

Efficacy of Ferrous Fumarate in Comparison to Carbonyl Iron in the Treatment of Iron Deficiency Anaemia during Pregnancy in Rajshahi, Bangladesh

Dr. Nahid Yusuf^{1*}, Dr. Mst. Manjila Khatun², Dr. Nazmun Nahar³, Dr. Rowshon Akhter⁴, Dr. Md. Zillur Rahman⁵, Dr. Md. Nasim Parvej⁶, Dr. Anika Ahmed⁷

¹Associate Professor (cc), Department of Obstetrics & Gynaecology, Rajshahi Medical College, Rajshahi, Bangladesh

²Medical Officer, Infectious Disease Hospital, Rajshahi Medical College, Rajshahi, Bangladesh

³Assistant Professor, Department of obstetrics & Gynaecology, Rajshahi Medical College, Rajshahi, Bangladesh

⁴Assistant Professor, Department of obstetrics & Gynaecology, Rajshahi Medical College, Rajshahi, Bangladesh

⁵Associate Professor, North Bengal Medical College, Sirajganj, Bangladesh

⁶Medical Officer, Upazilla Health Complex, Mohonpur, Rajshahi, Bangladesh

⁷Medical Officer, Upazilla Health Complex, Paba, Rajshahi, Bangladesh

DOI: [10.36348/sijog.2022.v05i05.001](https://doi.org/10.36348/sijog.2022.v05i05.001)

Received: 28.03.2022 | Accepted: 04.05.2022 | Published: 09.05.2022

*Corresponding author: Dr. Nahid Yusuf

Associate Professor (cc), Department of Obstetrics & Gynaecology, Rajshahi Medical College, Rajshahi, Bangladesh

Abstract

Introduction: Iron deficiency represents a spectrum ranging from iron depletion to iron deficiency anaemia. In iron depletion, the amount of stored iron is reduced but the amount of transport and functional iron may not be affected. Iron deficiency is a major problem worldwide especially in women of reproductive age. **Objectives:** This study was designed to compare efficacy of two commonly used oral iron preparations among anemic pregnant women in private chamber of gynecologists and outdoor of Rajshahi Medical college hospital, Rajshahi, Bangladesh. **Methods:** We conducted analysis of data collected from Pregnant women between 18 to 40 years of age, >8 weeks of gestation, having iron deficiency anaemia (serum hemoglobin levels <10 gm/dl or serum ferritin <30µg/l). The patients were divided into 2 groups (n=30) each and treated with Ferrous fumarate and carbonyl iron respectively. Hemoglobin gm/dl and serum Ferritin ng/dl were recorded after the interval of 3 months from baseline. Data was analyzed using SPSS 16. Efficacy variables between groups calculated using Chi square and T- test. **Results:** We observed that patients treated with Ferrous Fumarate (FF) showed significant rise in Hb 0.69(±0.83) which was greater than that of Carbonyl iron (CI) group 0.07(±1.11) g/dl. Mean (± SD) rise of serum ferritin was significantly higher in FF group (55.45 ±34.66) as compared to CI group (19.88 ±15.33) (t=5.14, df =58, P<0.001). **Conclusion:** It can be concluded that, ferrous fumarate still can be considered better effective medication than Carbonyl iron for the treatment of Iron deficiency anemia in pregnancy.

Keywords: Iron deficiency; Anaemia; Pregnant women.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Iron deficiency represents a spectrum ranging from iron depletion to iron deficiency anaemia. In iron depletion, the amount of stored iron (measured by serum ferritin concentration) is reduced but the amount of transport and functional iron may not be affected. Those with iron depletion have no iron stores to mobilize if the body requires additional iron. In iron-deficient erythropoiesis, stored iron is depleted and transport iron is reduced further; the amount of iron absorbed is not sufficient to replace the amount lost or

to provide the amount needed for growth and function [1].

In iron-deficiency anaemia, the most severe form of iron deficiency, there is shortage of iron stores, transport and functional iron, resulting in reduced hemoglobin (Hb) in addition to low serum ferritin, low transferrin saturation and increased erythrocyte protoporphyrin concentration. Iron deficiency is a major problem worldwide especially in women of reproductive age. Factors like malnutrition, blood loss during menstruation and delivery, depletion of stores

during pregnancy and nursing period, contributes to development of iron deficiency anaemia.

