Original Article

Comparative Efficacy Of Dapagliflozin And Empagliflozin For Blood Pressure Control In Type 2 Diabetes Mellitus With Hypertension

Shafaq Fatima[1], Irum Sohail[2], Hasina Sadiq[3], Mahrukh Fatima Zaidi[4], Marium Riaz[5]

Abstract

Objective: To compare oral ferrous bis-glycinate and ferrous sulfate as regards the mean change in haemoglobin, serum ferritin and tolerability in treating Iron Deficiency anaemia during pregnancy.

Methods: This Experimental Study was carried out in the outdoor department of the Gynaecology and Obstetrics department of Kahuta Research Laboratories (KRL) hospital in Islamabad from 26th September 2022 to 26th March 2023. A total of 150 pregnant patients with iron deficiency anaemia were included in the study. Group I was for oral ferrous sulfate, Group II was for oral ferrous Bis-Glycinate. Hb level, serum ferritin and tolerability were noted from both groups after 8 weeks.

Results: Mean Hb level was 9.760±0.63 g/dl in group I as compared to 10.853±0.81 g/dl in group II (p=0.000) after 8 weeks, and mean serum ferritin level was 23.640±1.14 ng/ml in group I as compared to 29.960±1.03 g/dl in group II (p=0.000) after 8 weeks.

Conclusion: Our study has concluded that ferrous bis-glycinate has a superior efficacy in increasing HB level and serum ferritin, and also has better tolerability.

Keywords: Pregnancy, Anaemia, Iron-Deficiency, Ferritins, Ferrous sulfate.

Introduction

Anaemia is one of the common health problems in obstetrics, and iron deficiency is considered the most prevalent cause of anaemia in pregnancy. Iron is essential to support the increase in maternal erythropoiesis and to meet the requirements of fetal organogenesis, the development of the central nervous system and hematopoietic tissues.[1] The total need for iron during pregnancy is significantly increased, reaching about 1240 mg.[2] However, suboptimal iron content in the average mother's diet and the presence of insufficient iron stores during their productive years are causes for this predominance of iron deficiency in pregnant females.[3] Anaemia has a significant impact on the health of the fetus and the mother. It is associated with increased preterm labour (28.2%)[4], preeclampsia(31.2%)[4]and maternal sepsis. It can also lead to fetal loss or even perinatal death.[4]

There is a wide variation in the prevalence of anaemia worldwide. In Pakistan, the prevalence of anaemia among pregnant women living in urban areas was reported from 29% to 50%[4]. A study conducted in India in 2015 showed that the prevalence of Iron deficiency anaemia in developing countries is approximately 52%versus25% in developed countries.[5] The ideal treatment for IDA with pregnancy still represents a great challenge. Oral iron preparations are the routine line used for correction of IDA with pregnancy because of their safety, effectiveness and low cost. Oral iron preparations for the correction of iron deficiency include different salts, like combination with sulphate, fumarate, gluconate, Iron chelators and ferric hydroxide complexes.[2]

Different studies conducted in various regions of the world compared ferrous bis-glycinate and ferrous sulfate in the treatment of iron deficiency anaemia, concluded that ferrous bis-glycinate is more efficient in increasing haemoglobin level and has tolerable adverse effects with high compliance.[3,6] A Study conducted in Egypt in 2018 had its results as a mean rise of Hb in ferrous bis-glycinate was 11.63$\pm$0.73 g/dL versus 10.58$\pm$0.82 g/dL [2] in the ferrous glycine sulphate group. Increase in serum ferritin levels in ferrous bis-glycinate was 30.2$\pm$4.54 ug/L, in ferrous glycine sulphate it was 24.9+4.48/ug/L.[2] In terms of tolerability with no adverse effects, ferrous bis-glycinate had 87.1% while ferrous glycine sulphate was 70.2%.[2]

This study aims to compare the mean change of haemoglobin, serum ferritin and tolerability of iron amino acid chelate, i.e. ferrous bis-glycinate and ferrous sulfate, in the treatment of IDA during pregnancy so that a drug with a faster rate of improvement of haemoglobin level and one with better tolerance can be given to the patients. Health care providers can also prescribe them with confidence. Moreover, no such comparative study has been done in our country and can be found in the literature.

