

## ORIGINAL RESEARCH

### Evaluation of therapeutic efficacy of intravenous ferric carboxymaltose in pregnant women with anaemia in OBG dept at tertiary care teaching hospital

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#### Abstract

**Background:** Anemia is a frequent and treatable disease among pregnant women all over the world, and it contributes to maternal and perinatal death.

**Aim:** The aim of this study was to assess the effect of Intravenous Ferric Carboxymaltose (FCM) on haemoglobin response among patients with anaemia.

**Materials and Methods:** This was a prospective study which was conducted in Department of Obstetrics and Gynaecology, Santhiram Medical College & General hospital, Nandyal. This study was conducted between the period of July 2018 to Jan 2019. Sample size was 117.

**Results:** The patients approaching for FCM treatment were mostly between the age group of 26-30years with 57.2% followed by 21-25 years with 24%. The haemoglobin profile shows that patients were more frequently recorded between the Hb ranges of 7.1-7.5g/dl with 20.5% followed by 6.1-6.5g/dl with 18.8%. The prevalence of anaemia was high in 26-30years age group. The severity of anaemia shows that 59 patients were recorded with moderate anaemia between 7.1-10.0g/dl. An increase in Haemoglobin with 2-3g/dl was seen for a period of 4 weeks.

**Conclusion:** The study concluded that a single dose of 1000mg IV infusion is safe and effective in improving Hb concentration by more than 2-3g/dl in pregnant women with anaemia. FCM demonstrated an improvement in the laboratory biomarker Hb in a short period of time as well as improved patient compliance and fewer hospital visits. The therapeutic efficacy of IV FCM in anaemic pregnant women, primarily in the late second and third trimesters.

**Keywords:** Ferric carboxymaltose (FCM), Haemoglobin, Anaemia.

#### Introduction

Anaemia during pregnancy can be mainly caused by iron deficiency and it can lead to severe threat to both mother and fetus. Anaemia in pregnancy is due to insufficient intake of iron and nutrients, which intern leads to insufficient RBC production. Due to this oxygen carrying capacity to mother tissue and for fetus growth may be altered. FCM is a novel iron complex a consist of polynuclear iron hydroxide carbohydrate complex which helps for control release of iron to the target receptor. The iron is reuptake by after 24days of FCM administration. Patients with 50kgs or above 50kgs: 1000mg of drug should be given twice at a time interval of 7days at a minimum time period of 15min. Anemia is common in pregnancy, with a frequency of 33-89 percent and a 42 percent incidence (WHO, 2015). It is responsible for

