



“Ferric Carboxymaltose and Iron Sucrose for Treatment of Iron Deficiency Anemia in Pregnancy”

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Review

According to WHO stats, 40% children between 6-59 months, 37% of pregnant women and 30% women belongs to 15-49 years of age worldwide are anemic [2]. In Indian population according to NFHS 5(2019-2021) data 57.0% women age 15-49 years, 57.2% Non-pregnant women age 15-49 years (<12.0 g/dl), 52.2% Pregnant women age 15-49 years compared to NFHS-4 data in which 50.4% pregnant woman were anemic [3]. The 65th world health assembly committed to be held on 2025 wants to reduce the prevalence anemia by half among women of reproductive age [4]. The same target aligns with Sustainable Development Goals (SDGs) 2030 goal, as an indicator on anemia in same population. But, prevalence of anemia is still stagnated and world is not in track to achieve the same [5].

Anemia has complex aetiology, there can be multiple possible causes and risk factors, of which iron deficiency anemia is the most common, estimated to be contributing from 10% to over 60%, depending upon the population group [6,7] and rest of the causes include parasitic diseases, chronic diseases, inflammation, gynaecological and obstetric conditions, and inherited red blood cell disorders [8,9].

Low dietary intake of iron, poor bio-availability of iron, phy-tate-rich Indian diet, faulty food habits, chronic blood loss during menses and high prevalence of infections like malaria and hookworm infestations are the major contributing factors for anemia among Indian population.



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Anemia in pregnancy can range from mild to very severe depending on the hemoglobin levels, it can lead to increased susceptibility increased risk of perinatal morbidity and mortality [10]. Anemia at the time of delivery may need to be managed by blood transfusion, and is associated with increased cardiovascular risks, longer hospital stay, and problems in the postpartum period like reduced lactation, risk of infections or postpartum mood disorder [11].

Oral iron is advised prophylactically to meet increased requirement during the antenatal period. Patient compliance may be poor with oral therapy due to gastrointestinal side effects which mainly include bloating, diarrhoea, heartburn, nausea, constipation, and dark stools. Those with intolerance to oral iron can be managed in the 2nd and 3rd trimester of pregnancy by parenteral therapy to achieve better outcome, can significantly reduce blood transfusions in antenatal and postnatal period [12].

The most commonly used iron preparation for anemia in pregnancy is Iron Sucrose Complex (ISC). It has negligible safety issues and no test dose is required. The only disadvantage with iron sucrose is limited dose per sitting. The maximum permissible dose is 300 mg per sitting or 600 mg per week. This adds to the total cost of therapy as it requires multiple visits. The latest addition to i.v. iron preparations is Ferric Carboxymaltose (FCM), which is a dextran free type I iron complex. A lot of studies have been published on the use of FCM for treatment of anemia in the postpartum period and other diseases with associated anemia. But, there is limited literature on the use of FCM in pregnancy. There are very few prospective studies on FCM in pregnancy and randomized controlled studies comparing FCM and Iron sucrose complex in pregnancy. The present review was conducted to evaluate the efficacy, safety, cost effectiveness of FCM compared with ISC for treatment of moderate to severe iron deficiency anemia in pregnancy.

For the present study literature search was performed via two independent investigators (DR and RZ) using a pre-defined search strategy mentioned below published on *PubMed*, *Embase*, *Cochrane reviews*, *Cochrane trials*, *CTRI* since inception till 31st May 2023. Manual search was also performed to retrieve other relevant articles.

#4: ((Anaemia OR anemia OR Iron OR Fe OR Iron deficiency anaemia OR iron deficiency anemia OR Irondeficiency anemia OR Iron-deficiency anaemia) AND (Ferric carboxymaltose OR Ferinject OR Injectafer OR FCM)) AND (iron sucrose complex OR isc OR iron sucrose injection OR iron sucrose OR iron saccharate.

1. Anaemia OR anemia OR Iron OR Fe OR Iron deficiency anaemia OR iron deficiency anemia OR Iron-deficiency anemia OR Iron-deficiency anaemia.
2. Ferric carboxymaltose OR Ferinject OR Injectafer OR FCM.
3. iron sucrose complex OR isc OR iron sucrose injection OR iron sucrose OR iron saccharate.
4. #1 AND #2 AND #3.

The iron requirement in pregnancy increases by around 1000 mg. Anemia is associated with varied maternal and fetal effects

which include, postpartum haemorrhage requiring blood transfusion, caesarean deliveries, postpartum wound infections and delayed recovery in mother, and prematurity, higher rate of neonatal intensive care admissions in the new-born [13].

