"COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE VERSUS FERRIC CARBOXY MALTOSE IN THE TREATMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA"

Dissertation submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the regulations for the award of the degree of

MASTER OF SURGERY

IN

OBSTETRICS AND GYNAECOLOGY

BRANCH II

ESIC MEDICAL COLLEGE AND PGIMSR,

K.K.NAGAR, CHENNAI

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ENDORSEMENT BY THE DEAN

This is to certify that the dissertation titled, **"COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE VERSUS FERRIC CARBOXY MALTOSE IN THE TREATMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA"** submitted by **Dr. REVATHY. M** in partial fulfilment for the award of the degree of **MASTER OF SURGERY** in **OBSTETRICS AND GYNAECOLOGY** by The Tamil Nadu Dr. M.G.R Medical University, Chennai is a bonafide record of work done by her in **ESIC MEDICAL COLLEGE & PGIMSR, K.K. NAGAR, CHENNAI – 600 078** during the academic year **2019 -2022**.

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DECLARATION

I hereby declare that the dissertation titled, **"COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE VERSUS FERRIC CARBOXY MALTOSE IN THE TREATMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA"** was done by me in **ESIC MEDICAL COLLEGE & PGIMSR , K.K. NAGAR, CHENNAI – 600 078** during the period 2019 – 2022 under the guidance of **Dr. ANITHA A.M. M.S(OG).,** Associate Professor, Department Of Obstetrics and Gynaecology, ESIC Medical College & PGIMSR, K.K. Nagar, Chennai – 600 078 and submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Guindy, Chennai – 600 032**, in partial fulfilment of the requirements for the award of the degree of M.S. Obstetrics and Gynaecology (Branch II), examinations to be held on May 2022. I have not submitted this dissertation previously to any journal or any university for the award of any degree or diploma.

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I am grateful to my family members and friends for their moral support and encouragement.

Last but not the least, I am indebted to all my patients who willingly participated in this study.

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE VERSUS FERRIC CARBOXY MALTOSE IN THE TREATMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA"** of the candidate **Dr. REVATHY.M** with University registration number **221916554** for the award of **MASTER OF SURGERY** in the branch of **OBSTETRICS AND GYNAECOLOGY**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **8%** of plagiarism in the dissertation.

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The Institutional Ethics Committee (IEC) convened on 30 October 2019 between 2 and 4 PM at the Meeting Room, Third Floor, ESIC Medical College & PGIMSR, KK Nagar, Chennai 600078, to review research proposals.

The following is the decision of the Institutional Ethics Committee.

IEC No.	IEC/2019/2/5
Research Proposal Title	Comparative study of efficacy and safety of intravenous iron sucrose versus ferric carboxymaltose in the treatment of postpartum iron deficiency anaemia
Name of the Principal Investigator	Dr. Revathy M.
Name and Address of the Institution	ESIC Medical College & PGIMSR, KK Nagar, Chennai 600078
Type of Review	Full Board Review
Documents Reviewed with version	Full Proposal Dated 10.11.2019 Data Collection Proforma Dated 10.11.2019 Informed Consent form in English Dated 10.11.2019 Informed Consent form in Tamil Dated 10.11.2019
Decision of the IEC	Approved
Period of validity of the approval	11.11.2019 to 10.11.2021

The IEC gave the following recommendations:

- Make randomization in the ratio of 2:1 (FCM:Iron sucrose). Therefore, you will include lesser women in the iron sucrose groups thus reducing the need for women to undergo more infusions and more visits to the hospital.
- Include a long term 3 month follow up in your study.
- Your data collection proforma is wrong. It is currently including a lot of dummy tables. Remove all of them. There is no necessity to see difference between FCM and IS groups in terms of socio-economic status.
- Include qualitative interviews with women regarding their experiences of receiving the iron injections.
- Register your study under the clinical trials registry of India. - http://ctri.icmr.org.in/

The study proposal was revised based on these recommendations and the revised proposal and documents mentioned above were approved.

The IEC must be informed immediately in case of any adverse events and serious adverse events. A fresh IEC application must be filed in case of any change of study procedure, site or investigator. This IEC approval is only for the period mentioned above. Final report of the research must be submitted to the IEC on completion of the study. Members of IEC have right to monitor the study at any point with prior intimation.

Member Secretary
IEC, ESIC MC and PGIMSR, Chennai

Date: 11.11.2019
Place: Chennai 600078

LIST OF ABBREVATIONS

Hb	: Haemoglobin
MCV	: Mean Corpuscular Volume
MCHC	: Mean Corpuscular Haemoglobin Concentration
PCV	: Packed Cell Volume
MCH	: Mean Corpuscular Haemoglobin
SF	: Serum Ferritin
WHO	: World Health Organisation
IDA	: Iron Deficiency Anaemia
PPA	: Post-Partum Anaemia
IS	: Iron Sucrose
FCM	: Ferric Carboxy Maltose
CDC	: Centres for Disease Control
SVD	: Spontaneous Vaginal Delivery
SES	: Socio Economic Status
FDA	: Food and Drug Administration

ABSTRACT

COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE VERSUS FERRIC CARBOXY MALTOSE IN THE TREATMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA

BACKGROUND:

Childbirth should be a joyous event. However, unforeseen medical problems such as postpartum haemorrhage or postpartum anaemia can develop and make this time very difficult. Postpartum anaemia is observed in up to 27% of postpartum women. It is a major contributable factor and indirect cause of maternal death. Iron deficiency is the commonest treatable cause of postpartum anaemia. Parental iron therapy with Ferric carboxy maltose (FCM) which is the third generation compound results in faster and higher replenishment of iron stores with correction of Hb levels and better patient compliance compared to other parenteral compounds and oral drugs.

AIM OF THE STUDY:

To compare the efficacy and safety of intravenous ferric carboxy maltose versus intravenous iron sucrose in the treatment of postpartum iron deficiency anaemia

OBJECTIVES:

1. To compare the efficacy of intravenous ferric carboxy maltose versus intravenous iron sucrose in postpartum anaemia correction.
2. To compare the raise in haemoglobin and other indices such as serum ferritin, MCV, PCV, MCHC and MCH between the two groups.
3. To compare the adverse reactions between the two groups.

MATERIALS AND METHODS:

This was a prospective, randomized comparative study conducted between November 2019 to April 2021 in Department of Obstetrics & Gynaecology, ESIC Medical College & PGIMSR, K.K. Nagar.

Postpartum women with Hb – 7 to 9 g/dl detected 24 hours after delivery were included. Total Sample size obtained was 63. Iron Sucrose (IS) group included 21 postpartum women and Ferric Carboxy Maltose (FCM) group included 42 postpartum women in the ratio of 1:2. Randomisation was done by computerized random number generation method. Postpartum women who fulfills the inclusion criteria were included in the study after obtaining their informed consent. The demographic profile and baseline clinical data such as age, parity, SES, educational status, presence of antenatal anaemia and mode of delivery was compared between both the groups. Iron requirement was calculated by GANZONI FORMULA and transfused intravenously. No test dose required in both the drugs. Pretransfusion vitals documented and patients were monitored for any adverse reactions such as pain, itching, rash, headache,

dizziness, nausea and vomiting post transfusion. Baseline values of Haemoglobin, ferritin, MCV, MCHC, PCV and MCH were noted and repeated at the end of 4 weeks and 12 weeks of therapy. The observed values were compared and analysed.

RESULT:

The improvement in Haemoglobin, ferritin, MCV, MCHC, PCV and MCH was better and more rapid with ferric carboxy maltose than iron sucrose and it was found to be statistically significant. Also, the use of high single dose of FCM reduced the number of infusions, enabling the possibility of cost reductions compared to multiple administrations. FCM lacks dextran and less immunogenic, so adverse reactions are also low. The occurrence of adverse reactions in FCM group was not significant compared to iron sucrose ($p=0.54$). The overall satisfaction reported by the postpartum patients was better as they received the drug with minimum hospital stay in a single dose.

CONCLUSION:

The ability to deliver a high dose of iron within a short time, with single prick and less adverse effects make FCM suitable for patients requiring quicker restoration of iron stores in postpartum period and can be recommended for anaemic postpartum women.

KEYWORDS:

Ferric carboxy maltose, Iron sucrose, Postpartum anaemia, Haemoglobin, Serum Ferritin, Iron deficiency.

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INTRODUCTION

INTRODUCTION

Anaemia is defined as decreasing oxygen carrying capacity of blood. The problem of anaemia during antepartum and postpartum is far more prevalent in developing countries than in western societies. [1] As per WHO, anaemia affects up to one-quarter of the global population, around 62 billion people.[2]

The postpartum period, the period beginning just after childbirth up to the subsequent 6 weeks, serves as a time to restore iron lost during pregnancy and delivery. The prevalence of IDA in postpartum women is 10-30% in developed countries and 50-80% in developing countries. [3]

Postpartum anaemia needs a major concern since it accounts for 20% of maternal deaths worldwide and 36% maternal deaths in India. [4,5] Nutrition Surveillance System estimated around 29.8% of non-anaemic antepartum women became anaemic after delivery.[6] It is mostly continuum of antepartum anaemia or could be precipitated by postpartum haemorrhage. The most common type of anaemia in pregnancy and postpartum period is iron deficiency anaemia.

The iron requirements doubles during third trimester and postpartum than in early pregnancy due to increased requirement for the growing foetus and anticipated blood loss during delivery. [7] Iron rich diet alone is not sufficient for such huge amounts of iron, because of poor bioavailability and decreased absorption. [8] All this makes iron supplementation, a basic necessity in all pregnant and postpartum women. Oral iron is the preferred route of administration for mild to moderate anaemia, but it has its own limitations like gastrointestinal adverse effects like metallic taste, constipation,

vomiting and long course of therapy. Noncompliance with oral iron is common, and even in compliant patients, limited intestinal absorption fails to compensate for the high iron requirement of pregnancy and postpartum period. [9] Also oral iron is often incapable of replenishing severe iron deficits in short time.

Parenteral iron therapy is effective alternative to oral iron. The intramuscular iron formulation is available but complications like pain, skin discolouration, allergic reaction, abscess formation, fever, lymphadenopathy and rarely anaphylaxis limits its use. Iron sucrose (IS) is an II generation compound widely being used all over the world with a good safety profile in pregnancy and postpartum. [10] Main disadvantage of IS is that it cannot be administered more than 600mg per week. Higher dose is associated with the risk of toxicity, thus requires divided doses and frequent visits to the hospital which creates a heavy burden on the hospital resources. [11]

With the challenge of optimizing iron delivery, new intravenous iron complexes have been developed in the last few years. [12] Intravenous Ferric Carboxy maltose (FCM) is a III generation novel iron complex which consists of a ferric hydroxide core stabilized by a carbohydrate shell. FCM is neutral at body pH (5.0 – 7.0) and its unique physiological osmolarity property adds to the advantage of administering maximum dose in a shorter period of time (1000mg over 15 minutes) when compared to other parenteral preparations.[13] It has a very low immunogenic potential and therefore not predisposed to anaphylactic reactions. Properties like ultra-short duration of treatment, better compliance and fewer side effects makes FCM the first-line drug in the management of postpartum iron deficiency anaemia.

There is a paucity of good quality clinical trials concerning the use of FCM in pregnancy as it lacks FDA approval.[14] Even in postpartum anaemia, FCM is not widely used compared to iron sucrose in developing countries like India.