Materials And Methods

This was a Quasi-experimental study conducted over six months from 26th September 2022 to 26th March 2023. Data for this study were collected from patients who met the inclusion criteria and presented through the

Contributions:
SF, IS, HS, MFZ - Conception, Design
SF, IS, HS, MFZ, MR - Acquisition, Analysis, Interpretation
SF, IS, HS, MFZ, MR - Drafting
SF, IS, HS, MFZ, MR - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

Conflicts of Interest: None
Financial Support: None to report
Potential Competing Interests: None to report

Institutional Review Board Approval
KRL-HI-ERC/Apr22/07
07-04-2022
KRL Hospital, Islamabad.

Review began 19/11/2024
Review ended 01/09/2025
Published 30/12/2025

How to cite this article: Fatima S, Sohail I, Sadiq H, Zaidi MF, Riaz M. Comparison of Efficacy and Safety of Ferrous Bisglycinateand Ferrous Sulphate in Iron Deficiency Anemia (IDA) of Pregnant Patients: Comparative Analytical study. JRMC. 2025 Dec. 31;29(4).

https://doi.org/10.37939/jrmc.v29i4.2787

outpatient department at KRL Hospital, Islamabad. After taking institutional ethical approval of the study, pregnant patients presenting to antenatal OPD with mild to moderate iron deficiency anaemia after 14 weeks of gestational age were enrolled in the study. Written Informed consent was taken. Recruited women were assessed through detailed history, clinical examination, and BMI calculation (Weight was measured on a standard weighing machine and height was measured in meters with measuring tape without shoes). Full blood count done during the first trimester was reviewed to rule out other causes of anaemia.

All pregnant patients after 14 weeks of gestation, who are sure of their dates, have a singleton pregnancy and mild to moderate iron deficiency anaemia, were included. Patients with Severe anaemia <7g/dl, having Multiple Pregnancies, Malabsorption Syndromes, Hepatic/Renal/Cardiac/Gastrointestinal diseases, Hemoglobinopathies, Preeclampsia/pregnancy-induced hypertension, Hyperemesis gravidarum, Allergic to iron

At the time of enrollment, the patient was categorised into either mild or moderate iron deficiency anaemia based on Laboratory investigations. This will include Haemoglobin in g/dL, serum ferritin in ug/L. Patients were divided into one of the two groups, via flipping a coin, i.e. side of the side with having head was for Group I and the tail side was for Group II. Group I was for oral ferrous sulfate, Group II was for oral ferrous Bis-Glycinate. Informed consent was taken, and the patient was advised to get the respective tablet once daily for 8 consecutive weeks and then follow up at 4 and 8 weeks of treatment. Blood samples were repeated at 4 and 8 weeks, respectively, and serum ferritin was assessed at the end of 8 weeks of treatment. Patients were notified to record any adverse effects like metallic taste, abdominal pain, nausea, vomiting, diarrhoea and constipation during treatment. Any discontinuation of therapy or reversion to another drug, including the reasons to do so, would be noted. A structured proforma was filled in by an equal number of the enrolled participants.

The data was collected and entered into a Microsoft Access database then was analysed using Statistical Package for the Social Sciences (SPSS version 22). Quantitative data (like age, parity, BMI, gestational age, haematological indices) were presented in terms of mean ±SD and then compared using a student's t-test between both groups. Qualitative variables (like adverse effects) were presented as frequency and percentage. Student's t-test was used for comparison between groups. For analysis, $p \leq 0.05$ was considered significant. Effect Modifiers like age, parity, educational level, BMI and gestational age were stratified using post-stratified Student t' t-test.

Results

Mean age in this study was 27.920±2.88 years, mean parity 1.426±1.32, mean BMI 26.146±1.27 Kg/m^2, mean gestational age 18.200±2.94 weeks, mean Hb level after 8 weeks 9.760±0.63 g/dl and mean serum ferritin levels were 23.640±1.14 ng/ml in Group I and mean age of 27.813±2.55 years, mean parity 1.320±1.25, mean BMI 25.693±1.22 Kg/m^2, mean gestational age 18.280±3.08 weeks, mean Hb level after 8 weeks 10.853±0.81 g/dl and mean serum ferritin levels were 29.960±1.03 ng/ml in Group II as shown in Table-1.