WHO has accepted 11 gm/dl as the normal haemoglobin (Hb) level in pregnancy [2]. In view of the relative plasma expansion being particularly marked in the second trimester, there is a variation in definition of normal Hb levels in pregnancy. A level of ≥ 11 g/dl appears adequate in the first trimester and ≥ 10.5 g/dl in the second and third trimesters. Postpartum anaemia is defined as $Hb < 10$ g/dl [1].

Serum ferritin is generally considered the best test to assess iron deficiency in pregnancy. Even though the ferritin level may be influenced by the plasma dilution later in pregnancy, a concentration < 15 μ g/l indicates iron depletion in all stages of pregnancy¹. According to the WHO report, the prevalence of iron deficiency anaemia in pregnant women in developing countries is 35-75% [3]. Anaemia has a significant impact on the health of the fetus as well as that of the mother. It impairs the oxygen delivery through the placenta to the fetus and interferes with the normal intrauterine growth, leading to fetal loss and perinatal deaths and increased preterm labors [4]. Iron supplements improve the iron status of the mother during pregnancy and during the postpartum period, even in women who become pregnant with reasonable iron stores [5]. The amount of iron absorbed from the diet is not sufficient to meet the requirements during pregnancy, when physiological iron requirements are the highest. Iron supplementation is necessary to control iron deficiency anemia. Folic acid is added to iron since the combination gives an enhanced hematological response [6]. Iron salts like ferrous sulphate, ferrous fumarate and ferrous gluconate are extensively prescribed for the prevention and treatment of iron deficiency.

Relatively high concentrations of elemental iron are present in ferrous fumarate. Each 200 mg of ferrous fumarate containing 65 mg of elemental iron [7]. Whereas the same amount of elemental iron is present in 300 mg of carbonyl iron [8].

However, gastrointestinal symptoms such as nausea, epigastric pain and constipation are commonly associated with iron salts. Food and/or chelating drugs in the gastrointestinal tract may interfere with absorption and decrease the concentration of the bioavailable iron [9]. This leads to variability in the Hb correction during anemia in pregnancy. Another formulation of iron called carbonyl iron has been introduced into the market with claims of higher bioavailability and safety. However, there have been reports of low bioavailability of carbonyl iron [10]. Additionally, ferrous fumarate as iron prophylaxis in pregnant women is reported to be safe with no significant gastrointestinal side effects [11].

Therefore, the present study was conducted to compare the efficacy and tolerability of a preparation containing ferrous fumarate and folic acid versus a preparation containing carbonyl iron and folic acid in the treatment of iron deficiency anemia of pregnancy.

OBJECTIVES

General objective

- To compare the efficacy and tolerability of ferrous fumarate with carbonyl iron in the treatment of iron deficiency anemia in pregnancy.

Specific objective

- To measure Complete blood count, Peripheral Blood film and serum ferritin of both group at booking visit.
- To measure Haemoglobin at the end of 3 month.
- To measure serum ferritin at the end of 3 month.
- To compare between ferrous fumarate and carbonyl iron.

MATERIALS & METHODOLOGY

This non-randomized clinical trial study was conducted in the department of Obs. & gynae OPD, private chambers of obstetricians of Rajshahi Medical College, Rajshahi, Bangladesh. The time duration was from January 2017 to December 2018 (1 year). Purposive sampling was used to collect the study subjects. Pregnant women with iron deficiency anaemia attending OPD, RMCH & private chambers. Patient who fulfilled the eligibility criteria were consecutively included in the study and were randomly assigned to either ferrous fumarate or carbonyl iron group. Ethical clearance from the Ethical Review Committee of Rajshahi Medical College, Rajshahi was taken to carry out this study. All women enrolled in the study were explained about the nature and purpose of the study and who gave consent were included in the study. The exact nature and the purpose of the study was explained to the pregnant women attending outdoor of obstetrics and gynecology department and private chambers of obstetricians. Written consent was taken. After that detailed history and clinical examination was done. Blood sample was taken and investigations were done. All pregnant women who are anemic (hemoglobin < 10 g/l or serum ferritin < 30 μ g/l) at first trimester are diagnosed as iron deficiency anaemia by peripheral blood film. Total 60 patients who fulfill the selection criteria were enrolled in the study. At first, we selected two groups randomly by lottery method. One group was given ferrous fumarate and carbonyl iron to other group for a period of 3 months. For treatment outcome follow up done at after 3 months. All the collected data were recorded in predesigned data sheet. Data were analyzed with Statistical Package for Social Science. Results obtained were evaluated and analyzed statistically.

