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# EFFICACY AND SAFETY OF FERRIC CARBOXYMALTOSE (FCM) IN MODERATE TO SEVERE IRON DEFICIENCY ANEMIA IN PREGNANCY (IDA)

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**ABSTRACT**

**Background:** Iron deficiency anemia is indeed a significant health issue in underdeveloped nations like Pakistan. According to recent statistics its prevalence is 45% in Pakistan. WHO states that every fifth woman is suffering from this condition in Pakistan.

**Objective:** To determine the efficacy and safety of ferric carboxymaltose in moderate to severe iron deficiency anemia in pregnancy.

**Methodology:** After IRB and written informed consent from the patients this prospective study was conducted in Gynae department of Sahiwal teaching hospital, Sahiwal from 15-02-2024 to 15-08-2024. Eighty one women with singleton pregnancy of gestational age > 20 weeks with moderate to severe anemia were included. FCM was transfused. All the patients were evaluated after four weeks for the efficacy and safety of FCM.

**Results:** The mean Hemoglobin and serum ferritin levels before treatment were 7.74 ± 0.89 g/dl and 11.87 ± 3.34 µg/l and after treatment were 12.67 ± 2.49 g/dl and 18.97 ± 2.77 µg/l respectively. Efficacy along with safety of ferric carboxymaltose in moderate to severe anemia was found to be 95.06% and 96.30% respectively.

**Conclusion:** A substantial increase in Hemoglobin and serum ferritin levels four weeks after transfusion of FCM was achieved as compared to baseline values. The current study concluded that efficacy as well as safety of ferric carboxymaltose in moderate to severe anemia is very high.

**Key words:** Iron deficiency anemia, Ferric carboxymaltose ,efficacy, safety, pregnancy

## INTRODUCTION

Iron deficiency anemia during pregnancy is a considerable global health concern affecting fetomaternal health. In developing countries its prevalence is much higher, around 50% [1]. The consequences of iron deficiency anemia includes increase in risk of heart failure, poor performance, compromised immune system leading to increased susceptibility to infection and illness. The concerning risks for the fetus include birth before 37 weeks, development challenges, low birth weight, still birth, distress at birth and weak immunity leading to more risk of infections [2,3]. Comprehensive strategies that address both prevention and treatment can make a substantial difference. Women with severe anemia during pregnancy have approximately 2.36 times more risk of mortality when compared with women

of normal hemoglobin levels. This elevated risk is attributed to complications such as severe blood loss during delivery, cardiovascular strain, and other associated health issues [4,5]. Many Studies suggest that children born to anemic mothers may have a higher risk of cardiovascular issues, intellectual problems, obesity later in life, possibly due to metabolic changes during fetal development. They also have higher likelihood of developing anemia in themselves [6]. Iron deficiency is indeed the most prevalent cause of anemia, accounting for above 50% cases of anemia during pregnancy all over the world. This widespread issue can significantly impact maternal and fetal health [7].

The iron requirement is raised significantly due to increased maternal erythropoiesis, fetal growth.[1] When the available iron in body fails to meet the increased need, iron stores get depleted and anemia manifests. Prophylactic oral iron supplements are widely recommended to address these concerns. But the patient's compliance with oral iron may get compromised due to its gastrointestinal side effects [8]. Iron sucrose and ferric carboxymaltose are notable parenteral preparations that do not contain dextran. Both are better in comparison to oral iron in terms of safety and efficacy [9]. While there are rare detrimental outcomes associated with iron sucrose but minor reactions accounts for about 18% of cases. Ferric carboxymaltose offers several advantages over older formulations. It doesn't contain dextran and pH is near neutral. Another benefit of increased bioavailability is due to its physiological osmolarity [10]. Absolutely, these properties make it a best option regarding efficacy along with safety profile. Moreover it is convenient in usage [11]. Gaikwad HS reported the efficacy of ferric carboxymaltose as 70% [7]. Another study demonstrated efficacy of ferric carboxymaltose 97.50% and safety 97.20%.[8] Anemia during pregnancy is a complex issue in our society which may result in serious fetomaternal complications. To address these grave concerns of anemia, there is an increased requirement of blood transfusions which is not free from hazards. So here is need of an effective medicine which can rapidly build up hemoglobin and replenish iron stores as well. It will definitely reduce the need for blood transfusions and ultimately improve maternal and neonatal outcomes. Although the efficacy of ferric carboxymaltose is well established, the novelty of this study lies in its prospective real-world evaluation in pregnant women with moderate to severe anemia in a high-burden, resource-limited public-sector setting. It provides population-specific evidence from Pakistan, documents short-term hematologic response and safety within a standardized four-week follow-up, and supports transfusion-sparing anemia management in routine clinical practice.