Table 1: Mean±SD of patients according to age, parity, BMI, gestational age, Hb level and serum ferritin in both groups, n=150

Demographics	Group I n=75 Mean±SD	Group II n=75 Mean±SD
Age(years)	27.920±2.88	27.813±2.55
Parity	1.426±1.32	1.320±1.25
BMI (Kg/m^2)	26.146±1.27	25.693±1.22
Gestational age (weeks)	18.200±2.94	18.280±3.08
Hb level (g/dl)	9.760±0.63	10.853±0.81
Serum ferritin (ng/ml)	23.640±1.14	29.960±1.03

Mean Hb level was 9.760±0.63 g/dl in group I as compared to 10.853±0.81 g/dl in group II (p=0.000) after 8 weeks, as shown in Table II. Mean serum ferritin level was 23.640±1.14 ng/ml in group I as compared to 29.960±1.03 g/dl in group II (p=0.000) after 8 weeks, as shown in Table 2.

Table 2: Comparison of mean Hb level and mean serum ferritin in both groups, n=150

	Group I n=75	Group II n=75	T	P value
Hb level (g/dl)	9.760±0.63	10.853±0.81	-9.160	0.000
Serum ferritin (ng/ml)	23.640±1.14	29.960±1.03	-35.474	0.000

Nausea was observed in 5 (6.7%) patients in group I as compare to 2 (2.7%) patients in group II, vomiting 6 (8%) versus 2 (2.7%), constipation 17 (22.7%) versus 8 (10.7%), metallic taste 3 (4%) versus 1 (1.3%), black stool 3 (4%) versus 1 (1.3%) and diarrhea was 5 (6.7%) versus 2 (2.7%) respectively as shown in Table 3.

Iron deficiency anaemia (IDA) is one of the most prevalent micronutrient deficiencies globally, affecting nearly half of all pregnant women. IDA during pregnancy is associated with increased risks of low birth weight, preterm delivery, and perinatal mortality. Oral iron supplementation is recommended as first-line treatment for IDA in pregnancy to improve maternal and infant health outcomes. The two most widely available forms of supplemental iron are ferrous sulfate and ferrous bis-glycinate.

Table 3: Symptoms in group 1 and group 2

Variable	n=75 Group I	n=75 Group II	P Value
Nausea			
1 **Yes**	5 (6.7%)	2 (2.7%)	
2 **No**	70 (93.3%)	73 (97.3%)	0.245
Total	75 (100%)	75 (100%)	
Vomiting			
1 **Yes**	6 (8%)	2 (2.7%)	
2 **No**	69 (92%)	73 (97.3%)	0.146
Total	75 (100%)	75 (100%)	
Constipation			
1 **Yes**	17 (22.7%)	8 (10.7%)	
2 **No**	58 (77.3%)	67 (89.3%)	0.049
Total	75 (100%)	75 (100%)	
Metallic Taste			
1 **Yes**	3 (4%)	1 (1.3%)	
2 **No**	72 (96%)	74 (98.7%)	0.311
Total	75 (100%)	75 (100%)	
Black Stool			
1 **Yes**	3 (4%)	1 (1.3%)	
2 **No**	72 (96%)	74 (98.7%)	0.311
Total	75 (100%)	75 (100%)	
Diarrhea			
1 **Yes**	5 (6.7%)	2 (2.7%)	
2 **No**	70 (93.3%)	73 (97.3%)	0.245
Total	75 (100%)	75 (100%)	

Discussion

This study demonstrates that ferrous bis-glycinate is effective and well-tolerated in pregnant women with second-trimester IDA. In addition, women who used ferrous bis-glycinate for 8 weeks could give birth to healthy newborns rather than ferrous glycine sulfate. Moreover, ferrous bis-glycinate more rapidly and effectively established normalised HB levels and replenished iron stores than ferrous glycine sulfate. Anaemia is the most common health problem affecting pregnant women in both developed and developing countries.[7] Oral iron is considered the first choice to correct IDA and replace iron stores, as this allows the normal mechanism of absorption, besides its low cost and effectiveness.[8]