The aim of the present study was to evaluate and compare the efficacy and safety of intravenous Ferric carboxy maltose versus intravenous Iron Sucrose in the treatment of iron deficiency anaemia in postpartum women.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The prevalence of postpartum anaemia is 27 % and a postpartum haemoglobin level less than 8 g/dl is observed in 10 % of women.[1,2] Anaemia results from inadequate dietary intake, parasitic or malaria infection and could be exacerbated by the physiological effects of pregnancy and blood loss at the time of birth. Under corrected antenatal anaemia along with postpartum haemorrhage is the major cause for postpartum anaemia and it is a major cause of maternal morbidity and mortality in poor resource countries. [3–6]

The traditional treatment for postpartum anaemia is oral iron supplementation, while blood transfusion is reserved for more severe cases of anaemia. High doses of oral iron usually cause some side effects including constipation, nausea and gastric irritation, which affect compliance of the postpartum women. Though blood transfusion gives excellent results, it is associated with a high risk of infections particularly with hepatitis B and C and human immunodeficiency virus and serious transfusion reactions. In such a scenario, intravenous iron has been considered as an alternative.

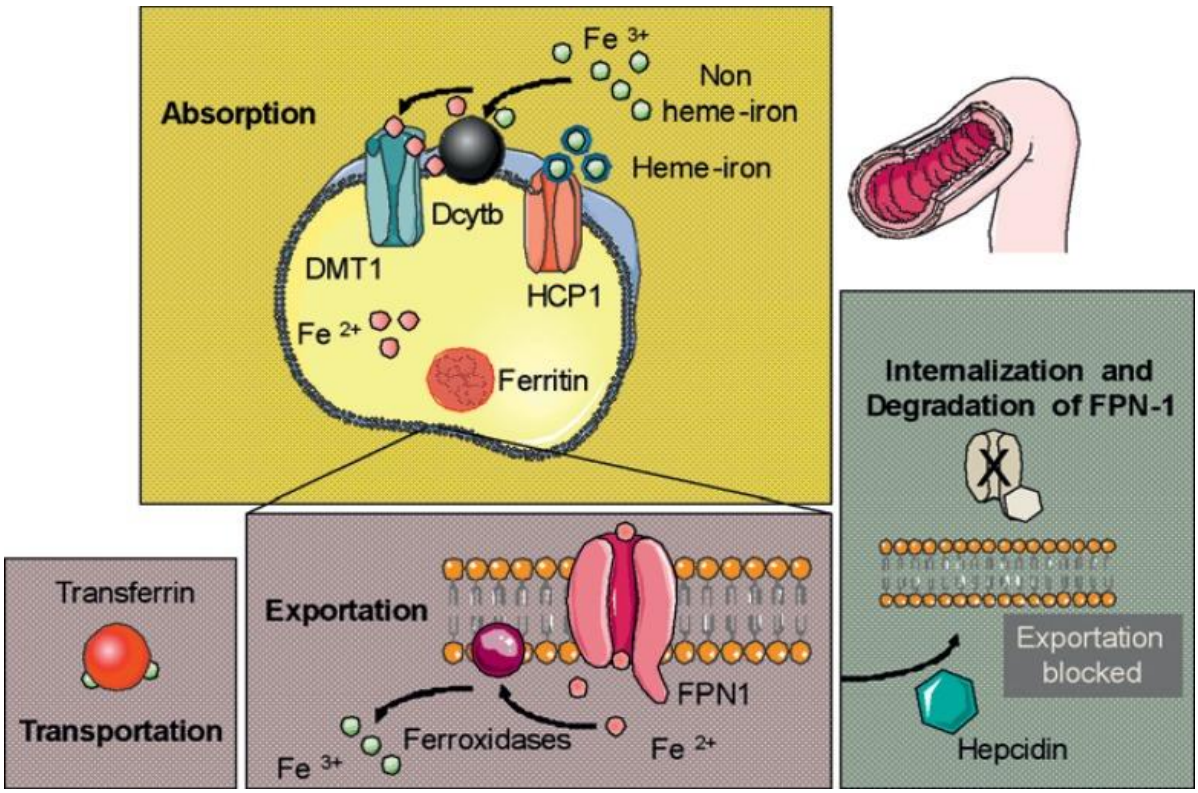
PATHOPHYSIOLOGY OF IRON DEFICIENCY IN ANAEMIA

The total body iron content is around 3–4 g, which is maintained by continuous recycling of iron from the senescent erythrocytes by splenic macrophages.[15] Senescent erythrocytes supplies around 20–25 mg/day of iron needed for bone marrow haematopoiesis.

Iron absorption is the result of complex mechanisms that takes place in the upper parts of the gastro intestinal (GI) tract, notably in the duodenum and the proximal

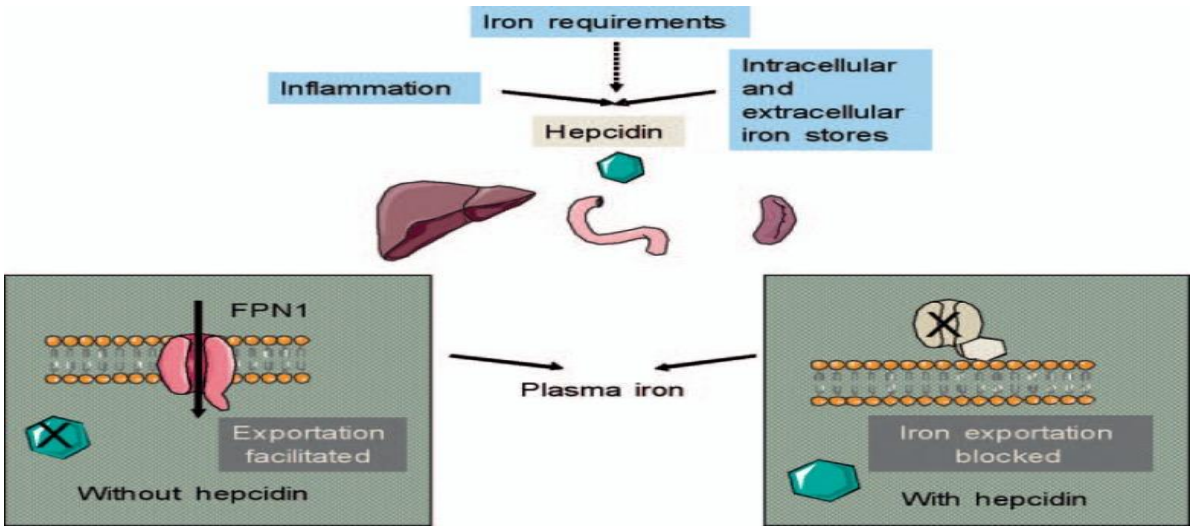
jejunum.[16] Both the heme and nonheme-iron are absorbed by specific pathways, including divalent metal transporter-1 (DMT-1) and heme carrier protein (HCP1), in association with the ferrireductase and duodenal cytochrome B (Dcytb) (figure1). Non-heme iron is present in various storage proteins, including ferritin, whereas heminic iron is present in hemoproteins such as myoglobin or Hb. At acidic pH in the stomach, heme is dissociated from hemoproteins, whereas non-heme iron stabilizes in its reduced form (Fe^{2+}).[17] Ascorbic acid and other acidic components derived from the diet can increase iron absorption. The metal is exported by protein ferroportin (FPN1) and transported into blood by transferrin. Within the cell, iron can be stored within the ferritin molecule.

Figure 1: Absorption of iron in GI tract



Hepcidin is a 25 amino acid peptide hormone, mainly produced by hepatocytes. The hepcidin peptide is encoded by the *HAMP* gene [18] which codes for the precursor protein pro-hepcidin which then is cleaved into the active hepcidin. Hypoxia, endocrine, metabolic and inflammatory processes (figure 2) modulate hepcidin biosynthesis which in turn regulates the availability of iron to erythropoiesis.

Figure 2: Key role of hepcidin in iron metabolism

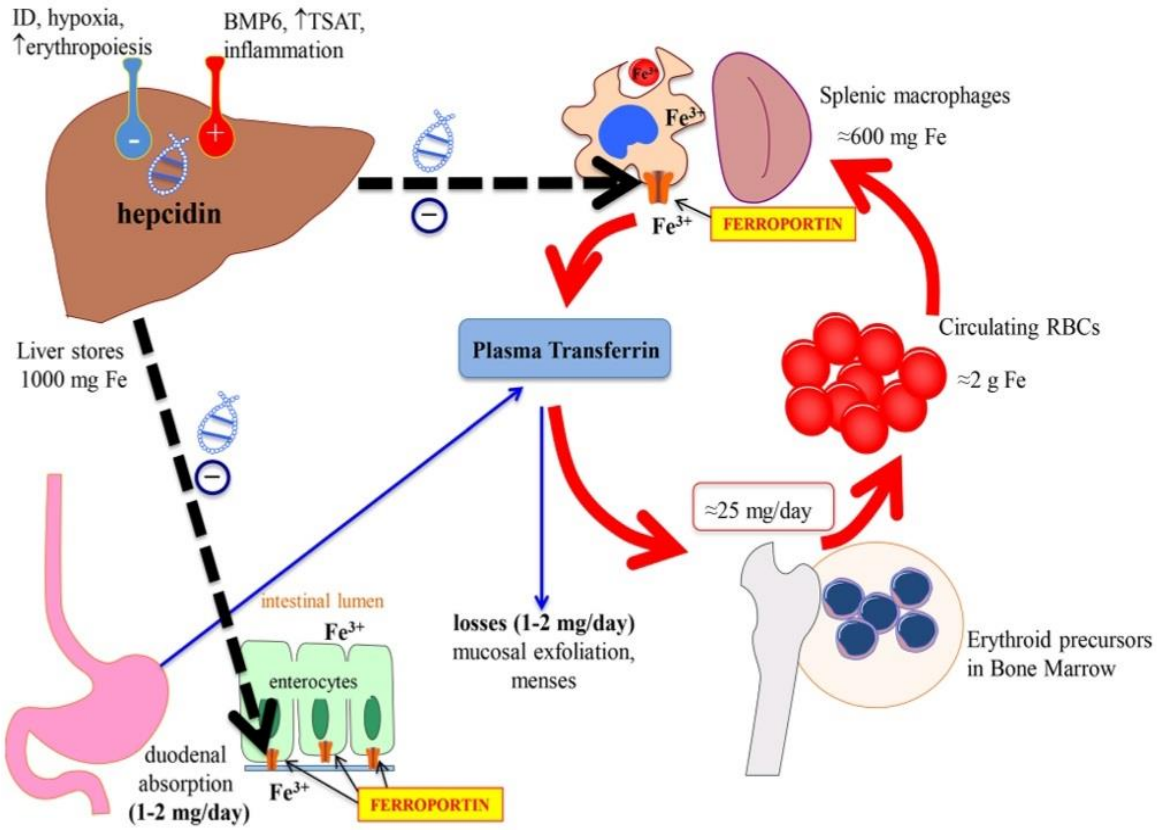


Ferroportin is a multidomain transmembrane protein. It is highly expressed in cells critical for iron handling like duodenal enterocytes, splenic red pulp macrophages and hepatocytes. In presence of hepcidin, ferroportin is internalized and degraded by lysosomes.[19] Thus, iron exportation is blocked. Inversely, in the absence of hepcidin, iron transportation is facilitated. High heme iron intake leads to increased body iron stores which is significantly associated with higher risk to develop type 2 diabetes mellitus.[20] Iron is a strong pro-oxidant and increased level of oxidative stress damages the pancreas by subsequent cell apoptosis causing diabetes. In contrast, total dietary iron, non-heme iron and intake of iron supplements were not associated with type 2

diabetes mellitus. Thus, heme iron which has maximum bioavailability has its own limitations. It emphasizes the use of parenteral iron even in anaemic compliant patients.