40% of maternal mortality in impoverished nations, with 25% of those deaths being due to direct causes.<sup>1</sup> The prevalence is 53% in non-pregnant women (NHS-3). According to the ICMR, 87 percent of pregnant women are anaemic, with 10% having severe anaemia. According to the NFHS-2, 46% of metropolitan women are anaemic. Anemia in pregnancy is defined by haemoglobin (Hb) levels of 11 gm percent and hematocrit of 33 percent, according to the WHO.<sup>2</sup> Anemia in pregnancy is defined as Hb 10.5 gm% in the first and third trimesters, and Hb 11 gm% in the second trimester, according to the CDC (Centers for Disease Control and Prevention).<sup>3</sup> The Indian Medical Council and Research (ICMR) has classified anaemia during pregnancy as mild (Hb -10-10.9 gm%), moderate (Hb-7- 9.9 gm%), severe (Hb-4-6.9 gm%), and extremely severe (Hb -4 gm%). In India, anaemia during pregnancy is directly responsible for 20% of maternal deaths and 50% of deaths due to related causes.<sup>4</sup> Susceptibility to infection, intrauterine growth retardation, early birth, and increased perinatal morbidity and mortality are all key outcomes of moderate to severe anaemia during pregnancy.<sup>5</sup> Blood transfusions are also required more frequently during delivery as a result of increased cardiovascular issues, longer hospital stays, decreased lactation, and postpartum mood disorders. Nutritional deficiency, a strict vegetarian diet, repeated pregnancies or pregnancy losses at very short intervals, pregnant females not taking supplementary medications, chronic blood loss such as in malaria, hookworm infestation, haemorrhoids, iatrogenic, cancers, suppressed bone marrow erythropoiesis, renal related, autoimmune disease, trauma or ruptures, unknown aetiology. Anemia is characterised by easy weariness, palpitation, giddiness, attention loss, depression, and diminished general mental, physical, and cognitive function, as well as skin and mucosal pallor on inspection. Low ferritin levels, together with a reduced Hb content, are regarded the gold standard for diagnosing anaemia. Iron, folic acid, vitamin B12, vitamin C, amino acids, traces of zinc, and erythropoietin are all required for Erythropoiesis.<sup>6</sup> Pregnancy is a high iron-demanding state, requiring an average of 1000mg in a typical singleton pregnancy (500mg for maternal Hb increase, 300mg for foetus and placenta, and 200mg for body waste via gut, skin, urine, and other routes). In 1970, India developed the National Nutritional Anemia Control Programme (NNARCP), which suggested that pregnant women take an iron tablet once a day for 100 days after the first trimester (1 tab = 100mg elemental iron and 500mcg folic acid). Parenteral iron therapy is utilised in chronic blood loss, gastrointestinal issues, and reduced iron absorption because it is more compliant, effective, and has a greater tolerance. It also allows for a faster replenishment of iron storage. Type I complexes have a high risk of anaphylaxis due to the gradual release of iron, but type II complexes are safer. Type III complexes are unstable and cause tissue toxicity. In November of 2000, the FDA approved iron sucrose (FeS) for producing an iron hydroxide sucrose complex in water with a molecular weight of 34000-60000 Dalton. With no test dose and a maximum daily dosage of 200 mg, it is given as an intravenous bolus injection over 5-10 minutes or as an infusion in 100ml normal saline over 15-20 minutes. Metal taste, nausea, dizziness, and local irritation are some of the side effects. Ferric carboxymaltose (FCM) is given in injection/infusion form contains iron in stable ferric state with complexation to carbohydrate polymer designed to deliver iron for the transportation to the target site and for the storage proteins in the body like transferrin and ferritin. FCM is effective in increasing the haemoglobin (Hb) and serum ferritin concentrations in patients with mild to moderate iron-deficiency anemia. The aim of this study was to assess the effect of Intravenous Ferric Carboxymaltose (FCM) on haemoglobin response among patients with anaemia. To increase Compliance to the drug. To make awareness for use of these drug[FCM]whenever required by evaluating the Haemoglobin levels.

## Materials and Methods

This was a prospective study which was conducted in Department of Obstetrics and Gynaecology, Santhiram Medical College & General hospital, Nandyal. This study was conducted between the period of July 2018 to Jan 2019. Sample size was 117. Patients who had been suffering from anaemia, second and third trimester of pregnancy, patients willing to join the study were included in the study. Patients who had hypersensitivity reactions to ferric elements, those who were not willing to join the study, those patients who were not co-operative and who were unable to understand the protocol and informed consent form were excluded from the study. Informed consent form was taken from all patients. Institutional ethical committee was obtained. Study participants interested in participating in the study will be included after taking consent form the participant. The merits and demerits of the study will be explained prior to the consent to the study subjects. Evaluating the Improvement of Hb levels after 3-4weeks. The data was analyzed using Graphpad Prism statistical version 7.0. P-Value is calculated using one way ANOVA and T-Test to check the efficacy of FCM and  $P < 0.05$  was taken as statistically significant. Percentage for categorical variables is reported relevant and for the data entry Microsoft word and MS EXCEL spreadsheets has been used to generate graphs and tables.