Inclusion Criteria

- Pregnant women between 18 to 40 years of age,
- >8 weeks of gestation,
- Having iron deficiency anaemia (serum hemoglobin levels <10gm/dl or serum ferritin <30µg/l) were included in the study.

Exclusion Criteria

- Pregnant women with Hb<7gm%,
- History of severe oral intolerance of oral iron preparations,
- Excessive emesis,
- Bleeding piles,
- Active peptic ulcer,
- Other GIT problem,
- High obstetric risk pregnancies like multiple pregnancy and
- Other anaemia other than iron deficiency anaemia.

RESULT

In the present study, each group of 30 participants were administered ferrous fumarate and carbonyl iron for a period of 3months. Serum hemoglobin and ferritin was done at booking and after three months of treatment.

The baseline hemoglobin (10.16 in FF and 10.03 in CI) and ferritin (15.84 in FF and 21.13 in CI) values did not differ significantly at the beginning in both the group. After 3 months of treatment hemoglobin level increases significantly in both group (10.86 in FF and 10.09 in CI group). Serum ferritin level increases significantly in FF group (71.29) than CI group (41.02). Mean (\pm SD) in Ferrous fumarate group was 27.30 (\pm 5.23) & in Carbonyl iron group was 26.93 (\pm 5.01). Highest frequency was observed between 25-29 years of age, both in Ferrous fumarate 13 (43.3%) and carbonyl iron 11(36.7%) group. Lowest frequency was observed between < 20 years of age, both in Ferrous fumarate 1 (3.3%) and carbonyl iron 2(6.7%) group. No significant difference in mean age was observe between two groups ($t = 0.277$, $d=58$, $P>0.05$) (Table-1). Regarding socio-economic condition, most patients came from middle class in both groups, in FF 18(60%) & in CI 22(73.3%) (Figure-1). Mean Hemoglobin (\pm SD) at booking visit in Ferrous fumarate group was 10.16 (\pm 1.06) & in Carbonyl iron group was 10.03 (\pm 0.93). Most patients came with mild anemia (8-10g/dl) 80% in Ferrous fumarate and 86.7% in Carbonyl iron. No significant difference in mean Hemoglobin was observed between two groups ($t = 0.54$, $d = 58$, $P > 0.05$) (Table-3). Mean Hemoglobin (\pm SD) after 3 months of treatment in Ferrous fumarate group was 10.86 (\pm 0.8) & in Carbonyl iron group was 10.09 (\pm 0.93). Significant difference in mean Hemoglobin was observed between two groups (t