Both iron deficiency and iron overload are detrimental and have to be corrected.[21] The saturation of transferrin is a strong indicator of iron overload. Total body iron homeostasis is balanced between unavoidable daily losses (figure 3) and intestinal absorption of dietary iron (1–2 mg/day).

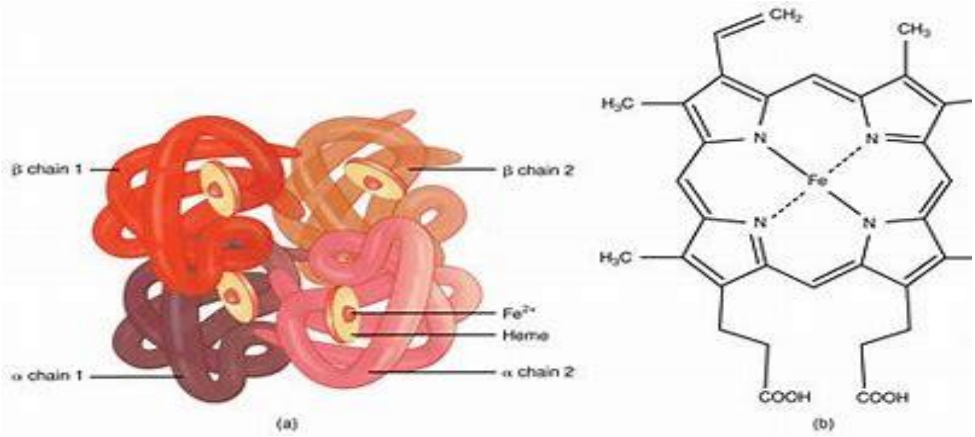
Figure 3: Maintenance of iron homeostasis



ROLE OF IRON IN HAEMOGLOBIN SYNTHESIS

Heme is an iron porphyrin compound. Porphyrin is a tetrapyrrole structure.

Figure 4: Structure of haemoglobin



Ferrous iron occupies the centre of the porphyrin ring and it forms linkages with all the four nitrogens of all the pyrrole rings. It is also linked to the nitrogen of the imidazole ring of histidine present in the globin part. Globin part is made of four polypeptide chains, two identical α-chains and two identical β-chains in normal adult haemoglobin (figure 4). Each chain contains a "heme" in the so-called 'heme pocket'. So one Hb molecule carries four heme units.

Hb molecule contains hydrophobic amino acids inside and hydrophilic ones on the surface. Heme pockets of α-subunits are of just adequate size to give entry to an oxygen molecule. Entry of oxygen into heme pockets of β-subunits is blocked by a valine residue. Varieties of normal human Hb are

- **Hb-A1** (two α-chains and β-chains)
- **Hb F** (two α-chains and ¥ chains)
- **Hb-A2** (two α-chains and delta-chains)

- **Embryonic Hb** (two α-chains and €-chains)
- **Hb-A3** (Altered from Hb-A found in old red cells)
- **HbA1C** (Glycosylated Hb, present in a concentration of 3 to 5% of total Hb). In diabetes mellitus, it is increased to 6 to 15%.

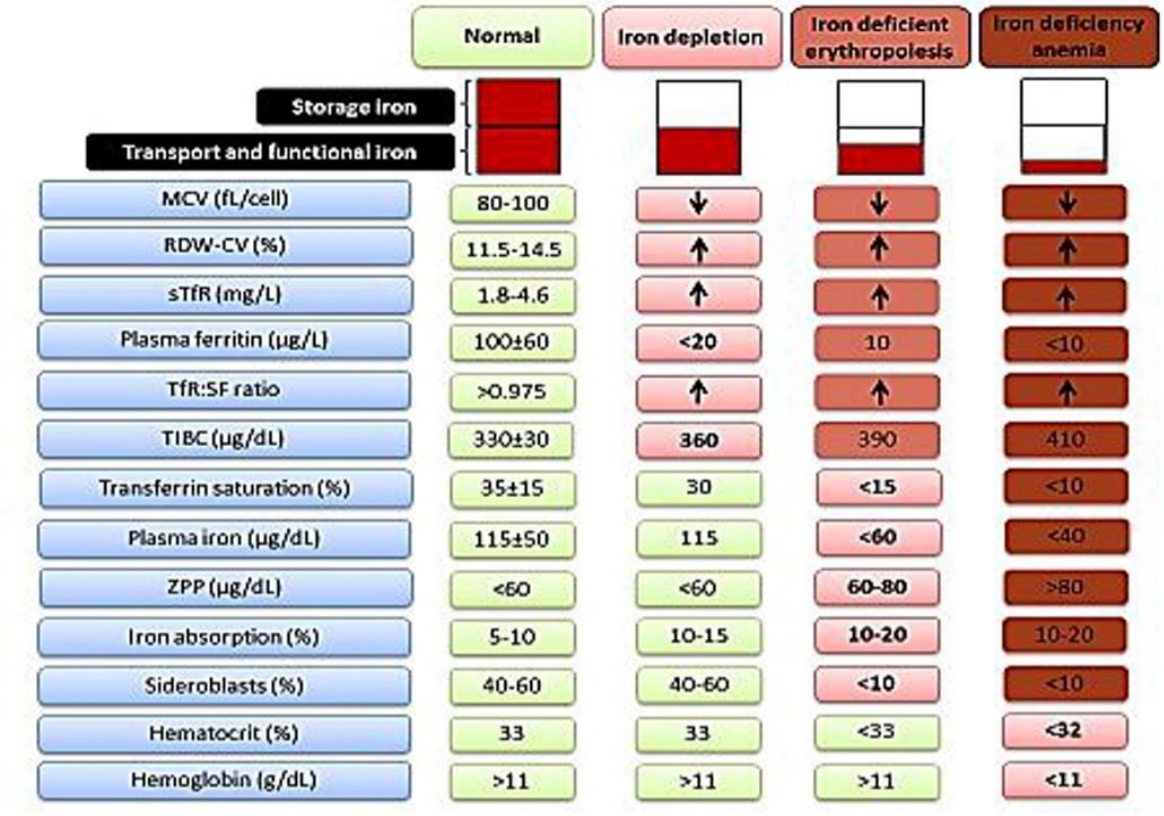
All immature red cells in reticulocyte stage are able to take up iron, while mature erythrocytes do not. At the time when the nucleus disappears from the cell, heme synthesis is nearly complete. [22] The iron which is taken up by the developing red cell is either converted to heme, temporarily stored or remains permanently as a non-heme fraction within the RBC. The developing red cell with nucleus is called sideroblasts and without nucleus is called siderocytes.[23]

STAGES OF IRON DEFICIENCY ANAEMIA

There are three stages of development of iron deficiency anaemia [24] (figure 5)

1. Storage iron depletion
2. Iron deficient erythropoiesis
3. Iron deficiency anaemia

Figure 5: Stages of iron deficiency anaemia



SIGNS AND SYMPTOMS

Majority of the patients of IDA presents with tiredness, weakness sometimes passing worms in stool. Iron is required for normal body homeostasis. Normal pinkish appearance of the eyelids, tongue, nail beds, and palm is due to sufficient iron content in body. Severe iron deficient patients may have alopecia, atrophy of lingual papillae or dry mouth due to reduced salivation. [25, 26] These changes were caused by result of a reduction of iron-containing enzymes in the epithelia and the gastrointestinal tract. The restless leg syndrome might be a striking neurological sequalae prevalent in pregnancy.[27] Pica, the eating disorder in which there is an appealing desire to lick or eat non-food items such as gypsum, chalk, soil, ice (pagophagia) or paper, is commonly

prevalent in pregnant women.[28, 29] Pagophagia (intense desire to eat ice) is quite specific to iron deficiency and responds quickly to treatment.

Plummer-Vinson syndrome (PVS) or Paterson-Brown-Kelly syndrome. [30] Is a rare condition characterized by the classic triad of dysphagia, iron-deficiency anaemia and oesophageal web. Although genetic predispositions, immune dysregulation and several other mechanisms have been postulated, iron deficiency appears to consistently playing an important role. The iron deficiency induces iron-dependent enzyme dysfunction, leading to oxidative stress and DNA damages in the epithelia of the oesophageal mucosa. Repeated injury to epithelia due to iron deficiency leads to atrophy of mucosa and degradation of pharyngeal muscles, leading to the development of oesophageal webs. Elemental iron in the range of 150 to 200 mg is generally required for the correction of iron deficiency anaemia. Dysphagia in many patients resolves with just iron supplementation.

LABORATORY TEST

There are four groups of tests available for assessment of IDA [31] as follows,

1. Hb, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), red cell distribution width (RDW), reticulocyte Hb content, percentage of hypochromic cells, red cell size factor and low Hb density,
2. Direct measurement of iron stores in the body through assessment of serum iron, total iron binding capacity (TIBC), percentage saturation, serum ferritin, bone marrow biopsy,

3. Assessment of heme iron form through assessment of free erythrocyte protoporphyrin (FEP),
4. Assessment of iron uptake is performed by measurement of the soluble serum transferrin receptor (sTfR).

Iron deficiency anaemia is typically characterized by microcytic red blood cells. Other conditions which cause microcytic RBCs include anaemia of chronic disorders, beta-thalassemia and sideroblastic anaemia.[32] The iron marker tests which are performed to differentiate the causes of microcytic anaemia are shown in the table 1 below.[33-35]

Table 1: Differential diagnosis of microcytic hypochromic anaemia

Indicator	Iron deficiency anaemia	Beta thalassemia	Sideroblastic anaemia	Acute chronic inflammation
Haemoglobin	Decreased	Normal or decreased	-	Decreased
Ferritin	Decreased	Normal Increased	Normal or Increased	Normal or Increased
Serum iron	Decreased	Normal or increased	Normal or Increased	Normal or Decreased
Total iron binding capacity	Increased	Normal	Normal	Slightly decreased
Transferrin saturation	Decreased	Normal to increased	Normal to decreased	Normal to slightly Decreased
Serum Transferrin	Increased in severe IDA	>100 mg/L	-	Normal
FEP	Increased	Normal	-	Increased
MCV	Decreased	Decreased	Normal	Normal or decreased
RDW	Increased	Normal to increased	Increased	Normal
Reticulocytes	Decreased	-	-	Normal or decreased

Mentzer index (MCV/ Total RBC count) has been shown as the most reliable index with high sensitivity to differentiate between thalassemia trait and IDA. The index <13 suggests patient has the thalassemia trait. The index >13 suggests patient has iron deficiency anaemia.[36]

Serum ferritin is a sensitive marker to detect IDA in pregnant women. In pregnant women with adequate iron stores, serum ferritin initially rises and later a gradual fall is seen by 32 weeks (due to haemodilution), followed by a slight rise in the third trimester.

Fall in the serum concentration of serum ferritin below 15 μg/L indicates depletion of iron stores in pregnancy.[37] Treatment is indicated when the concentration falls below 30 μg/L which implies early stage of iron depletion.