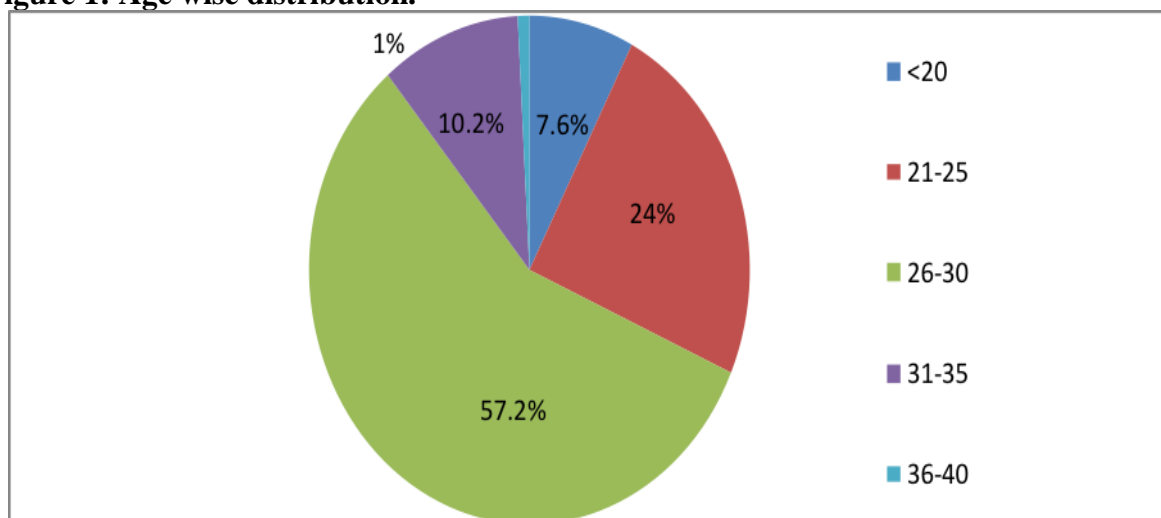
## Results

**Table 1: Age wise distribution**

Age (in years)	No. of patients	Percentage
<20	9	7.6%
21-25	28	24%
26-30	67	57.2%
31-35	12	10.2%
36-40	1	1%
Total	117	100%

Table 1 shows that the age wise study shows that the patients approaching for FCM treatment were mostly between the age group of 26-30years with 57.2% followed by 21-25 years with 24%. The less frequently approaching patients were between the age group of 36-40years with 1%.

**Figure 1: Age wise distribution.**



**Table 2: Haemoglobin wise distribution**

Hb ranges (g/dl)	No. of patients	Percentage
4-4.5	2	1.7%
4.6-5	3	2.5%
5.1-5.5	6	5.1%
5.6-6	10	8.5%
6.1-6.5	22	18.8%
6.6-7	15	12.8%
7.1-7.5	24	20.5%
7.6-8	15	12.8%
8.1-8.5	17	14.5%
8.6-9	3	2.5%

Table 2 shows that the haemoglobin profile shows that patients were more frequently recorded between the Hb ranges of 7.1-7.5g/dl with 20.5% followed by 6.1-6.5g/dl with 18.8% and less frequently recorded between 4.0-4.5g/dl with 1.7%.

**Table 3: Haemoglobin level wise distribution based on age.**

S.No.	Hb levels(g/dl)	Age in years				
		<20	21-25	26-30	31-35	36-40
1.	4.0-4.5g/dl	1	0	1	0	0
2.	4.6-5g/dl	1	1	1	0	0
3	5.1-5.5g/dl	0	1	5	0	0
4.	5.6-6g/dl	2	1	4	3	0
5.	6.1-6.5g/dl	2	5	12	3	0
6.	6.6-7g/dl	1	3	9	2	0
7.	7.1-7.5g/dl	1	5	16	1	1
8.	7.6-8g/dl	1	8	5	1	0
9.	8.1-8.5g/dl	0	4	11	2	0
10.	8.6-9g/dl	0	0	3	0	0

Table 3 shows that prevalence of anaemia is high in 26-30years age group. According to WHO classification of anaemia, more women are reported with severe anaemia followed by moderate anaemia.

