

The adherence outcomes in this study further support the tolerability advantage of IPC. A greater proportion of participants in the IPC group completed more than 90% of their prescribed doses, consistent with results from a study which reported higher compliance rates in patients receiving ferric polymaltose therapy (19). Despite the consistency in hematologic improvement across groups, some studies suggest a slight edge in iron store repletion with IPC. For instance, a study observed higher hemoglobin levels in IPC recipients at eight weeks, though not at earlier points (20). Similarly, a study reported a statistically significant rise in hemoglobin following a 30-day IPC regimen in pregnant women, indicating rapid and sustained hematological response (21). This study's strengths include a robust randomized design, adequate sample size, real-world antenatal settings, and detailed adverse event monitoring, which enhance the validity and applicability of the findings. Additionally, objective tools such as CBC and serum ferritin assessments at multiple time points improved the accuracy of efficacy measurements.

Nonetheless, the study had limitations. The follow-up period was limited to 12 weeks, which may not capture long-term differences in maternal or neonatal outcomes. Although adherence was assessed through pill counts and self-reports, the possibility of recall or reporting bias cannot be ruled out. Cost-effectiveness, a relevant aspect of treatment selection in low-resource settings, was not explored in depth. Furthermore, the study was restricted to urban tertiary care centers, potentially limiting generalizability to rural or primary care populations. Future studies could address these limitations by including longer follow-up durations, exploring cost-effectiveness parameters, and evaluating maternal-fetal outcomes beyond hematologic indices. Research into patient satisfaction and quality of life associated with different iron formulations would also provide meaningful insight for patient-centered care (22,23). In conclusion, while both iron salts and IPC were effective in treating pregnancy-related anemia, IPC showed superior tolerability and adherence, making it a potentially preferred option for women who experience side effects from conventional iron salts. These findings support a more individualized approach to anemia management in pregnancy, guided by both efficacy and patient comfort.

CONCLUSION

This study concludes that both oral iron salts and iron polymaltose complex are effective in treating pregnancy-related anemia; however, iron polymaltose complex demonstrated superior gastrointestinal tolerability and higher adherence. These findings support IPC as a practical alternative for pregnant women who experience poor tolerance with conventional iron salts, promoting better compliance and treatment outcomes in antenatal care.

AUTHOR CONTRIBUTION

Author	Contribution
Kiran Jabbar	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Areeba Farooqui*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Maryam Asim Khan	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Maham Maooz Ansari	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Manahil Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Naeem	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Breymann C. Treatment of anemia using parenteral iron supplements. Infusion & Chemotherapy. 2020.
2. Elmore C, Ellis J. Screening, Treatment, and Monitoring of Iron Deficiency Anemia in Pregnancy and Postpartum. J Midwifery Womens Health. 2022;67(3):321-31.
3. Saboor M, Zehra A, Hamali HA, Mobarki AA. Revisiting Iron Metabolism, Iron Homeostasis and Iron Deficiency Anemia. Clin Lab. 2021;67(3).
4. Munro MG, Mast AE, Powers JM, Kouides PA, O'Brien SH, Richards T, et al. The relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia. Am J Obstet Gynecol. 2023;229(1):1-9.
5. Kirthan JPA, Somannavar MS. Pathophysiology and management of iron deficiency anaemia in pregnancy: a review. Ann Hematol. 2024;103(8):2637-46.
6. Ebea-Ugwuanyi PO, Vidyasagar S, Connor JR, Frazer DM, Knutson MD, Collins JF. Oral iron therapy: Current concepts and future prospects for improving efficacy and outcomes. Br J Haematol. 2024;204(3):759-73.
7. Wani R, Gupte S, Gopinath P, Swami O, Mukhopadhyay A, Sharma J, et al. A meta-analysis of ferric carboxymaltose versus other intravenous iron preparations for the management of iron deficiency anemia during pregnancy. RBGO Gynecology & Obstetrics. 2024;46.
8. Cappellini MD, Santini V, Braxs C, Shander A. Iron metabolism and iron deficiency anemia in women. Fertil Steril. 2022;118(4):607-14.
9. Al-Naseem A, Sallam A, Choudhury S, Thachil J. Iron deficiency without anaemia: a diagnosis that matters. Clin Med (Lond). 2021;21(2):107-13.
10. Moisidis-Tesch CM, Shulman LP. Iron Deficiency in Women's Health: New Insights into Diagnosis and Treatment. Adv Ther. 2022;39(6):2438-51.
11. Auerbach M, DeLoughery TG, Tirnauer JS. Iron Deficiency in Adults: A Review. Jama. 2025;333(20):1813-23.
12. Petraglia F, Dolmans MM. Iron deficiency anemia: Impact on women's reproductive health. Fertil Steril. 2022;118(4):605-6.
13. Kumar SB, Arnipalli SR, Mehta P, Carrau S, Ziouzenkova O. Iron Deficiency Anemia: Efficacy and Limitations of Nutritional and Comprehensive Mitigation Strategies. Nutrients. 2022;14(14).
14. James AH. Iron Deficiency Anemia in Pregnancy. Obstet Gynecol. 2021;138(4):663-74.
15. Tang GH, Sholzberg M. Iron deficiency anemia among women: An issue of health equity. Blood Rev. 2024;64:101159.
16. McWilliams S, Singh I, Leung W, Stockler S, Ipsiroglu OS. Iron deficiency and common neurodevelopmental disorders-A scoping review. PLoS One. 2022;17(9):e0273819.

17. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. BMJ Open Gastroenterol. 2022;9(1).
18. Lewkowitz AK, Stout MJ, Cooke E, Deoni SC, D'Sa V, Rouse DJ, et al. Intravenous versus Oral Iron for Iron-Deficiency Anemia in Pregnancy (IVIDA): A Randomized Controlled Trial. Am J Perinatol. 2022;39(8):808-15.
19. Benson AE, Shatzel JJ, Ryan KS, Hedges MA, Martens K, Aslan JE, et al. The incidence, complications, and treatment of iron deficiency in pregnancy. Eur J Haematol. 2022;109(6):633-42.
20. Lewkowitz AK, Tuuli MG. Identifying and treating iron deficiency anemia in pregnancy. Hematology Am Soc Hematol Educ Program. 2023;2023(1):223-8.
21. Farghali M, Amer O, Abdelazim IA. Ferric polymaltose complex in treatment of iron deficiency and iron-deficiency anaemia with pregnancy. 2021.
22. Fischer JAJ, Cherian AM, Bone JN, Karakochuk CD. The effects of oral ferrous bisglycinate supplementation on hemoglobin and ferritin concentrations in adults and children: a systematic review and meta-analysis of randomized controlled trials. Nutr Rev. 2023;81(8):904-20.
23. Skolmowska D, Głąbska D, Kołota A, Guzek D. Effectiveness of Dietary Interventions in Prevention and Treatment of Iron-Deficiency Anemia in Pregnant Women: A Systematic Review of Randomized Controlled Trials. Nutrients. 2022;14(15).