The salient haematological changes in pregnancy are

- Decrease in Haemoglobin and haematocrit
- Increase in White cell count
- Decrease in Platelets
- Increase in Fibrinogen, Factors V, VII VIII, X, XII and Von Willebrand Factor
- Antithrombin III and protein C remains the same
- Decrease in Protein S and plasminogen activator inhibitor
- Total blood volume increases around 1.5 litres, mainly to supply the demands of the new vascular bed, growth of the foetus and to compensate for blood loss occurring at delivery.[38]

Haematological changes in puerperium:

The haematocrit may initially drop because of blood loss associated with delivery but tends to rise again. The plasma volume will decrease due to diuresis and haemoconcentration. The haematocrit values will return to normal in 3-5 days postpartum as plasma volume starts increasing.

The discrepancy seen in haemoglobin values in the postpartum period is due to the variability in the plasma volume. Studies done to evaluate the values of haemoglobin in the postpartum period indicate that it takes at least 4-6 months to restore the pregnancy-induced fall in Hb to non-pregnant state.[39]

IRON REQUIREMENT IN PREGNANCY

The total iron requirement for an average sized pregnant woman is approximately 1000 mg throughout the pregnancy.[40]

Considering the daily needs, trimester wise iron requirement is

- 0.8 mg of iron in the first trimester,
- 4 and 5 mg every day during the second trimester
- 6 mg every day in the third trimester.

It has been stated that only 15% of iron is absorbed form the daily diet. This amount of dietary iron suffices for the daily requirements of a non-pregnant woman, and not enough for the requirement of large iron stores in pregnancy.[41]

Even with recommended optimal diet in pregnancy, the amounts of iron being absorbed is lesser especially in later part of the pregnancy.[42] Also the need increases

during mid and later part of pregnancy and during delivery due to increased demand by growing foetus and labour process per se. So iron supplementation becomes necessary in pregnancy and also in postpartum period

Table 2: WHO recommendation for anaemia detection in pregnancy[43]

PREGNANCY	NORMAL(g/dl)	MILD(g/dl)	MODERATE(g/d)	SEVERE(g/dl)
1st trimester	11 or higher	10-10.9	7-9.9	Less than 7
2nd trimester	10.5 or higher	10-10.4	7-9.9	Less than 7
3rd trimester	11 or higher	10-10.9	7-9.9	Less than 7

ICMR defines anaemia in pregnancy when Hb values are less than 11 g/dl in all three trimesters. ICMR and WHO recommendation for detection of postpartum anaemia is when Hb value is lesser than 10gm/dl. [44, 45]

SIGNIFICANCE OF POSTPARTUM ANAEMIA CORRECTION

The early detection and correction of postpartum anaemia is essential as it ensures healthy puerperium, better mother baby bonding, build up iron stores, better quality of life, minimizes anaemia in next pregnancy and improves cognitive function in newborn. It also prevents puerperal sepsis, tiredness and breathlessness, postpartum depression, stress, maternal morbidity, prolonged hospital stay and breast feeding difficulties.[46] The most common causes for postpartum anaemia includes postpartum haemorrhage and under corrected antenatal anaemia.

MANAGEMENT OF IRON DEFICIENCY ANAEMIA

Management of IDA can be achieved at two levels, at the individual level or at public health level. Prevention strategies developed by WHO comprise food-based approach, iron supplementation, improvement in health services and sanitation. Other strategies recommended to prevent IDA are control of hookworm, malaria and parasitic infestations.[47]

RECOMMENDATIONS FOR IRON DEFICIENCY ANAEMIA CORRECTION

The Ministry of Health and Family Welfare (MoHFW) recommends all pregnant women should be started with 100 mg of elemental oral iron and 500 µg of folic acid daily (Table 3) at least for 100 days starting from 14-16 weeks of gestation and to be continued for 6 months post-partum.[48]

Prophylactic supplementation of all pregnant women with 60 mg elemental iron and 400 µg folic acid daily, till term in pregnancy and continuation of same dose during 3 months of lactation in countries where prevalence is more than 40% is recommended by WHO.[49] Both guidelines recommend offering standard prophylactic dose after the Hb is normalized for remaining term of pregnancy.[50]

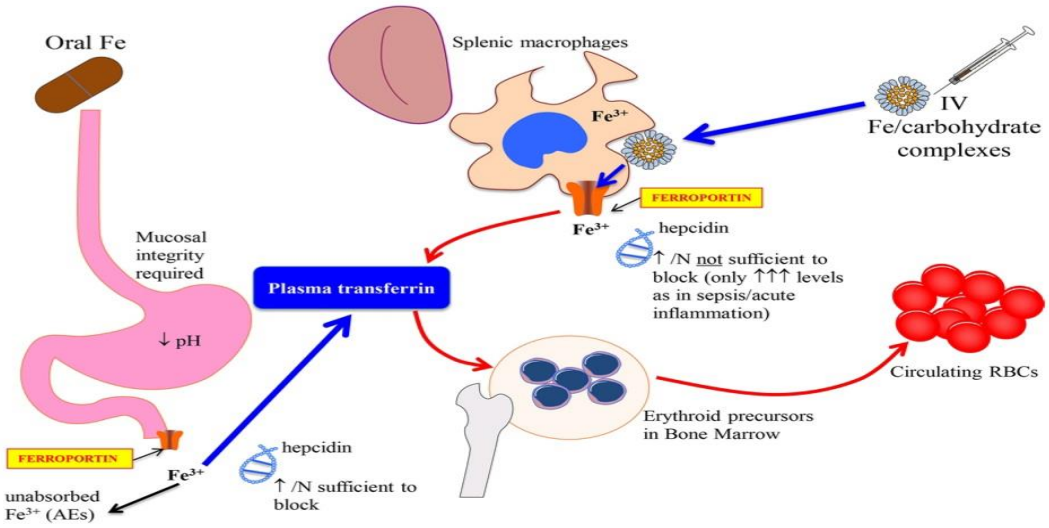
Table 3: Recommendations by WHO and MoHFW for anaemia prophylaxis and treatment

	During pregnancy		**Postpartum**
	Prophylaxis	**Treatment**	
WHO	Daily 60mg iron+400 µg folic acid till term	Daily 120mg iron+400 µg folic acid till term	Daily 60mg iron and 400 µg folic acid-3months
MoHFW	Daily 100mg iron+500 µg folic acid- 6 months	Mild anemia-2 IFA tablets/day-100 days. Moderate anaemia- IM iron therapy +oral folic acid. Severe anaemia-IV iron therapy	Daily 100mg iron+500 µg folic acid- 6 months

PARENTERAL IRON OVER ORAL IRON

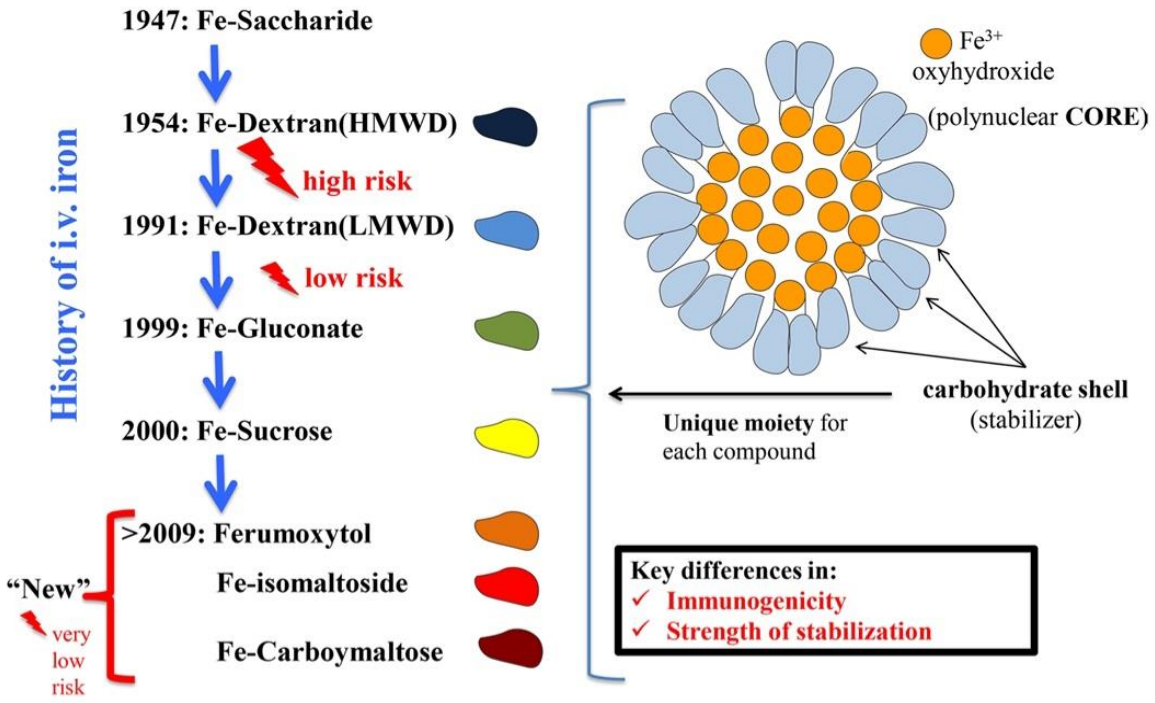
Oral iron therapy is currently the treatment of choice for the majority of patients with iron deficiency anaemia but it has demerits like poor absorption, poor compliance and gastro-intestinal side effects.

Figure 6: Significance of parenteral iron in bypassing iron absorption



Oral iron is incorporated into plasma transferrin after release from the basolateral membrane of intestinal cells. Its absorption is limited by condition causing malabsorption like celiac disease, autoimmune or chronic gastritis. By contrast, parenteral iron compounds are first taken up by macrophages (figure 6) and then released into the bloodstream overcoming the effects of hepcidin so parenteral iron helps in restoring iron stores faster and more effectively than oral iron. [51]

Figure 7: History of iv iron



HISTORY OF PARENTERAL IRON COMPOUNDS

Iron has been used to treat anaemia for more than 300 years.

- The use of oral iron started when treatment of chlorosis was improved with oral iron which was reported by US scientist in late 16TH century.
- In 1832, Pierre Blaud, French scientist introduced ferrous sulphate and reported cure of chlorosis by supplementing with ferrous sulphate. They reported that the iron deficiency was responsible for the pathology of chlorosis. Thus, oral iron therapy became the standard care for anaemia correction.
- First introduced parenteral iron form was Ferric hydroxide solutions which were designed for subcutaneous and intramuscular use in patients with hypochromic anaemia

and the observed haemoglobin rise was proportional to the amount of iron administered. The lack of a carbohydrate shell resulted in immediate iron release and is associated with severe toxic reactions which has limited the use of this therapy.