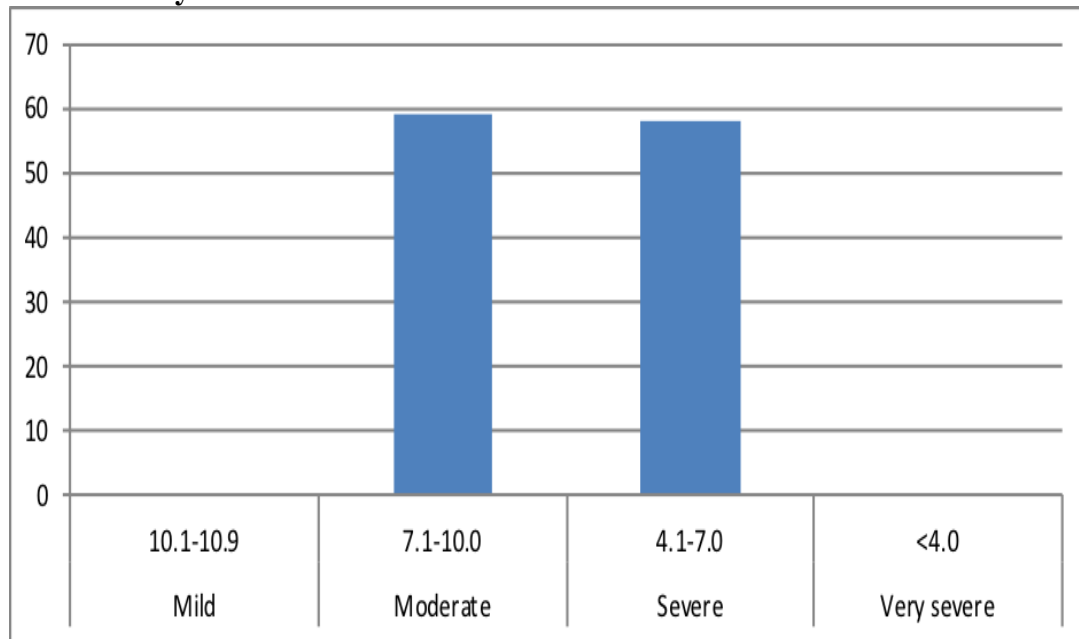
**Table 4: Severity wise distribution**

Anemia Severity	Haemoglobin level (g/dl)	No. of patients
Mild	10.1-10.9	0
Moderate	7.1-10.0	59
Severe	4.1-7.0	58
Very Severe	<4.0	0

Table 4 shows that among 117 pregnant women, the severity of anaemia shows that 59 patients were recorded with moderate anaemia between 7.1-10.0g/dl followed by 58 patients

with severe anaemia between 4.1-7.0g/dl. No patients were recorded with mild and very severe anaemia.

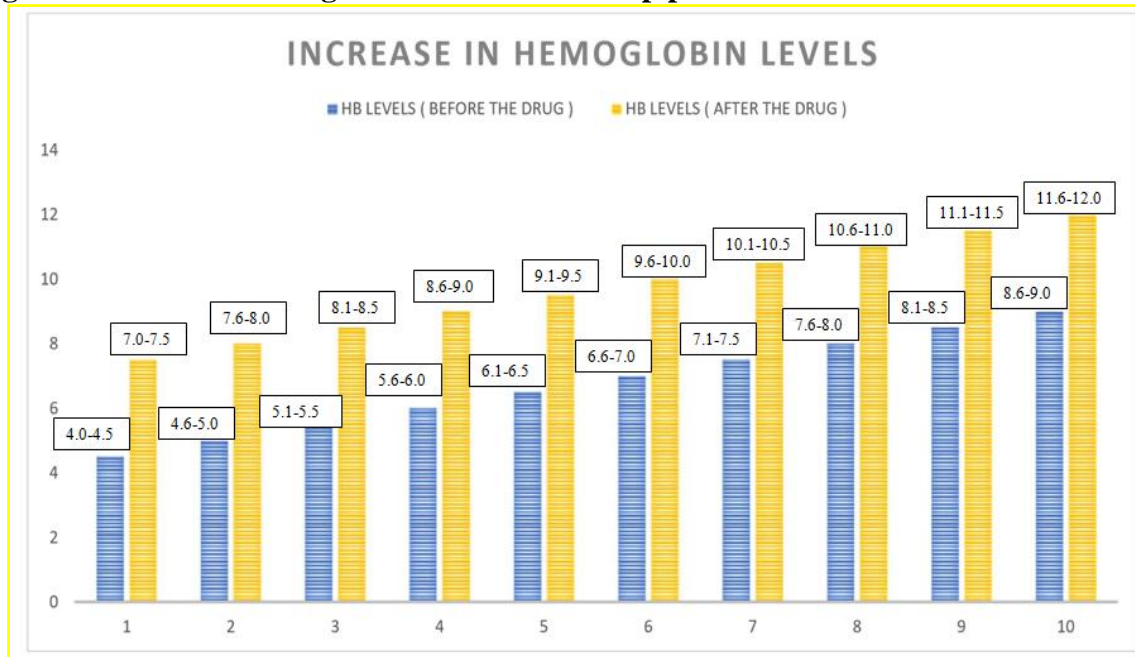
**Figure 2: Severity wise distribution.**