## METHODOLGY

This Quasi experimental study was carried out at the Gynaecology department of Sahiwal Teaching hospital, Sahiwal after taking approval from institutional review board for a period of one year 01-07-2023 to 30-06-2024 with letter no. 106/IRB/SLMC/SWL dated 04-04-2023. The sample size of 81 patients was calculated with WHO calculator keeping confidence level 95% with margin of error 10% and taking efficacy of ferric carboxymaltose in moderate to severe anemia as 70% [7].Non probability consecutive sampling was employed. This study included both primiparous and multiparous women with singleton pregnancy of gestational age>20 weeks presenting with moderate anemia (Hb 7 to 9 gm/dl ) as well as severe iron deficiency anemia (Hb below 7 gm/dl) between 18-40 years of age. While the women who has history of allergic reactions to iron, deranged renal function tests, liver disease, HIV infections, hemochromatosis, significant cardiovascular disease and intolerance to iron derivatives were excluded. Informed written consent was taken. Patient's age, gestational age, parity, baseline hemoglobin & ferritin levels, place of living and monthly income were noted. Inj. FCM 500mg in 100ml Normal Saline was given intravenously to the selected patients over a time span of 20-30 minutes. Patients were observed for any reactions. All patients were followed after 4 weeks. The whole data was recorded on a specially designed proformas. Analysis was done by using SPSS version 25.0. For patient's age, gestational age, baseline hemoglobin and ferritin post-therapy hemoglobin and ferritin levels, mean and standard deviation were calculated. Efficacy as well as safety (No complication e.g. local skin irritation, nausea, and headache) of treatment, parity, income per month, residential place, and literacy level were calculated with frequency and percentages. Independent t-test was used to calculate Hemoglobin and ferritin levels before and after the treatment and p-value $\leq 0.05$ was taken as significant. Age, gestational age, parity, residential place, income per month, education level and baseline hemoglobin levels were controlled through stratifications. Chi square was applied post-stratification and p-value $\leq 0.05$ was considered significant.

## RESULTS

Eighty-one patients were selected after fulfilling the criteria. Patients taken were between 18- 40 years of age making mean of $32.36 \pm 3.07$ years. The majority of the patients, 71.60% were falling in 31-40 years, while the rest 28.40 % were from 18-30 years. Mean gestational age was $24.46 \pm 4.33$ weeks. In distribution of parity, 38.27% were primiparous and 61.73% were multiparous. From the rural area contribution was 60.49 % while 39.51% from urban area. Distribution of patients according to monthly income was, 30.86% (<20,000), 51.85% (20,000-40,000) and 17.28% (>40,000). In this study population, 11.11% were illiterate,

12.35% up to primary school education and 24.69% up to middle, 38.27% matric and 13.58% were of Graduation level (Table 1).

**Table 1: Comparison of Hemoglobin and ferritin levels Pre and Post Treatment**

| | **Pre-therapy** | **Post-therapy** | **p-value** |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| **Hb (g/dl)** | 7.74 ± 0.89 | 12.67 ± 2.49 | **0.0001** |
| **Ferritin (µg/L)** | 11.87 ± 3.34 | 18.97 ± 2.77 | **0.0001** |

The mean baseline Hemoglobin (Hb) and ferritin levels were 7.74 ± 0.89 g/dl and 11.87 ± 3.34 µg/L and post-therapy were 12.67 ± 2.49 g/dl and 18.97 ± 2.77 µg/L, respectively (Table I). Ferric carboxymaltose was efficacious in 95.06% of cases, while safety found were 96.30% (Table II). Patient's age, gestational age, parity, place of living, monthly income, education level, and baseline hemoglobin levels stratification was done for efficacy as well as for safety.

**Table 2: Efficacy and Safety of ferric carboxymaltose in moderate to severe anemia**

| | Yes | No |
|---|---|---|
| **Efficacy** | 77 (95.06%) | 04 (4.94%) |
| **Safety** | 78 (96.30%) | 03 (3.70%) |

Ferric carboxymaltose was well tolerated among the study participants, with the majority of patients (96.3%) experiencing no adverse events. Only three patients (3.7%) developed minor adverse reactions, including mild infusion-related symptoms such as headache or nausea (2.47%) and a localized injection-site reaction (1.23%).