In this study, the mean age of included patients was 27.920±2.88 and 27.813±2.55 years in both groups, respectively. This coincides with previous studies on pregnant women with IDA, and this reflects the high prevalence of IDA in young pregnant women.[9] Early age at marriage and pregnancy is common in developing countries, thus associated with exhaustion of iron stores that are already low in teenagers.[10] All recruited pregnant women had mild to moderate IDA in the second trimester because correction of anaemia at this age avoids the development of severe anaemia at term. The mean rise in HB level was significantly observed in both groups as therapeutic iron supplementation stimulates erythropoiesis in iron-deficient women. However, the mean HB in the ferrous bis-glycinate group was significantly higher, 10.853±0.81 versus 9.760±0.63 g/dL in the ferrous glycine sulfate group (p 0.000) after 8 weeks of treatment. This may be attributed to the higher rate of adverse effects reported with ferrous glycine sulfate, like nausea, vomiting, and constipation, leading to malabsorption of iron. Our results were similar to Youssef et al.,[11] who reported a mean increase in HB level of 2.12 g/dL with ferrous bis-glycinate. A previous study by Szarfarc et al.,[12] between ferrous bis-glycinate and ferrous sulfate reported that both groups showed a significant increase in HB level; however, the ferrous bis-glycinate group had a significant rise in serum ferritin. Moreover, Youssef et al.,[13] reported a significant increase in serum ferritin level with ferrous bis-glycinate than other iron preparations (p<.05). Our results coincide with their study as serum ferritin in the ferrous bis-glycinate group was significantly higher after 8 weeks of treatment than ferrous glycine sulfate (p=0.000).

Adverse effects of oral iron therapy are a common problem in the treatment of patients with IDA. In our study, ferrous bis-glycinate was well tolerated in pregnant women during their second trimester with fewer GIT adverse events than ferrous glycine sulfate. The safety profile was consistent with what has been previously reported about amino acid chelated iron preparations [14]. Our results were matched with the meta-analysis by Tolkien et al.,[14] reported that ferrous sulfate is associated with a significant increase in GIT adverse effects. The tolerability of amino acid chelated iron preparations in comparison to traditional iron salts was confirmed in a lot of previous studies.[15-17]

The strengths of our study include that it was a randomised controlled trial. In addition, we were able to recruit our calculated sample size for achieving sufficient power to detect a clinically significant difference in our primary outcome. Moreover, the ability to record the obstetric outcome of women with IDA in terms of gestational age at delivery, mode of delivery, maternal complications and neonatal outcomes (neonatal weight, Apgar score, cord HB level) in cases delivered inside our hospital; however, our study was not powered enough to detect the differences in these outcomes. Future trials should focus on the use of ferrous bisglycinate in non-anaemic women as a routine supplementation during the second trimester to prevent the occurrence of IDA. In addition, a well-designed study comparing the effect of ferrous bis-glycinate versus intravenous iron in women remote from term with moderate IDA should be carried out.

Conclusions

Our study has concluded that ferrous bis-glycinate has a superior efficacy in increasing HB level and serum ferritin than ferrous glycine sulfate in pregnant women with IDA. Overall, the adverse effects of ferrous bis-glycinate were low. It also had a good compliance and low discontinuation rate.

Author Information

1,4,5. Post Graduate Trainee, KRL Hospital, Islamabad 2. Consultant, KRL Hospital, Islamabad 3. Senior Registrar, Shifa College of Medicine, Islamabad
Corresponding author: Dr. Shafaq Fatima shafaqfatima968@gmail.com