Prophylactic oral iron is administered to all antenatal women in India to meet the demands in pregnancy, however oral iron is associated with major gastrointestinal adverse effects and many pregnant women are not able to consume it [14]. Moreover Oral iron is less suitable for correcting moderate to severe anemia in later half of pregnancy due to compliance issues. Iron sucrose is a widely used preparation which is recommended in most settings for treatment of iron deficiency anemia in pregnancy. However iron sucrose has its own disadvantages of requiring multiple hospital visits and cannulations causing discomfort to the patient. Ferric Carboxymaltose is an attractive option compared to iron sucrose avoiding the above mentioned issues with iron sucrose. As of now, there are a very few studies comparing iron sucrose to ferric Carboxymaltose for treatment of iron deficiency anemia in pregnancy. Of the 4 studies available for review, three were excluded for various reasons (Table 1).

The only study eligible for review was by Jose A et al., 2019 [14] and Patel AR et al., 2020 [15].

Jose A et al., 2019 [14] recruited 100 antenatal women with 50 in each group. After calculating total iron deficit, patients in the FCM group were administered i.v. with the maximal dose of 1000 mg IV infusion per sitting. Further does if needed were administered on day 7 and day 14. Patients in Iron sucrose group were administered IV ISC as 300 mg IV infusion (twice weekly till dosage was completed, not to exceed 600 mg per week. They followed all the patients after All patients were followed up after 3, 6 and 12 weeks of initiation of treatment. All the patients completed the treatment in both the groups. All the patients in both groups received complete calculated dose of drug. No serious adverse events were noted in either group. Notable adverse effects were that of injection site reaction in 1 patient in FCM group and 2 in ISC group. Preterm delivery rate was 14% in FCM group and 12 % in ISC group. The mean birth weight in FCM group was 2834.1 g and in ISC group was 2864.7 g; p value: 0.73). The cost of total therapy was significantly higher in FCM group, where the cost included only drug cost and consumables, Personal costs borne by the patients in view of multiple hospital visits and absence from work was not included. FCM group had significantly higher mean rise in hemoglobin (P-value < 0.01). Number of visits were significantly less in FCM group. No serious adverse events were noted in either group (Table 2).

Patel AR et al., 2020 [15] performed a prospective interventional comparative study which was conducted during May 2016 to April 2018 among 100 pregnant women from gestation period 28 to 34 weeks with moderate to severe anemia. A mean rise in Hb with Fe Sucrose noted as 1.8 gm% and with FCM as 2.6gm% respectively. In the study one woman developed severe anaphylactic reaction who was receiving iron sucrose. This study concluded, IV FCM is better and safe when compared to Fe sucrose and has several advantage to administer large dose in a single setting (Table 2).

Table 1: List of studies comparing Ferric Carboxymaltose with Iron Sucrose.

Author and Year	Study Design	Remarks
Jose A et al., 2019 [14]	Open-label randomized clinical trial	Included in the present review
Patel AR et al., 2020 [15]	Prospective interventional comparative study	Included in the present review
Muhammad H et al., 2021 [16]	Prospective	Eligible for including in review but sufficient data not available hence, excluded.
Christoph P et al., 2012 [17]	Observational (retrospective analysis)	Excluded because of different study design
Rajwani S et al., 2020 [18]	RCT	Eligible for including in the present review on the basis of abstract screening but full text not available hence, excluded.

Table 2: List of studies comparing Ferric Carboxymaltose with Iron Sucrose.

Author and Year	Duration	Disease severity	POG	Subjects	Sample Size	Follow up	Time required to administer the total drug dose	Rise in Hb
Jose A et al., 2019 [14]	January 2016– August 2017	Moderate to Severe	16 to 36	Hb > 60 g/L and < 100 g/L and iron deficiency anemia (IDA)	100 (50=FCM and 50=ISC)	Till 12 weeks	1 week in FCM group (2 doses on day 0 and 7); and in ISC group 3 weeks (2 doses per week).	FCM= 29.6 ± 8.2; and ISC= 22.1 ± 8.2
Patel AR et al., 2020 [15]	May 2016 to April 2018	Moderate to Severe	28 to 34	Hb 6 gm% to 9.9 gm % and s. Ferritin < 30 ng/ml.	100 (50=FCM and 50=ISC)	Till 3 weeks	-	Mean rise in Hb with Fe sucrose was 1.8 gm% and with FCM was 2.6 gm%.
Muhammad H et al., 2021 [16]	May 2020 to July 2021		24 to 37	Hb 7-8g/dl	400 (400=FCM and 400=ISC)	Till 37 weeks POG	-	FCM= 29.6 ± 8.2; and ISC= 22.1 ± 8.2 3.600±0.48
Christoph P et al., 2012 [17]	2005 to 2008		Above 13	Ferritin lev- els ≤30 µg/L	206 (103=FCM and 103=ISC)	FCM =28.4±31.2; and ISC =41.2±27.3	-	FCM= 3.714 ± 0.45; and ISC= 3.600±0.48
Rajwani S et al., 2020 [18]	Full text not available							

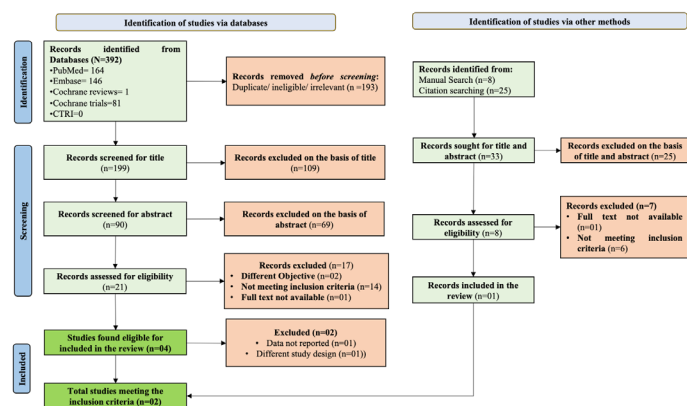


Figure 1: The PRISMA study flow diagram.