- In 1947, Nissim introduced iron saccharide for intravenous use and concluded that this form of iron therapy was safer and more suitable for parenteral administration.
- In 1954, Baird and Podmore in UK [52] introduced Imferon (High Molecular Weight Iron Dextran - HMW ID) which is a type of iron saccharide preparation. Advantage of Imferon being the Dextran content which covers the iron oxide core, reduces the release of free iron during infusion which accounts for a decreased incidence of adverse reactions. Bioavailability of iron occurs via the uptake of the iron dextran particles into the reticuloendothelial system with subsequent degradation but large dextran molecule can produce anaphylaxis. HMW ID was the only parenteral iron product which was available until 1990s.(figure7)
- In 1980, the first prospective study on the clinical use of Imferon was conducted in the United States.[53] Four hundred and seventy-one patients with IDA received Imferon in required doses. All the patients responded, but three of them were considered to have had "anaphylactoid" reactions, with symptoms and signs including respiratory arrest, hypotension, purpura, cyanosis, dyspnoea, syncope, wheezing, and hives. There were no recorded deaths in the series.
- The authors concluded that Imferon should be reserved for those conditions in which oral iron could not be used. So HMW ID remained on the pharmacopoeia and was a minor product until the introduction of recombinant human erythropoietin (epoetin alfa) the first erythropoiesis stimulating agent introduced in 1989. Chertow et

al in their retrospective review reported that the exposure to HMW ID was associated with significantly higher risk of adverse events, compared with LMW ID.[54]

- In 1999, ferric gluconate (FG) is a safer alternative to iron dextran due to the lack of dextran envelope. Even though the maximum recommended dose of Ferric gluconate is 125 mg given as a bolus or short infusion, 250 mg has been reported to be given safely over 1 hour. Higher doses are associated with vasoactive reactions which include hypotension, acute onset of diarrhoea and swelling of the extremities.
- In November 2000, iron sucrose (IS) was approved for use by FDA. It lacked a dextran coat and was reported to have a safety profile similar to Ferric gluconate. Both FG or IS does not require test dose before transfusion.

The following parenteral iron generations have been introduced till date

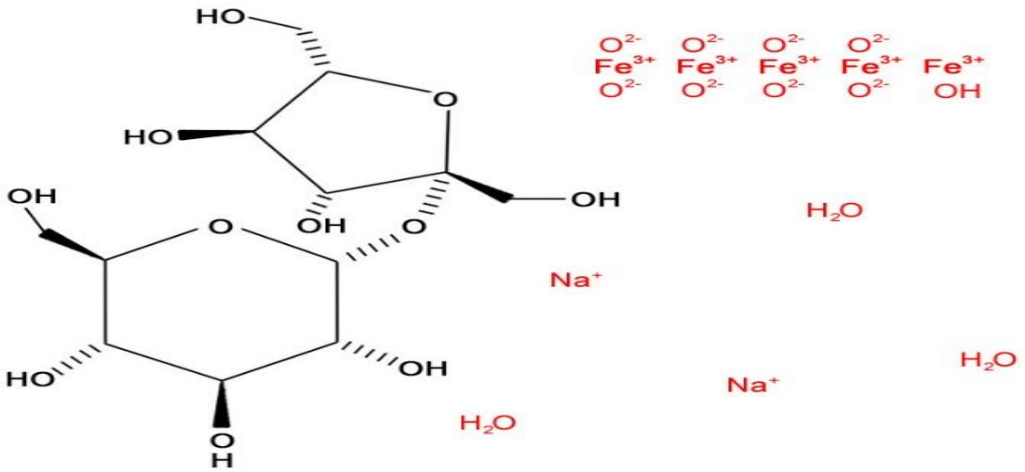
- **I Generation:** Iron dextran use restricted due to severe anaphylactic reaction.
- **II Generation:** Iron sucrose and ferric gluconate are safer but require multiple doses.
- **III Generation:** ferric carboxy maltose, iron isomaltoside and Ferumoxytol.

In this study we compare the efficacy of II generation iron sucrose with III generation ferric carboxy maltose iron therapy in postpartum anaemia correction.

IRON SUCROSE

The chemical formula of iron sucrose is $C_{12}H_{29}Fe_5Na_2O_{23}$. The iron sucrose molecule is a polymer consisting of two main molecules; sucrose (chemical formula $C_{12}H_{22}O_{11}$) and an iron (III) hydroxide ($Na_2Fe_5O_8•3(H_2O)$). (Figure 8)

Figure 8: Molecular structure of iron sucrose



These two components are in solution together, but are not bound to one another. Iron sucrose is a type II complex which is made up of two oxygen atoms bonded to each iron atom.

It is administered intravenously and is indicated only in patient with iron deficiency not responding to oral iron.[22] It is a generally effective drug, with greater than 80% of patients responding to treatment. Iron sucrose has ~20 mg of iron per mL of solution. (figure9) A typical adult patient can safely receive 600 mg of iron sucrose per week, administered in divided doses of 200–300 mg. Administration usually takes around fifteen to thirty minutes.

Figure 9: Ampoule of iron sucrose

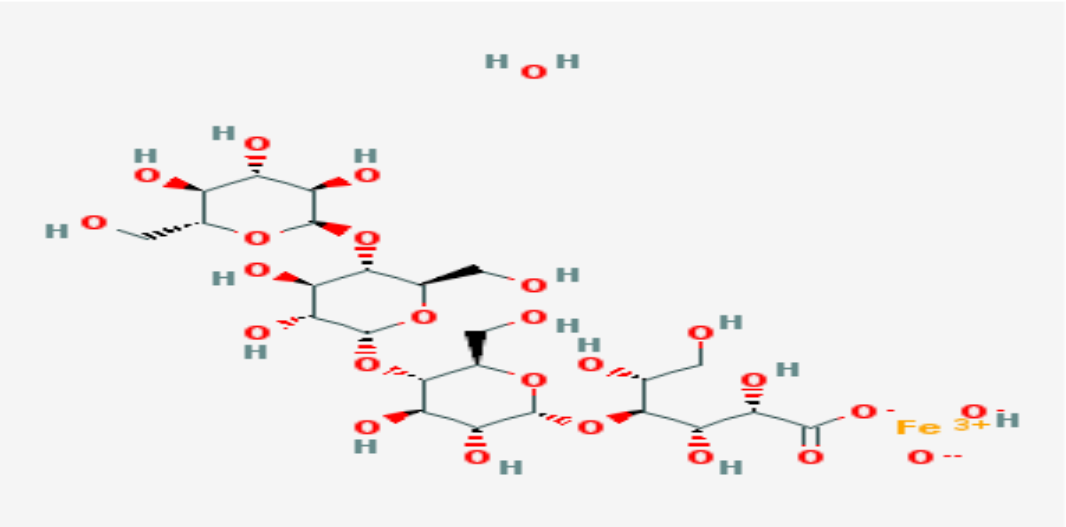
Once iron sucrose has been administered, it is transferred to ferritin, the normal iron storage protein. [36] Then, it is broken down in the liver, spleen, and bone marrow. The iron is then either stored for later use in the body or taken up by plasma. The plasma transfers the iron to haemoglobin, where it is used in red blood cell production.

Less serious symptoms of iron sucrose infusion includes sweetly-scented breath, nausea, chills, eye pain, irritation, swelling, diarrhoea, pain at the injection site, myalgia or weakness.

FERRIC CARBOXY MALTOSE

Ferric carboxy maltose (Ferinject(R)) is a novel iron complex that consists of a ferric hydroxide core stabilized by a carbohydrate shell. (figure10)

Figure 10: Molecular structure of ferric carboxymaltose



It is a non-dextran III generation iron with low immunogenic potential. FCM can be administered as a single large dose (1000mg within 15 minutes) and has better compliance with less hospital stay.

Ferric carboxy maltose is a macromolecular ferric hydroxide carbohydrate complex, which allows for controlled delivery of iron within the cells of the reticuloendothelial system. It then accounts for the subsequent delivery of iron to the iron-binding proteins such as ferritin and transferrin, with minimal risk of release of large amounts of ionic iron in the serum.

Ferric carboxy maltose is rapidly cleared from the circulation and is distributed primarily to the bone marrow (approximately 80%) and also to the liver and spleen.

Commonly reported drug-related adverse events include headache, dizziness, nausea, abdominal pain, constipation, diarrhoea, rash and injection-site reactions which are quickly reversible.[13]

Figure 11: Vial of ferric carboxy maltose

POTENTIAL BENEFITS OF FCM OVER IRON SUCROSE

- Faster increase in Hb status and replenishment of iron stores (serum ferritin)
- Less pricks and less chances of infection
- Less hospital stay
- Better compliance
- Less side effects
- Less economic burden to health resources

STUDIES REGARDING POSTPARTUM ANAEMIA AND ITS TREATMENT

Many trials have been conducted till date to compare the efficacy of oral iron with different parenteral iron therapy among antenatal and postpartum anaemic women. The following studies emphasizes on the role of FCM in the postpartum anaemia correction comparing with other modalities.

David B conducted a randomised trial in 2007 [55] to estimate the efficacy of ferric carboxy maltose with oral iron (Ferrous sulphate) and observed increase in haemoglobin levels by 2 gm/dl within 7 days and 4gm/dl within 2-4 weeks in FCM. The increase in Serum ferritin was better in FCM patients without adverse drug reactions.

A prospective trial conducted by Setu Rathod et al [56] in tertiary care centre of Odisha, compared the safety and efficacy of FCM, IS and oral iron in postpartum anaemia with Hb < 10 g/dl. The mean increase in Hb after 2 weeks was 0.8, 2.4 and 3.2 g/dL and at 6 weeks was 2.1, 3.4 and 4.4 g/dL in oral iron, IS and FCM groups respectively. The mean increase in serum ferritin levels after 2 weeks was 2.5, 193.1, and 307.1 ng/mL and after 6 weeks was 14.2, 64, and 106.7 ng/mL in oral iron, IS and FCM groups, respectively. They concluded that FCM elevates Hb level and restores iron stores faster than IS and oral iron without any severe adverse reactions with increased acceptance among patients who received FCM treatment.

A multicentre randomized controlled trial by Seid et al [57] was conducted among 291 postpartum women of 56 tertiary care centres and reported that ferritin level increase upto 238 ng/ml after 6 weeks of FCM therapy, while the increase in serum

ferritin in oral iron group was only 21ng/ml. They concluded that FCM was safe and well tolerated with superior efficacy compared to oral iron in severe anaemia.

A randomised prospective trial conducted by Pervez [58] in 2018 showed that women receiving FCM had higher haemoglobin concentrations compared to oral iron at postpartum. There was an increased likelihood of skin flushing and a decreased likelihood of constipation and dyspepsia observed in FCM group. The anaphylaxis was observed in 0.6% of participants in FCM group and concluded that FCM could be used as a viable option for postpartum iron deficiency anaemia.

A randomized comparative trial by Breymann et al [59] was conducted to compare safety and efficacy of intravenous FCM with oral ferrous sulphate in the treatment of postpartum IDA. 227 women received FCM of 1000 mg maximum dose (up to 3 weekly doses) and 117 women received oral ferrous sulphate 100 mg twice daily for 6 weeks. They concluded that parenteral FCM was a safe and effective treatment option for postpartum anaemia, with advantages of a shorter treatment period, better compliance, rapid normalization of iron storages and lower incidence of gastrointestinal side effects.

A retrospective study [60] was conducted in 2015 to assess the efficacy and safety of FCM among PPA patients in tertiary care centres. Mean increase in Hb – 2.76± 1.00 g/dl ($p<0.001$) with maximum increase from baseline was observed. Adverse reactions reported were urticaria and rash which were quickly reversible. They concluded that FCM was effective in improving Hb in PPA patients and was well tolerated with least adverse reactions.

Verma et al [61] in their prospective comparative study among 100 postpartum women who were followed at 2, 4, 6 and 12 weeks of iron therapy. In FCM group mean rise of Hb level was 3.95 g/ dl while in IS group mean rise was 3.32 g/dl. In FCM group 100% patients achieved target Hb at 12 weeks after therapy while in IS group 98% patients achieved target Hb at 12 weeks after therapy.