$=3.42$, $d = 58$, $P< 0.05$) (Table-4). Mean MCV (\pm SD) at booking visit in Ferrous fumarate group is 82.90 (\pm 6.08) & in Carbonyl iron group is 82.07 (\pm 7.40). No significant difference in mean MCV was observed between two groups ($t=0.47$, $d=58$, $P>0.05$) (Table-5). Mean MCV (\pm SD) after 3 months of treatment in Ferrous fumarate group was 86.96 (\pm 4.99) & in Carbonyl iron group was 83.43 (\pm 5.91). No significant difference in mean MCV was observed between two groups ($t = 2.5$, $d = 58$, $P > 0.05$) (Table-6). Mean MCH (\pm SD) at booking visit in Ferrous fumarate group is 27.40 (\pm 2.29) & in Carbonyl iron group is 26.34 (\pm 2.76). No significant difference in mean MCH was observed between two groups ($t= 1.61$, $d = 58$, $P > 0.05$) (Table-7). Mean MCH (\pm SD) after 3 months of treatment in Ferrous fumarate group is 29.27(\pm 1.87) & in Carbonyl iron group is 27.51(\pm 1.60). Significant difference in mean MCH was observed between two groups ($t=3.94$, $d = 58$, $P < 0.001$) (Table-8). Mean MCHC (\pm SD) at booking visit in Ferrous fumarate group was 31.24 (\pm 2.19) & in Carbonyl iron group is 31.94 (\pm 1.58). No significant difference in mean MCHC was observed between two groups ($t= 0.39$, $d = 58$, $P > 0.05$) (Table-9). Mean MCHC (\pm SD) after 3 months of treatment in Ferrous fumarate group was 31.03 (\pm 2) & in Carbonyl iron group is 31.18 (\pm 1.7). No significant difference in mean MCHC was observed between two groups ($t = 1.79$, $d = 58$, $P > 0.05$) (Table-10). Mean Ferritin (\pm SD) at booking visit in Ferrous fumarate group was 15.84 (\pm 10.48) & in Carbonyl iron group is 21.13 (\pm 22.75). No significant difference in mean Ferritin was observed between two groups ($t=- 1.16$, $d = 58$, $P > 0.05$) (Table-11). Mean Ferritin (\pm SD) after 3 months of treatment in Ferrous fumarate group is 71.29(\pm 36.47) & in Carbonyl iron group is 41.02(\pm 26.64). Significant difference in mean Ferritin was observed between two groups ($t = 3.67$, $d = 58$, $P < 0.05$) (Table-12). After 3 months of follow up mean (\pm SD) hemoglobin increase in Ferrous fumarate (FF) group was 0.69 (\pm 0.83) Carbonyl iron (CI) group was 0.07(\pm 1.11) g/dl. The mean hemoglobin increase was significantly higher in FF group compared to CI group ($t =2.479$, $dt = 58$, $p<0.05$). Mean (\pm SD) increase of MCV in FF group was 4.07(\pm 4.12) and in CI group was 1.36(\pm 3.05) fl. The difference was statically significant ($t = 2.90$, $dt=58$, $p< 0.01$). Mean (\pm SD) increase in MCH in FF group was 1.87(\pm 1.65) pg and in CI group was 1.16(\pm 1.53) pg. The mean (\pm SD) increase in MCHC in FF group was 0.69(\pm 0.95) g/dl and in CI group was 0.15(\pm 1.30)g/dl. The differences of increase in MCH & MCHC were higher in FF group but it was statistically insignificant ($t = 1.73$, $df =58$, $p>0.05$ & $t=1.86$, $df = 58$, $p>0.05$ respectively). But mean (\pm SD) rise of serum ferritin was significantly higher in FF group (55.45 \pm 34.66) as compared to CI group (19.88 \pm 15.33) ($t = 5.14$, $df = 58$, $P < 0.001$) (Table-13).

Table 1: Distribution of study patients by age (years). (N=60)

Age (years)	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
<20	1(3.3%)	2(6.7%)	3(5%)
20-24	8(26.7%)	7(23.3%)	15(25%)
25-29	13 (43.3%)	11(36.7%)	24(40%)
30-40	4 (13.3%)	7(23.3%)	11(18.3%)
>35	4(13.3%)	3(10%)	7(11.7%)
Total	30(100%)	30(100%)	60(100%)

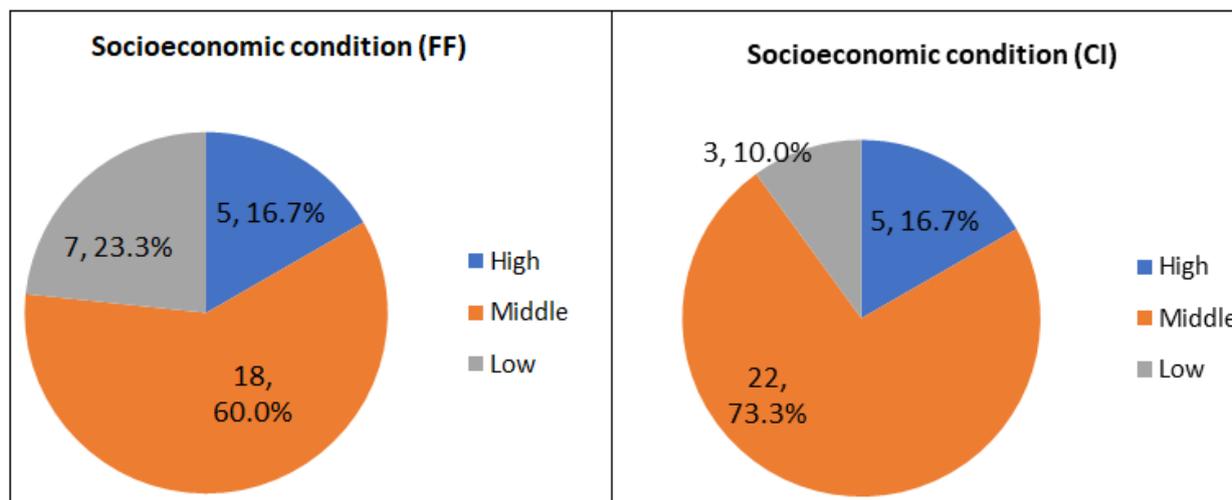


Figure-1: Socio-economic condition of the patients (N=60)