References

1. Bumrungpert A, Pavadhgul P, Piromsawasdi T, Mozafari MR. Efficacy and safety of ferrous bisglycinate and folinic acid in the control of iron deficiency in pregnant women: a randomized, controlled trial. Nutrients. 2022 Jan 20;14(3):452. https://doi.org/10.3390/nu14030452
2. Abbas AM, Abdelbadee SA, Alanwar A, Mostafa S. Efficacy of ferrous bis-glycinate versus ferrous glycine sulfate in the treatment of iron deficiency anemia with pregnancy: a randomized double-blind clinical trial. The Journal of Maternal-Fetal & Neonatal Medicine. 2019 Dec 17;32(24):4139-45. https://doi.org/10.1080/14767058.2018.1482871
3. Moety GA, Ali AM, Fouad R, Ramadan W, Belal DS, Haggag HM. Amino acid chelated iron versus an iron salt in the treatment of iron deficiency anemia with pregnancy: A randomized controlled study. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2017 Mar 1;210:242-6. https://doi.org/10.1016/j.ejogrb.2017.01.003
4. Shams S, Ahmad Z, Wadood A. Prevalence of iron deficiency anemia in pregnant women of district Mardan. Pakistan. J Preg Child Health. 2017 Feb;4(6):1-4. https://doi.org/10.4172/2376-127X.1000356
5. Singhal SR, Kadian V, Singh S, Ghalaut VS. Comparison of various oral iron salts in the treatment of iron deficiency anemia in pregnancy. Indian J Obstet Gynecol Res. 2015;2(3):155-8. https://doi.org/10.5958/2394-2754.2015.00005.3
6. Milman N, Jønsson L, Dyre P, Pedersen PL, Larsen LG. Ferrous bisglycinate 25 mg iron is as effective as ferrous sulfate 50 mg iron in the prophylaxis of iron deficiency and anemia during pregnancy in a randomized trial. Journal of perinatal medicine. 2014 Mar 1;42(2):197-206. https://doi.org/10.1515/jpm-2013-0153
7. Bah A, Wegmuller R, Cerami C, Kendall L, Pasricha SR, Moore SE, Prentice AM. A double blind randomised controlled trial comparing standard dose of iron supplementation for pregnant women with two screen-and-treat approaches using hepcidin as a biomarker for ready and safe to receive iron. BMC pregnancy and childbirth. 2016 Jul 13;16(1):157.https://doi.org/10.1186/s12884-016-0934-8
8. Reveiz L, Gyte GM, Cuervo LG, Casasbuenas A. Treatments for iron-deficiency anaemia in pregnancy. Cochrane database of systematic reviews. 2011(10). https://doi.org/10.1002/14651858.CD003094
9. Darwish AM, Khalifa EE, Rashad E, Farghally E. RETRACTED ARTICLE: Total dose iron dextran infusion versus oral iron for treating iron deficiency anemia in pregnant women: a randomized controlled trial. The Journal of Maternal-Fetal & Neonatal Medicine. 2019 Feb 1;32(3):398-403. https://doi.org/10.1080/14767058.2017.1379988
10. Chandra-Mouli V, Camacho AV, Michaud PA. WHO guidelines on preventing early pregnancy and poor reproductive outcomes among adolescents in developing countries. Journal of adolescent health. 2013 May 1;52(5):517-22. https://doi.org/10.1016/j.jadohealth.2013.03.002
11. Youssef AM, Shata AF, Kamal HM, El-Saied Y, Ali OF. A comparative study of efficacy, tolerability, and compliance of oral iron preparations for iron deficiency anemia in pregnant women. Am J Med Med Sci. 2014;4(6):244-9. https://doi.org/10.3390/nu14030452
12. Szarfarc SC, Cassana LM, Fujimori E, Guerra-Shinohara EM, Oliveira IM. Relative effectiveness of iron bis-glycinate chelate (Ferrochel) and ferrous sulfate in the control of iron deficiency in pregnant women. Archivos Latinoamericanos de Nutricion. 2001;51(1):42-7. https://doi.org/ 10.3390/nu14030452
13. Hertrampf, Olivares. Iron amino acid chelates. International journal for vitamin and nutrition research. 2004 Nov 1;74(6):435 43.https://doi.org/10.1024/0300-9831.74.6.435
14. Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PloS one. 2015 Feb 20;10(2):e0117383. https://doi.org/10.1371/journal.pone.0117383
15. Milman NT, Bergholt T. Low-dose prophylactic oral iron supplementation (Ferrous Fumarate, ferrous Bisglycinate, and ferrous sulphate) in pregnancy is not associated with clinically significant gastrointestinal complaints: Results from two randomized studies. Journal of Pregnancy. 2024;2024(1):1716798. https://doi.org/10.1515/jpm-2013-0153
16. Khan A, Muhammad L, Ali S, Abdulhaq A, Rahman Z. Efficacy of Ferrous Bis-Glycinate versus Ferrous Sulphate in Children with Iron Deficiency Anemia: Efficacy of Ferrous Bis-Glycinate versus Ferrous Sulphate. Pakistan Journal of Health Sciences. 2023 Nov 30:39-43. https://doi.org/10.7759/cureus.84826
17. Suva MA, Tirgar PR. Comparative evaluation of different oral iron salts in the management of iron deficiency anemia. DARU Journal of Pharmaceutical Sciences. 2024 Dec;32(2):485-94. https://doi.org/10.1007/s40199-024-00517-y
18. Parveen A, Raja NF, Khan IM, Shaheen H, Imran M, Ahmed RS. Comparison of conventional and newer iron preparations for the treatment of iron deficiency anaemia in children. Journal of Rawalpindi Medical College. 2020 Jun 26;24(2). https://doi.org/10.37939/jrmc.v24i2.1160