**Table 5: Increase haemoglobin levels in follow up patients.**

S.No	No. of Patients	Hb level (before the drug)	Hb level (after the drug)
1	1	4.0-4.5g/dl	7.0-7.5g/dl
2	2	4.6-5.0g/dl	7.5-8.0g/dl
3	3	5.1-5.5g/dl	8.0-8.5g/dl
4	8	5.6-6.0g/dl	8.5-9g/dl
5	12	6.1-6.5g/dl	9.0-9.5g/dl
6	8	6.6-7.0g/dl	9.5-10g/dl
7	14	7.1-7.5g/dl	10.0-10.5g/dl
8	11	7.6-8.0g/dl	10.5-11.0g/dl
9	11	8.1-8.5g/dl	11.0-11.5g/dl
10	3	8.6-9.0g/dl	>11.5g/dl

Table 5 shows that the objective evidence for anaemic patients shows the improvement of Hb levels before and after use of IV FCM. An increase in Haemoglobin with 2-3g/dl was seen for a period of 4 weeks.

**Figure 3: Increase haemoglobin levels in follow up patients.**

## Discussion

The present study was conducted for a period of 6 months in SRMC & SRGH during the study period a total of 117 patients were assessed to evaluate the therapeutic efficacy by IV FCM in pregnant women. Almost 80% of pregnant are anaemic out of them maximum are teenage pregnant women from low socio-economic group, heavy periods and short duration between pregnancies. The diagnosis is made by examining the blood cells and noted low haemoglobin concentration. Since the population under study was not homogenous, the main cause of anaemia was diverse such as short duration between pregnancies, heavy bleeding during periods, early pregnancy. The patient population was identified on the basis of laboratory biomarker Hb. The decision regarding the continuation of oral therapy of interruption was taken on the basis of laboratory biomarker. A well balanced diet is always recommended along with iron supplements, if the patient is complaining any side effect to iron supplements or even at second and third trimester women are in severe or moderate anaemic stage, the better treatment option is injection of IV FCM for 15minutes at a single dose of 1000mg after 28weeks of gestation. This new IV FCM shown lower risk of complications than other injectables. Infusion of FCM is only 15minutes for a dose of 1000mg compared with longer IV administration times like iron sucrose and iron dextran. The study shown that treatment with FCM was not associated with any unacceptable side effects or adverse effects. The study is consistent with other reported studies on FCM. In this trial, patient treated with FCM achieved Hb rise of 2-3g/dl in 2-4weeks. In our study the mean increase after 3weeks was recorded as 2g/dl from baseline value in case of patients treated with FCM. In a study by Seid and Colleagues, the increase in Hb was 3g/dl or more in 15days consistence with our study. None of the patients reported any serious ADR requiring hospitalization. FCM was better tolerated in pregnant women with no reported ADR which is in consistence with the study by Breyman and Colleagues<sup>7</sup>. Patients seeking FCM treatment were predominantly in the age bracket of 26-30 years, with 57.2 percent, followed by 21-25 years, with 24 percent. Patients between the ages of 36 and 40 were the least likely to be approached, accounting for 1% of the total. Patients were more frequently recorded between the Hb ranges of 7.1-7.5g/dl with 20.5 percent, followed by 6.1-6.5g/dl with 18.8 percent, and less frequently recorded between 4.0-4.5g/dl with 1.7 percent, according to the haemoglobin