Conclusion

Based on the available literature, FCM is a safe intravenous agent in pregnancy and is non-inferior to the iron sucrose complex therapy for the treatment of iron deficiency anemia in pregnancy. Advantages of FCM over ISC include larger dosage administration per sitting, early rise in hemoglobin, and lesser number of hospital visits due to lesser number of doses. Therefore cost associated with multiple hospital visits, equipment

at each visit and discomfort to patient due to multiple needle prick is avoided in those receiving FCM. Improvement in fatigue scores were better with FCM over 12 weeks. Significantly shorter duration of treatment when considered in a community setting with the patient friendly dosing, may translate to better patient compliance to treatment.

Present review was registered on **Prospero (Registration number: CRD42022385539)**, but because of less number of studies available a meta-analysis was not possible to conduct.

References

1. Comparative quantification of health risks: Global and regional burden of disease attributable to selected major risk factors / edited by Majid Ezzati [et al.]. 2023.
2. Anaemia. 2023.
3. NFHS-5_Phase-II_0.pdf. 2023.
4. Comprehensive implementation plan on maternal, infant and young child nutrition. 2023.
5. Stevens GA, Paciorek CJ, Flores-Urrutia MC, Borghi E, Namaste S, et al. National, regional, and global estimates of anaemia by severity in women and children for 2000-19: A pooled analysis of population-representative data. *Lancet Glob Health*. 2022; 10:

- e627-39.
6. Petry N, Olofin I, Hurrell RF, Boy E, Wirth JP, et al. The Proportion of Anemia Associated with Iron Deficiency in Low, Medium, and High Human Development Index Countries: A Systematic Analysis of National Surveys. *Nutrients*. 2016; 8: 693.
 7. Wirth JP, Woodruff BA, Engle-Stone R, Namaste SM, Temple VJ, et al. Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr*. 2017; 106: 416S-427S.
 8. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. *Ann N Y Acad Sci*. 2019; 1450: 15-31.
 9. Safiri S, Kolahi AA, Noori M, Nejadghaderi SA, Karamzad N, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990-2019: Results from the Global Burden of Disease Study 2019. *J Hematol Oncol* *J Hematol Oncol*. 2021; 14: 185.
 10. Van Wyck DB, Martens MG, Seid MH, Baker JB, Mangione A. Intravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anemia: a randomized controlled trial. *Obstet Gynecol*. 2007; 110: 267-78.
 11. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum iron deficiency anemia - PubMed. 2023.
 12. Kriplani A, Mahey R, Dash BB, Kulshreshta V, Agarwal N, et al. Intravenous iron sucrose therapy for moderate to severe anaemia in pregnancy. *Indian J Med Res*. 2013; 138: 78-82.
 13. Georgieff MK. Iron Deficiency in Pregnancy. *Am J Obstet Gynecol*. 2020; 223: 516-24.
 14. Jose A, Mahey R, Sharma JB, Bhatla N, Saxena R, et al. Comparison of ferric Carboxymaltose and iron sucrose complex for treatment of iron deficiency anemia in pregnancy- randomised controlled trial. *BMC Pregnancy Childbirth*. 2019; 19: 54.
 15. Patel AR, Patel VS, Patel PR. A comparative study of ferric carboxymaltose and iron sucrose as a parenteral iron treatment in iron deficiency anaemia during pregnancy. *Int J Reprod Contracept Obstet Gynecol*. 2020; 9: 2437-41.
 16. Muhammad H, Ansar A, Ansar S, Ahmad I, Latif A. Pharmacotherapy in Anaemia of Pregnancy: Comparison of Oral Ferrous Sulphate, Intravenous Iron Sucrose. *Pak J Med Health Sci*. 2021; 15: 2154-6.
 17. Christoph P, Schuller C, Studer H, Irion O, De Tejada BM, et al. Intravenous iron treatment in pregnancy: Comparison of high-dose ferric carboxymaltose vs. iron sucrose. *J Perinat Med*. 2012; 40: 469-74.
 18. Rajwani S, Kshirsagar N, Patil S. Randomized clinical trial of IV iron sucrose and IV ferric carboxymaltose in the treatment of moderate iron deficiency anaemia in pregnancy. *Int J Res Pharm Sci*. 2020; 11: 4937-43.