**Table 3: Safety Outcomes Following Ferric Carboxymaltose Administration (n = 81)**

| **Safety Parameter** | **Frequency (n)** | **Percentage (%)** |
|---|---|---|
| No adverse events | 78 | 96.30 |
| Any adverse event | 3 | 3.70 |
| Mild infusion-related reactions (e.g., headache, nausea) | 2 | 2.47 |
| Local injection-site reaction | 1 | 1.23 |
| Serious adverse events | 0 | 0.00 |
| Anaphylaxis / hypersensitivity | 0 | 0.00 |

## DISCUSSION

Anemia is a critical issue affecting developing countries. Although it is known that anemia affects a significant proportion of pregnant women in these regions, comprehensive and accurate data on its burden and the associated risk of maternal mortality are lacking. Daru et al used the data on Maternal and Newborn Health from the WHO Multicountry Survey to assess the relationship between maternal death and severe anemia. They analyzed that there is are higher risk of maternal mortality with severe anemia [12].

In moderate to severe anemia, rapid replacement of iron stores cannot be done with oral iron; it needs iron infusions. Moreover, when iron is not tolerated orally, intravenous iron is the best alternative. Different intravenous iron formulations are available, including ferric carboxymaltose, iron sucrose, and ferric gluconate. All of these have been proven efficacious and safe. Few allergic reactions have been reported with these preparations. Josh et al. conducted an RCT that compared FCM and iron sucrose. Iron sucrose has traditionally been used as a standard parenteral iron therapy, but it has a drawback of dose limitation & multiple visits, while FCM can be transfused in a large dose at one visit. This RCT also showed an increase in hemoglobin levels in patients who were given FCM when compared with other patients who were given iron sucrose with greater symptomatic improvement as well [13]. Another meta-analysis conducted by Gupte et al. stated that FCM was more efficacious compared to other intravenous iron preparations [14]. There was a notable rise in Hemoglobin and ferritin in the FCM group versus iron sucrose/iron polymaltose. There were no adverse reactions in any group. The real-world study conducted in Turkey on 103 anemic patients with age $\geq$ 18years suggested that the treatment with FCM was notably effective in improving key markers of anemia (Hemoglobin, Ferritin, hematocrit and transferrin saturation) with a significant p-value ($P<0.05$) [15]. Krishna and

colleagues reported that FCM raised hemoglobin levels≥3 g/dl and serum ferritin levels more quickly compared to other iron preparations with a lower frequency of adverse events. One notable drawback was the higher cost of FCM compared to other iron supplements. Although ferric carboxymaltose offers several benefits in the treatment of iron deficiency anemia, particularly in terms of rapid efficacy and patient convenience, but its higher cost might be a consideration for both patients and healthcare systems [16]. Kumari and Singh also compared iron sucrose and FCM. Their results indicated that the FCM group experienced a significant increase in hemoglobin levels, specifically rise in Hemoglobin was 11.83 ± 0.79 gm/dl from baseline which was 8.305 ± 0.609 gm/dl. There was a notable rise in hemoglobin levels, ≥3gm/dl after 3-4 weeks in FCM group [16,17]. This data supports and highlights its effectiveness as compared to iron sucrose, and underscores its potential advantages in treating anemia more swiftly and effectively [17].

A retrospective real-world analysis was done by LaVellee C and colleagues on 2966 patients with iron deficiency anemia. Data provided compelling evidence of the advantages of ferric carboxymaltose compared to ferumoxytol, sodium ferric gluconate in sucrose, iron dextran, and iron sucrose. Post-treatment outpatient visits within one year were less in the FCM group compared to the ferumoxytol group (5.9 vs 9.2, $p \leq 0.001$) and other iron products (5.7 vs 11.8, $p \leq 0.001$). This data supports the use of FCM as an effective treatment option for managing iron deficiency anemia [18]. Motta et al. analyzed the effect of FCM in the hemodynamically stable patients reporting to the emergency department with severe iron deficiency anemia. They stated that the rise in Hemoglobin was 2.8 ± 1 g/dl in the FCM group within two weeks [19]. This study emphasized the potential benefits of FCM in emergency settings to minimize unnecessary blood transfusions. However, to establish its recommendations in the emergency department, further studies are needed. Holm and colleagues used another intravenous iron preparation, isomaltoside in comparison to oral iron. This study suggested that iron isomaltoside may be a more effective option for managing severe fatigue in the postpartum period, particularly after experiencing significant blood loss. Further research could help to solidify its role in postpartum care. The current study on moderate to severe anemia showed that the efficacy and safety of ferric carboxymaltose is 95.06% and 96.30% which is comparable to another study where efficacy and safety were 97.50% and 97.20% respectively [8].

## CONCLUSION

The current study concluded that high efficacy as well as safety of ferric carboxymaltose make it a valuable option in pregnancy for managing moderate and severe anemia. So, it should be recommended as a first line therapy in our routine practice for treating iron deficiency anemia. It can also be used in emergency department for hemodynamically stable anemic
patients. In this way, it will significantly improve maternal and neonatal outcomes and minimize the need for blood transfusions. Thus it will also prevent potential hazards associated with blood transfusions.

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