profile. Anemia is common in people between the ages of 26 and 30. According to the WHO classification of anaemia, severe anaemia is more common in women, followed by moderate anaemia. The degree of anaemia was documented in 117 pregnant women, with 59 patients having moderate anaemia between 7.1-10.0g/dl and 58 patients having severe anaemia between 4.1-7.0g/dl. There were no patients with mild or severe anaemia documented. D. L. Arnold et al.,<sup>8</sup> conducted a study on "Iron deficiency anemia, cigarette smoking and risk of abruption placenta" Anemia affects one-quarter of the world's population and is concentrated in preschool-aged children and women, making it a global public health problem. Data on relative contributions of causal factors are lacking, however, which makes it difficult to effectively address the problem. J. F. Murphy et al.,<sup>9</sup> conducted a study on "Relation of hemoglobin levels in first and second trimesters to outcome of pregnancy" Intravenously administered iron elevated serum Hb and restored iron stores better than oral iron (ferrous ascorbate). P. Galan et al.,<sup>10</sup> conducted a study on "Determining factors in the iron status of adult women in the SU.VI.MAX study. Supplementation en Vitamins et Minéraux Antioxydants" Intravenous administration of iron sucrose seems to be safe and it helps postpartum women recover early from anemia. R. L. Bergmann et al.;<sup>11</sup> conducted a study on "Diagnosis and treatment of iron deficiency and anemia during pregnancy and post partum" Although hematological parameters improved following infusion in both groups, FCM had a lower incidence of infusion- related adverse events compared to FeS. Although sample size is small, given decreased monitoring and infusion time required for FCM, it may become the preferred formulation for ID treatment in pregnancy. L.H.Allen et al.,<sup>12</sup> conducted a study on "Anemia and iron deficiency: effects on pregnancy outcome" Oral iron supplements are an inexpensive and effective way of treating IDA patients and their administration, in the absence of inflammation or significant ongoing blood loss, can correct anemia, provided significant doses of iron can be tolerated. The objective data for anaemic patients reveals that Hb levels improve before and after IV FCM treatment. For a period of four weeks, a rise in haemoglobin of 2-3g/dl was seen. Finally, the current study shows that the FCM was safe and efficacious among pregnant women to increase haemoglobin levels. The limited number of patients (population under study were only females) and the duration of the study is less are the limitations of this study. The study needs to be done on large population i.e., on both males and females population and the duration should be more to assess the long term effects of the FCM. Comparison of drug with other preparations available in the market should also be done.

## Conclusion

This study showed many gaps in our knowledge about the maternal anaemia on pregnancy outcome. Anaemia is widely spread and mostly overlook. Prophylactic treatment should be started in women with heavy bleeding during menstruation and in pregnancy to avoid anemia related complications. The conclusion of the study is to demonstrate that a single dose of 1000mg IV infusion is safe and effective in improving Hb concentration by above 2-3g/dl in treatment of anaemia in pregnant women. FCM had shown an improvement in laboratory biomarker Hb in short duration of time and along with better patient compliance and reduced number of hospital visits. The therapeutic efficacy of IV FCM on anaemic pregnant women mostly in late 2nd and 3rd trimester. Our study recommends a rational therapeutic approach to these anaemic pregnant women with the IV FCM in time. In light of this study, there is a need for clinician prescribed IV FCM to the patients after the laboratory investigations for early evaluation and treatment of anaemia & to prevent further complications in pregnant women with anaemia.

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