A prospective study conducted by Pfenniger et al [62] among 210 postpartum anaemic women. The safety and efficacy of high dose FCM with IS for the treatment of postpartum anaemia was compared. They reported rapid administration of FCM was as safe as IS in the management of postpartum anaemia despite five times of higher dosage. FCM was as effective as IS in changing Hb levels from the baseline. Women with severe anaemia showed the most effective responsiveness. The single application of FCM showed advantages of lower incidence of adverse effects at the injection site, a shorter treatment period and better patient compliance.

A randomised controlled trial was conducted by Van Wyck et al [63] comparing FCM with oral iron. FCM group achieved a higher and faster rise in Hb upto 3g/dl and they concluded that large-dose FCM administration is effective for the treatment of postpartum anaemia.

A prospective randomized controlled trial was conducted by Rathod et al [64] among 366 postpartum women with Hb<10 g/dl. The efficacy of oral iron, IS and FCM was compared. A significant increase in Hb and serum ferritin level was observed in all three groups, but the increase in FCM group was statistically significant ($p < 0.001$) than IS and oral iron group. The mean increase of Hb in oral iron, IS and FCM after 2

weeks was 0.8, 2.4, and 3.2 g/dL and after 6 weeks was 2.1, 3.4, and 4.4 g/dL respectively. The mean increase in serum ferritin levels after 2 weeks was 2.5, 193.1, and 307.1 and at 6 weeks was 14.2, 164, and 406.7 ng/L among 3 groups. They reported that FCM is highly effective in correcting anaemia and restoring iron stores faster than oral iron and IS in patients with PPA.

Daminneni et al [65] conducted a prospective study in postpartum women with Hb 7-10 g/dl. They compared oral iron with FCM. FCM treated women achieved higher Hb rise of 3.0 g/dL. FCM was better tolerated with complete adherence to treatment when compared to oral ferrous ascorbate.

A prospective follow up study was conducted by Calvet X et al [66] in Barcelona, Spain, among 111day care patients for one year with IS 200mg multiple infusions and 1000mg single dose FCM. They concluded that high doses of FCM reduces the number of infusions, enabling the possibility of cost reductions compared to multiple administrations. Patients were highly compliant as less pricks and lesser incidence of thrombophlebitis seen with FCM.

Khallafallah conducted a comparative follow up study [67] among anaemic antenatal women between oral iron and IS for a period of 32 months in Australia. 79% of women treated with oral iron had below normal ferritin levels whereas only 4.5% of women treated with IV iron had below normal ferritin levels and it was statistically significant ($p < 0.001$). Also they stated that Hb level <11.6g/dl at the time of delivery was found in 29% of women of oral iron group but only in 16% of women of the IV iron group.

In a prospective study conducted by Froessler [68] in 2014 among 65 anaemic pregnant women who received FCM up to 15 mg/kg between 24 and 40 weeks of pregnancy. Treatment effectiveness was assessed by repeat Hb measurements and patients' report of well-being in the postpartum period. They found that increased Hb values were observed till 8 weeks post infusion and postpartum ferritin values were above baseline and confirmed the safe and effective use of FCM in pregnancy.

Garg et al [69] in 2015 conducted a prospective study comparing FCM 1000mg single dose and IS 200mg alternate days 5 doses and reviewed Hb along with adverse drug reactions. They found that mean increase in Hb at 4 weeks was 3.95 g/dL in FCM group and 3.32 g/dL in IS group. The occurrence of adverse reactions were similar between both groups.

A prospective randomized controlled study was conducted by Hol Kkv et al [70] to assess the efficacy and safety of IS vs FCM in postpartum anaemia. 500mg iron was given for mild anemia and 1000mg for moderate anemia. The mean increase in Hb was 2.30 g % with IS and 2.52 g % with FCM therapy. The mean increase in serum ferritin was 37.97 with IS and 38.70 with FCM (p=0.67) in mild anemia patients whereas, 43.65 with IS and 44.40 with FCM (p=0.788) in moderate anemia patients. And concluded that FCM and IS was equally effective in treating postpartum mild and moderate anemia. FCM has good patient satisfaction compared to IS.

Patel et al [71] conducted a randomized trial comparing IS and FCM in pregnancy vs postpartum women. They observed raise on Hb, serum ferritin and occurrence of adverse reactions at 8 days and 15 days of therapy. The mean increase in Hb after 15days of therapy with FCM on pregnant women was 5.2 g/dl and 5.4 g/dl in PPA

women. In FCM group, adverse reactions were observed only in 16.67% of participants and in IS group 40% had adverse reactions. The study showed FCM improved Hb and iron stores more rapidly than IS. And was also safe and effective to blood transfusion in the postpartum period.

A prospective trial was conducted by Mishra [72] about the efficacy and safety of FCM in pregnancy and postpartum period among 200 women. They noticed improvement in Hb from 8.97 g/dl to 11.34 g/dl along with other indices such as PCV, TIBC, SF and SI after 3 weeks of FCM therapy. Patients had minimal adverse effects which were easily reversible. And concluded that FCM should be offered to postpartum women to reduce mortality and morbidity in improving all blood indices.

A prospective cohort study done in New Zealand [73] reviewed the benefits of FCM in 300 postpartum anaemic patients and showed that it was well tolerated with increase in Hb of maximum 3.4 g/dl within 4 weeks of therapy which was statistically significant.

A systemic literature review in Italy was performed by Rognoni C et al [74] from published Randomised controlled trails on the use of ferric carboxy maltose in iron deficiency. Significant improvements in serum ferritin and Hb was seen with FCM compared to ferric gluconate and placebo. All currently available intravenous iron preparations appeared to be safer and effective, but FCM seems to provide a better and quicker correction of Hb and serum ferritin levels in iron-deficient patients.

A prospective trial conducted by Aggarwal et al [75] in 2012 among the postpartum women with Hb< 10 g/dl comparing the efficacy and safety of oral iron, IS and FCM. The mean increase of Hb in oral iron, IS, FCM groups after 2 weeks was 0.8, 2.4, and 3.2 g/dL and after 6 weeks was 2.1, 3.4, and 4.4 g/dL respectively. The mean increase in serum ferritin levels after 2 weeks of therapy was 2.5, 193.1, and 307.1 and after 6 weeks was 14.2, 64, and 106.7 ng/mL in oral iron, IS and FCM groups respectively. Adverse drug reactions were significantly low ($p< 0.001$) in FCM group when compared with other two groups.

A randomized controlled trial was conducted by Singh et al [76] on 200 postpartum patients with anemia and observed that significantly higher number of women achieved Hb >11gm/dl in FCM group. 88 women in FCM group achieved Hb raise of 2 gm compared to only 24women in iron sucrose group after 21 days post therapy.

A prospective trial comparing IS vs FCM was done in 2016 by Joshi et al [77] in postpartum iron deficiency anemia and found that adverse effects were seen in 7.2% of IS group and 3.3% FCM group. Thus, FCM was found to be much safer than IS in postpartum anaemic women.

A similar prospective study was conducted [78] in 2018 among PPA women comparing IS and FCM. They reported that almost all anaemic patients belong to younger reproductive age group. And FCM replenished iron stores faster than iron sucrose in the given time period.

A randomized prospective comparative trial was conducted by Giannoulis et al[79] among 104 anaemic postpartum women who were treated with IS and oral iron. The criteria for the diagnosis of anaemia was Hb<8 g/dl and ferritin <10 µg/dl. Group A consisted of 50 women who received IS a total of 300 mg in 3 days and increase of Hb mean level was 4.6 g/dl and ferritin mean level was 105 mg/L. Group B consisted of 54 women, who received orally 800 mg iron protein succinylate daily for 4 weeks and increase in Hb mean level was 2.3 g/dl and ferritin mean level was 68 mg/L. And concluded that IS seems to be safer and effective in postpartum anaemia correction.

Singh RK conducted a study in 2016 [80] comparing the adverse events of parenteral iron with oral iron. They concluded that parenteral iron helps in restoring iron stores faster and more effectively than oral iron without gastrointestinal side effects like nausea, vomiting, metallic taste, gastritis, diarrhoea and constipation.

Mangione and his associates [81] in their study stated that inflammatory reaction secondary to surgically assisted deliveries leads to sequestration of iron in macrophages and decrease of intestinal absorption. So, administered oral iron is not available for erythropoiesis. To overcome this problem IV iron preparations were used.

A randomized controlled study conducted by Dev SM et al [82] comparing oral iron with parenteral iron among antenatal women. Even though oral iron helped in improving Hb, it could not meet the iron demand in pregnancy in view of increased demand of pregnancy. They finally arrived that parenteral iron supplementation was necessary in all pregnant women because of poor bioavailability of oral iron.

A prospective trial was conducted in 2015 [83] with IS vs oral ferrous sulphate in postpartum women and increase in Hb values were measured at 1st, 15th, 42nd day post infusion. The mean increase of Hb in IS and oral iron at day 1 was 7.62 and 8.50 ($p<0.001$). The achievement of target Hb after 42 days with IS and oral iron was 13.05 and 10.65 ($p<0.001$). The mean increase in ferritin in IS and oral iron (µg/L) at day 1 was 10.95 and 15.55 ($p<0.001$) and at day 42 was 119.56 and 71.04 ($p<0.001$). And concluded that IS was safer, well tolerated and help in replenishment of iron stores and Hb than oral iron.

A randomized trial was conducted by Vijayalaksmi et al [84] among 120 postpartum anaemic women comparing IS with ferrous sulphate. The mean increase in Hb in IS group after 28 days of therapy was 11.1g/dl. The mean increase in Hb after 28 days in ferrous sulphate group was 10.6g/dl. IS showed significant increase in Hb level within one month of postpartum iron therapy.

Jain conducted a study at Jharkhand [85] with IS and ferrous fumarate for Hb < 8 g/dl in postpartum anaemic women and found that mean rise in Hb in IS after 14 days was 2.4 g/dL. The mean increase in Hb in ferrous fumarate after 14 days was 1.2 g/dL. And concluded that Iron Sucrose is effective, well tolerated than ferrous fumarate in postpartum anemia.

A prospective randomized trial [86] was conducted among 200 postpartum anaemic women. IS group received 200mg thrice per week and ferrous sulphate group 200mg thrice daily for 28 days. They found that mean increase in Hb in ferrous sulphate group was from 7.43 to 8.2 g/dL. The mean increase in Hb in IS group was from 7.27 to 8.5 g/dL. The mean rise in hematocrit in ferrous sulphate group was 0.72% and mean

rise in hematocrit in IS group was 0.93% and concluded that iron sucrose was well tolerated, safe and effective drug.

Perwunsnyk and his colleagues [87] in their study stated that new iron–sucrose complex was very safe with hardly any adverse effects. Accumulation of IS in parenchyma of organs is less compared with iron dextran or iron gluconate and incorporation into the bone marrow for erythropoiesis is considerably faster.

Broche et al and his associates [88] did a retrospective study among severely anaemic postpartum women with IS and ferrous fumarate therapy. All patients who had a hemoglobin of less than 8 g/dL within 48 hours of delivery were included and divided into two groups. They found that mean increase in Hb of 1.9 g/dl was obtained in IS group participants within 7 days and 3.1 g/dl within 14 days without any serious adverse effect. This study concluded that blood transfusion could be avoided in young women, even though blood transfusion is indicated in the case of emergency.