Table-2: Gravida

Gravida	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
1	15(50%)	12(40%)	27(45%)
2	8(26.7%)	13(43.3%)	21(35%)
3	5(16.7%)	4(13.3%)	9(15%)
4	2(6.7%)	1(3.3%)	3(5%)
Total	30(100%)	30(100%)	60(100%)

Table-3: Hemoglobin level in both groups at booking

Hemoglobin	Type of iron used		Total (n=60)
	Ferrous fumarate (n=30)	Carbonyl iron (n=30)	
Normal (> 11g/dl)	5 (16.7%)	3 (10%)	8 (13.3%)
Mild anemia (8-10g/dl)	24 (80%)	26 (86.7%)	50 (83.3%)
Moderate anemia (7-8g/dl)	1 (3.3%)	1 (3.3%)	2 (3.3%)

Table-4: Hemoglobin in both groups after 3 months

Hemoglobin	Type of iron used		p- value
	Ferrous fumarate	Carbonyl iron	
Normal (>11g/dl)	15 (50%)	4 (13.3%)	P<0.05
Mild anemia (8-10 g/dl)	15 (50%)	26 (86.7%)	
Total	30 (100%)	30 (100%)	

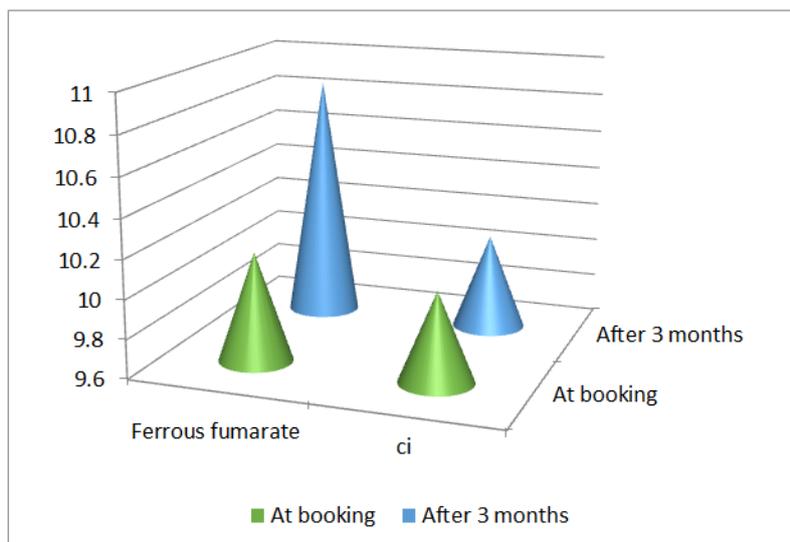


Figure-2: Showing mean Hemoglobin at booking and after 3 months of treatment

Table-5: MCV in both groups at booking

MCV	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 76 fl)	4 (13.3%)	7 (23.3%)	11 (18.3%)
Normal (76-94 fl)	26 (86.7%)	23 (76.7%)	49 (81.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-6: Serum MCV in both groups after 3 months

MCV	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 76 fl)	2 (6.7%)	6 (20%)	8 (13.3%)
Normal (76-94 fl)	28 (93.3%)	24 (80%)	52 (86.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-7: Serum MCHC in both groups after at booking

MCH	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 27pg)	10 (33.3%)	14 (46.7%)	24 (40%)
Normal (27-32pg)	20 (66.7%)	16 (53.3%)	36 (60%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-8: Serum MCH in both groups after 3 months.

MCH	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 27pg)	1 (3.3%)	5 (16.7%)	6 (10%)
Normal (27-32pg)	29 (96.7%)	25 (83.3%)	54 (90%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-9: Serum MCHC in both groups at booking visit.