A prospective randomized controlled trial [89] was conducted to compare IS with oral iron. Forty-four women with haemoglobin (Hb) <9 g/dl and ferritin of <15 microgram/l detected 24-48 hours postdelivery were included in the study. The mean increase in Hb level from baseline at day 5 was 2.5 g/dl in the IS group and 0.7 g/dl in the oral group and ferritin levels rose rapidly and remained significantly higher in IS group than oral iron. They concluded that IS increased the Hb level more rapidly than oral ferrous sulphate in women with postpartum IDA. It replenished iron stores more rapidly.

Danielson et al [90] in this study compared the effectiveness of IS vs oral ferrous fumarate in postpartum anemia correction. On day 14, the increase in mean Hb level in IS group was 2.4 g/dl in comparison to 1.2 g/dl in oral group. They found that high tolerance was partly because of lower allergenic effect of sucrose and very slow release of elementary iron from the complex.

The modern aspects of iron deficiency anemia correction was evaluated by Breymann [91] and his associates in Zurich. Indications for the use of iron sucrose complex in the study were preexisting (moderate–severe) anaemia, no effect of oral iron therapy, side effects of oral iron, refusal of blood transfusion, limited time until delivery and coexisting risk factors (eg, bowel disease, renal disease). Therefore, they concluded that IS, alone or in combination with recombinant human erythropoietin (rHuEPO) therapy, has been considered as an alternative in the management of iron deficiency.

A randomized comparative prospective clinical study in 2008 was conducted by Westad s et al [92] among 100 postpartum anaemic women with Hb – 6 to 8 g/dl after 24 hours postpartum. Mean rise in Hb level was 4.1 gm% with IS compared to 3.4 gm% with oral iron on day 30 of treatment with p value < 0.0001. Mean rise in PCV level was 12.22% with IS and 10.46% with oral iron on day 30. And concluded that IS increased the Hb level more rapidly than oral ferrous sulphate in postpartum anemia without any serious side effects.

A randomized trial was conducted by Crichton R and his colleagues [93] in Germany and they concluded that intra venous iron supplementation was highly effective in treating iron deficiency anemia in postpartum period, resulting in a much

rapid resolution of iron deficiency anemia. It had minimal adverse effects and good compliance.

A randomized prospective study was conducted by Bayoumeu [94] in Europe including 50 patients with hemoglobin levels between 8 and 10 g/dL and a ferritin value of <50 μg/L. An increase in hemoglobin was observed, rising from 9.6 g/dL to 11.11g/dL on day 30 in the IS group and from 9.7 g/dL to 11g/dL on day 30 in the oral iron group. The author concluded that iron sucrose appeared to be a treatment of choice without serious adverse effects and indicated in correction of anemia in pregnancy or iron stores depletion.

Gozzard et al [95] commented on conditions requiring high dose intravenous iron infusion and reviewed newer treatment options. FERUMOXYTOL can be administered in a maximum dose of 510 mg within one minute as a single dose, however the compound is contraindicated in patients with chronic kidney disease due to its toxicity. The next compound introduced is FERRIC CARBOXYMALTOSE which can be rapidly administered in doses of 15 mg/kg body weight, up to maximum of 1000 mg even without test dose. The latest introduction is IRON ISOMALTOSIDE with higher dose up to 20 mg/kg body weight. This will allow the clinicians to achieve high-dose repletion with single administration.

AIM AND OBJECTIVE

AIM AND OBJECTIVE

AIM OF THE STUDY:

To determine the efficacy and safety of intravenous ferric carboxy maltose versus intravenous iron sucrose in postpartum anaemia correction.

OBJECTIVE OF THE STUDY:

1. To compare the efficacy of intravenous ferric carboxy maltose versus intravenous iron sucrose in postpartum anaemia correction.
2. To compare the raise in haemoglobin and other indices such as serum ferritin, MCV, PCV, MCHC and MCH between the two groups.
3. To compare the adverse reactions between the two groups.

METHODOLOGY

MATERIALS AND METHODOLOGY

STUDY DESIGN:

This is a prospective comparative randomised interventional clinical Trial.

DURATION OF THE STUDY:

November 2019 – April 2021

STUDY PLACE:

This study was conducted in Department of Obstetrics &Gynaecology, ESIC Medical College & PGIMSR, K.K. Nagar, Chennai – 600 078

SAMPLE SIZE CALCULATION:

From the reference of JOSHI et al [65] with the prevalence of PPA of about 37%, sample size was obtained using the below mentioned formula considering 95% confidence interval, 80% power and allocation ratio of 1:2.

$$N = \sigma_p^2(Z_{1-\alpha} + Z_{1-\beta})^2 / (|\mu_A-\mu_B|-d)^2$$

Where,

d = Equivalent limit of the difference in means = 3

$|\mu_A-\mu_B|$ = Expected absolute difference in means = 2

σ_p = Standard Deviation(pooled)

$(\sigma_1^2+ \sigma_2^2)/2$ = 1.5

$1 - \alpha$ = 95% Confidence level

$1-\beta$ = 80% Power

Allocation ratio = 1:2 (A: B = 21:42)

Sample Size: The obtained sample size was 63 with 1: 2 allocation ratio.

Group A (IS group) – consisting 21 postpartum women

Group B (FCM group) – consisting 42 postpartum women

Inclusion criteria:

- ✓ 18-40 years old postpartum women delivered either by vaginal or caesarean delivery with Haemoglobin between 7 to 9 g/dl which was detected 24 hours after delivery.

Exclusion criteria:

Postpartum women with

- ✓ History of allergy to iron compound
- ✓ Anaemia due to other cause (B12/folate)
- ✓ CKD/ bronchial asthma/heart disease
- ✓ Hematologic disorder
- ✓ Recent blood transfusion/erythropoietin injection
- ✓ Hepatitis/HIV

METHODOLOGY:

63 eligible postpartum women with Hb between 7to9 g/dl were included after obtaining their informed consent. Iron requirement was calculated by GANZONI FORMULA and transfused intravenously among randomised participants of FCM and IS group. No test dose was required for both drugs. The demographic profile and clinical details such as age, parity, SES, presence of antenatal anaemia and mode of delivery

were noted and was compared between both the groups. Pretransfusion vitals documented and patients were monitored for any adverse reactions such as pain, itching, rash, headache, dizziness, nausea and vomiting post transfusion. Baseline values of Haemoglobin, ferritin, MCV, MCHC, PCV and MCH were noted and repeated at the end of 4 weeks and 12 weeks of therapy. The observed values were compared and analysed between both groups.

Randomization was done using computerized random number generator method.

- Random allocation done with opaque & sealed envelope.
- Informed consent obtained from the participants explaining the maintenance of confidentiality of the participants details. Anonymity maintained throughout the study. The patients were asked to select sealed envelope from a folder which indicated the drug to be infused.
- Iron sucrose group (Group A) was coded by numbers (A1, A2, A3,…..A21).
- FCM group (Group B) was coded by numbers (B1, B2, B3,…..B42).
- Since drug administration involved active participation of postpartum women, the participants and investigator could not be blinded after concealed allocation. Only the laboratory personnel were blinded.

DRUG ADMINISTRATION:

The target haemoglobin was taken as 11 g/dl. Iron requirement was calculated by using GANZONI's formula.

2.4 x Body weight in kg x (Target Hb – Actual Hb) + 500g

Where 500grams added for replenishment of iron stores.

IS and FCM was given intravenously and no test dose required for both. The calculated dose was rounded up to nearest multiple of 100 for each individual.

Iron sucrose: 200mg of IS (2 ampoules of 5 ml) diluted in 100ml 0.9% normal saline transfused over 15 to 20 minutes and same dose was repeated on alternate days till the calculated dose was completed.

Ferric carboxy maltose: The required calculated dose of FCM up to a maximum of 1000 mg / day (2 ampoules of 10 ml) diluted in 250ml of 0.9% NS was given over 15 minutes and the remaining dose of iron was given a week later.

ADVERSE EFFECTS MONITORED:

Patient vitals were recorded and were monitored for one hour post infusion for the development of any side effects like

- Pain at the injection site
- Itching and rash
- Abdominal pain, palpitations
- Headache, dizziness
- Nausea, vomiting

Baseline complete hemogram (Hb, MCV, MCHC, PCV, MCH) and serum ferritin were recorded and repeated after 4weeks and 12 weeks of IS and FCM therapy.

STATISTICAL ANALYSIS:

Data entry was made in the Microsoft Excel software and analysis was done with SPSS Version 20. The descriptive statistics presented for quantitative and qualitative data. Continuous variables were presented in the form of mean and standard deviation (SD). Qualitative data were presented in the form of frequency and percentage. To test the difference between two groups (IS and FCM); an independent t test was applied. The Chi square test was applied to find the association of demographical variables between two groups. The significance level was considered at p value <=0.05.

OBSERVATION AND ANALYSIS

OBSERVATION AND ANALYSIS

The results from present study were encouraging with satisfactory rise in Hb and serum ferritin, good patient satisfaction, minimal side effects and easy administration with FCM compared to IS.

Table 4: Distribution of the Study Participants

Group	Frequency	Percentage
Group A - Intravenous iron sucrose therapy	21	33.3
Group B - Intravenous ferric carboxy-maltose therapy	42	66.7

The study participants were randomly allocated into two groups in the ratio of 1:2 = IS: FCM.

Figure 12

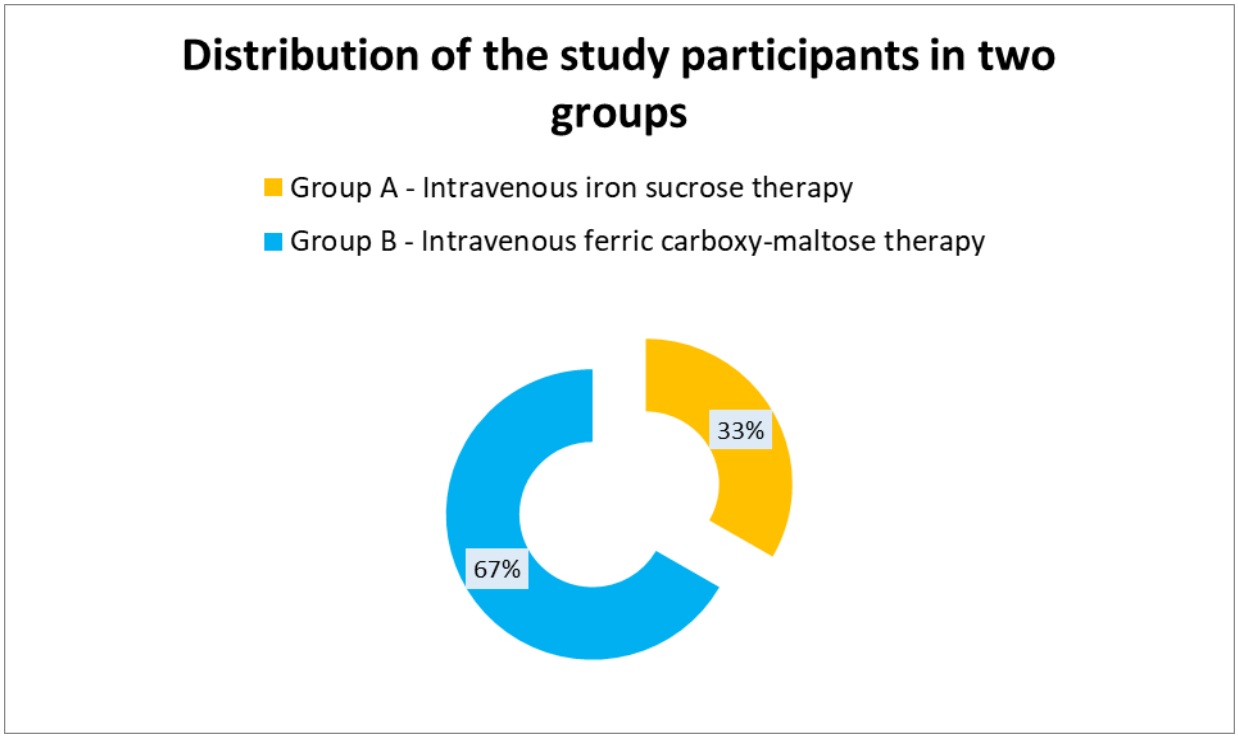


Table 5: Age wise comparison between IS group and FCM group

Age Category	Group A - Intravenous iron sucrose therapy		Group B - Intravenous ferric carboxy-maltose therapy		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
18-25	7	33.3	12	28.6	0.603
26-30	7	33.3	21	50.0	
31-35	5	23.8	7	16.7	
36-40	2	9.5	2	4.8	
Total	**21**	**100.0**	**42**	**100.0**	

Table 5 shows comparison of age between group A (IS) and group B (FCM) participants. Majority of the study participants in both the groups were aged between 25 to 30 years of age. Two participants each in both the groups were aged between 36-40 years. When statistically analysed age group was comparable between both the groups (p=0.603).