MCHC	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 29g/dl)	6 (20%)	6 (20%)	12 (20%)
Normal (29-34g/dl)	24 (80%)	24 (80%)	48 (80%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-10: Serum MCHC in both groups after 3 months

MCHC	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 29g/dl)	1 (3.3%)	3 (10%)	4 (6.7%)
Normal (29-34 g/dl)	29 (96.7%)	27 (90%)	56 (93.3%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-11: Serum ferritin in both groups at booking visit

Serum Ferritin	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low (< 30ng/ml)	27 (90%)	23 (76.7%)	50 (83.3%)
Normal (>30ng/ml)	3 (10%)	7 (23.3%)	10 (16.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-12: Increase level of serum ferritin in both groups after 3 months

Serum Ferritin	Type of iron used		Total
	Ferrous fumarate	Carbonyl iron	
Low(< 30ng/ml)	3 (10%)	13 (43.3%)	16 (26.7%)
Normal (> 30ng/ml)	27 (90%)	17 (56.7%)	44 (73.3%)
Total	30 (100%)	30 (100%)	60 (100%)

Table-13: Increase of hemoglobin, red cell indices and serum ferritin in both groups

Increase of	Type of iron used		P Value
	Ferrous fumarate	Carbonyl iron	
Hb (g/dl)	0.69 (± 0.83)	0.07 (± 1.11)	< 0.05
MCV (fl)	4.07 (± 4.11)	1.36 (± 3.05)	< 0.05
MCH (pg)	1.87 (± 1.65)	1.16 (± 1.53)	> 0.05
MCHC (g/dl)	0.69 (± 0.95)	0.15 (± 1.30)	> 0.05
Serum ferritin(ng/ml)	55.45 (± 34.66)	19.88 (± 15.33)	< 0.001

DISCUSSION

Iron deficiency anaemia is very common worldwide. In Bangladesh prevalence of anaemia in pregnancy is high. Pregnancy with anaemia has a significant impact on the health of fetus as well as that of the mother. The treatment of IDA is given to replenish Hb and iron stores by supplying sufficient iron. Oral iron supplementation is recommended to prevent and treat iron deficiency since dietary absorption cannot keep up with the increased iron demands. Iron deficiency anemia in pregnancy is associated with greater risk of perinatal mortality and morbidity, low birth weight leading to preterm delivery and lower infant APGAR scores. Since dietary absorption cannot keep up with the increased iron demands during pregnancy, it is mandatory to recommend oral iron supplements in the latter half of the pregnancy.

Various iron salts are available. Ferrous sulfate (32% elemental iron), ferrous fumarate (33% elemental iron) and ferrous gluconate (12% elemental iron) are some of the commonly used salts. An iron salt like ferrous fumarate, which is already in the reduced state, does not depend upon gastric acidity for absorption.

Another form of oral iron is carbonyl iron, which has been mainly used for the fortification of

foods. In the present study, the demographic and baseline values of Hb were not significantly different in both groups reflecting the lack of bias that might have skewed the results in favor of one of the groups.

Blood hemoglobin level is the most accurate measure of the degree of anemia in iron deficiency. Other parameters that are used to assess response to therapy include red cell indices and serum ferritin level.

For all statistical tests a 'p' value < 0.05 was considered as significant and 'p' value < 0.001 was considered as highly significant. A 'p' value > 0.05 was considered as insignificant. In the present study, hemoglobin and serum ferritin estimation was done on day 0 and 3 month after enrolment, in order to assess the efficacy of the iron supplements in improving the degree of anemia. After 3 months, when the final values in the treatment groups were compared with their respective baseline values, the improvement in the hemoglobin percentage (gm /dl) was significant (p <0.05) for both the treatment groups. Similar results were observed in the study conducted by Sagaonkar S *et al.*, [12], Patil SS *et al.*, [13].

In our study Carbonyl iron causes least rise in Hb compared to Ferrous fumarate (Table 5). In ferrous fumarate group hemoglobin level rises to 10.86 gm/dl from a baseline value of 10.16 gm/dl and in carbonyl

iron group reaches a level of 10.09gm/dl from a baseline value of 10.03 gm/dl (Table 4, Table 5 and Figure 1). The hematological response is in accordance with other reports in literature that state that a mild reticulocytosis usually begins within three to five days after the start of therapy, reaches a maximum within eight to ten days, and declines thereafter. After the first week, the hemoglobin concentration begins to increase, and is usually normal within six weeks. Alleviation of iron deficiency symptoms often occurs within the first few days of treatment.

Conflicting results were obtained by Pyarelal [14], and Geetha R *et al.*, [15]. They found that the increase in hemoglobin level was more in carbonyl iron group, as compared to the Ferrous fumarate group. In present study, a non-randomized clinical trial involving pregnant anaemic women we found carbonyl iron have lower efficacy than ferrous fumarate in increasing serum Hb. Serum ferritin levels were more effectively increased with ferrous fumarate than Carbonyl iron.

It can be suggested by findings of present study that the conventional Ferrous fumarate is more effective in the treatment of iron deficiency anemia in pregnant women as compared to carbonyl iron.

Limitations of the study

- The study population was selected from one selected hospital in Rajshahi, so the results of the study may not be reflecting the exact picture of the country.
- The sample size also a limitation of the present study, which decreases the statistical power.

In this study drug related adverse effects was not done.

CONCLUSION

Provision of iron supplements has long been recognized as a key strategy for reaching target populations at high risk of iron deficiency. Most commonly, iron supplements have been provided to women during pregnancy to prevent maternal anemia and to provide adequate iron to meet the needs of the fetus. In present study, ferrous fumarate showed highly significant increase in the hemoglobin level as compared to Carbonyl iron. It is superior in efficacy when compared to other drugs and is better tolerated.

REFERENCE

1. UK guideline, March, 2012.
2. WHO. (2001). Iron Deficiency Anemia. Assessment, Prevention, and Control. *A Guide for Programme Managers*.
3. World Health Organization. (1992). The prevalence of anaemia in women a tabulation of available information. 2nd ed. Geneva; *World Health organization*.

4. Saha, L., Pandhi, P., Gopalan, S., Malhotra, S., & kumar Saha, P. (2007). Comparison of efficacy, tolerability, and cost of iron polymaltose complex with ferrous sulphate in the treatment of iron deficiency anemia in pregnant women. *Medscape General Medicine*, 9(1), 1.
5. Allen, L. H. (2000). Anemia and iron deficiency: effects on pregnancy outcome. *The American journal of clinical nutrition*, 71(5), 1280S-1284S.
6. Juarez-Vazquez, J., Bonizzoni, E., & Scotti, A. (2002). Iron plus folate is more effective than iron alone in the treatment of iron deficiency anaemia in pregnancy: a randomised, double blind clinical trial. *BJOG: an international journal of obstetrics and gynaecology*, 109(9), 1009-1014.
7. Kumar, A., Sharma, E., Marley, A., Samaan, M. A., & Brookes, M. J. (2022). Iron deficiency anaemia: pathophysiology, assessment, practical management. *BMJ open gastroenterology*, 9(1), e000759.
8. Frewin, R., Henson, A., & Provan, D. (1997). ABC of clinical haematology: iron deficiency anaemia. *BMJ*, 314(7077), 360-363.
9. Kaltwasser, J. P., Werner, E., & Niechzial, M. (1987). Bioavailability and therapeutic efficacy of bivalent and trivalent iron preparations. *Arzneimittel-forschung*, 37(1A), 122-129.
10. Hallberg, L., Brune, M., & Rossander, L. (1986). Low bioavailability of carbonyl iron in man: studies on iron fortification of wheat flour. *The American journal of clinical nutrition*, 43(1), 59-67.
11. Milman, N., Byg, K. E., Bergholt, T., & Eriksen, L. (2006). Side effects of oral iron prophylaxis in pregnancy—myth or reality?. *Acta haematologica*, 115(1-2), 53-57.
12. Smita, S., Sukhija, S., Renu, T., & Sagaonkar, P. D. (2009). Pregnancy induced iron deficiency and the evaluation and comparison of the efficacy and safety of ferrous fumarate and carbonyl iron in its treatment-PERFECT trial. *J Obstet Gynecol India*, 59(6), 552-562.
13. Patil, S. S., Khanwelkar, C. C., Patil, S. K., Thorat, V. M., Jadhav, S. A., & Sontakke, A. V. (2013). Comparison of efficacy, tolerability, and cost of newer with conventional oral iron preparation. *Al Ameen Journal of Medical Sciences*, 6(1), 29-33.
14. Pyarelal. (2015). Comparative study of iron supplements: Its efficacy and tolerability. *Indian Journal of Basic and Applied Medical Research*, 4(4), 132-136.
15. Geetha, R., Rageshwari, S., Parvathavarthini, S., Sowmia, K. R., Vivekkumar, S. P., Nagesh, S. V., & Umamageswari, A. (2014). Comparative study of iron supplements in south Indian antenatal women with iron deficiency anemia. *J Evolut Med Dent Sci*, 3, 11379-85.