Figure 13

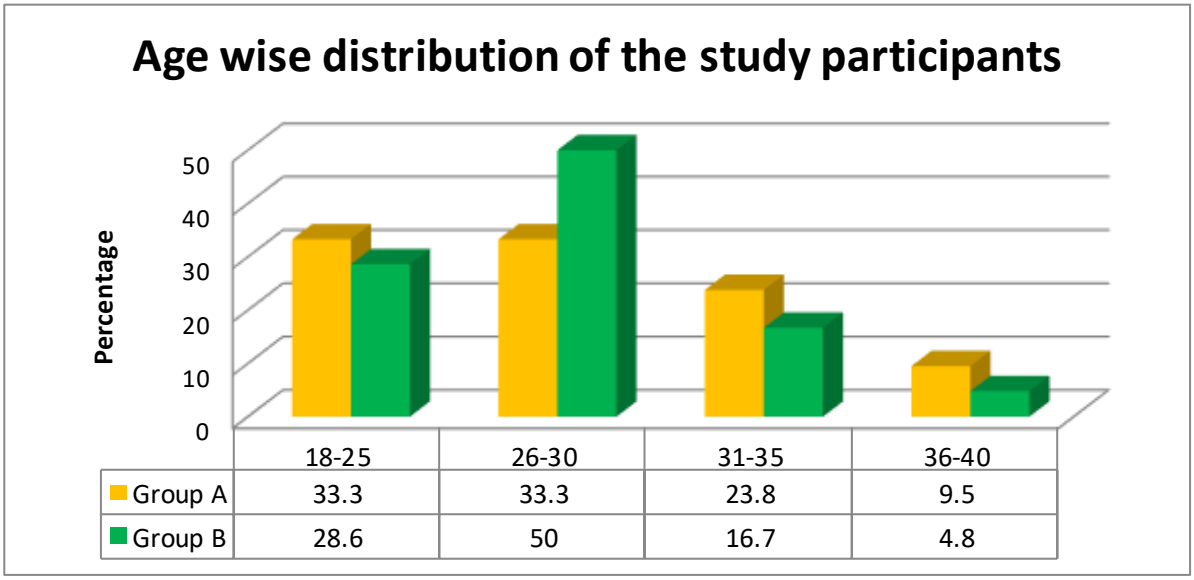


Table 6: Educational status comparison between IS group and FCM group

Education	Group A		Group B		pvalue(unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
Primary	2	9.5	4	9.5	0.974
High School	6	28.6	11	26.2	
Higher Secondary	8	38.1	19	45.2	
Graduate	4	19.0	7	16.7	
Illiterate	1	4.8	1	2.4	
Total	**21**	**100.0**	**42**	**100.0**	

In Iron sucrose group, 4.8% were illiterate and in FCM group 2.4% were illiterate. Majority had completed primary and higher secondary level of education. 4(19%) participants in IS group were graduates compared to 7(16.7%) participants in FCM group. There was no significant difference between the two groups with respect to education. (Table 6)

Figure 14

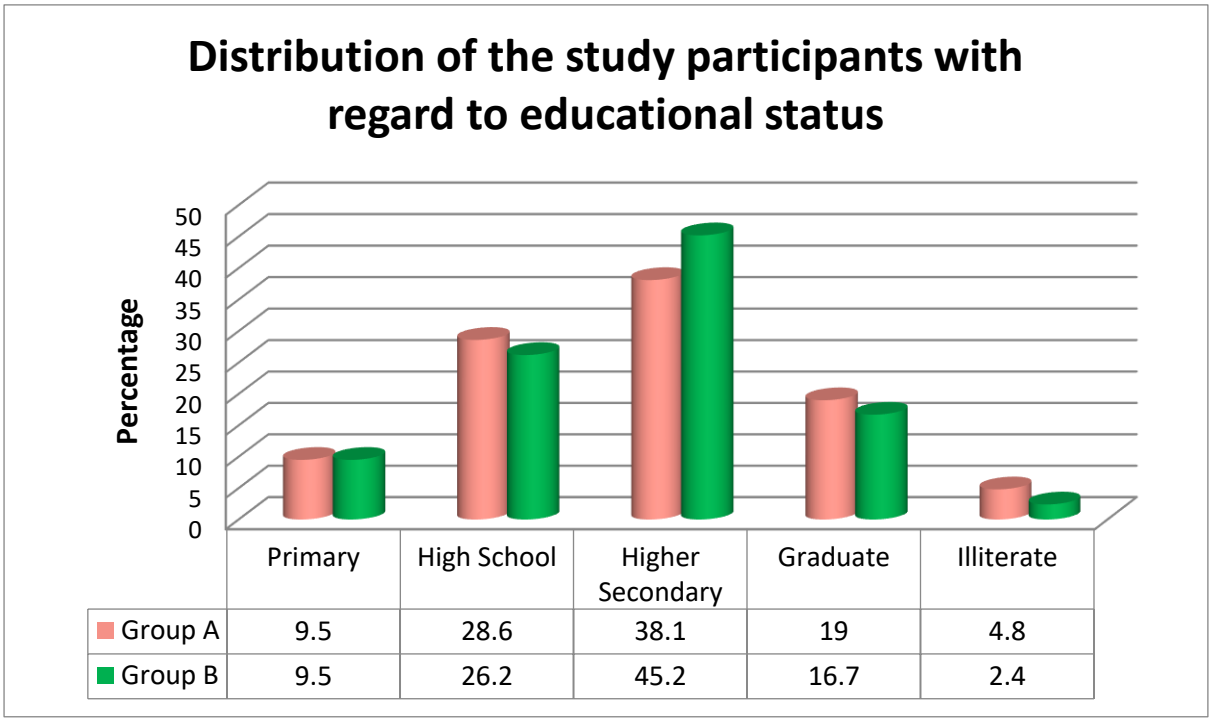


Table 7: SES comparison between IS group and FCM group

Modified Kuppusamy upgraded scale 2020 was used for classifying participants into different levels of SES.

Socio-economic status	Group A		Group B		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
Upper (I)	0	-	0	-	0.99
Upper middle (II)	1	4.8	2	4.8	
Lower middle (III)	10	47.6	20	47.6	
Upper lower (IV)	7	33.3	15	35.7	
Lower (V)	3	14.3	5	11.9	
Total	**21**	**100.0**	**42**	**100.0**	

There were no participants in upper class and majority belong to lower middle class (47.6%). The socioeconomic status between the two groups was comparable (p=0.99).

Figure: 15

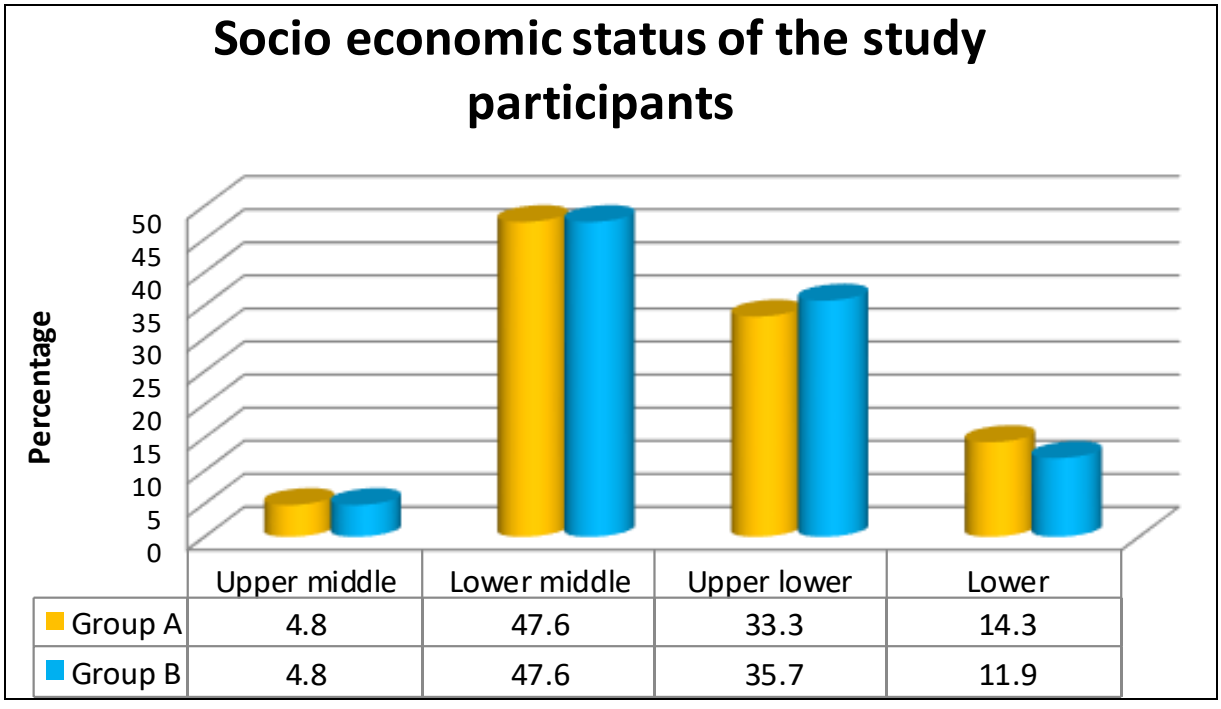


Table 8: Correction of antenatal anaemia between IS group and FCM group

Antenatal Anaemia	Group A		Group B		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
Nil	18	85.7	36	85.7	1.0
Corrected with Iron Sucrose	3	14.3	6	14.3	
Total	**21**	**100.0**	**42**	**100.0**	

Table 8 describes about the history of anaemia correction done in antenatal period. In both groups, only iron sucrose had been used for anaemia correction for mild and moderate grade. 3(14.3%) women had anaemia correction in IS group and 6(14.3%) women in FCM group. The need of antenatal anaemia correction was statistically not significant between the two groups (p=1.0).

Figure 16

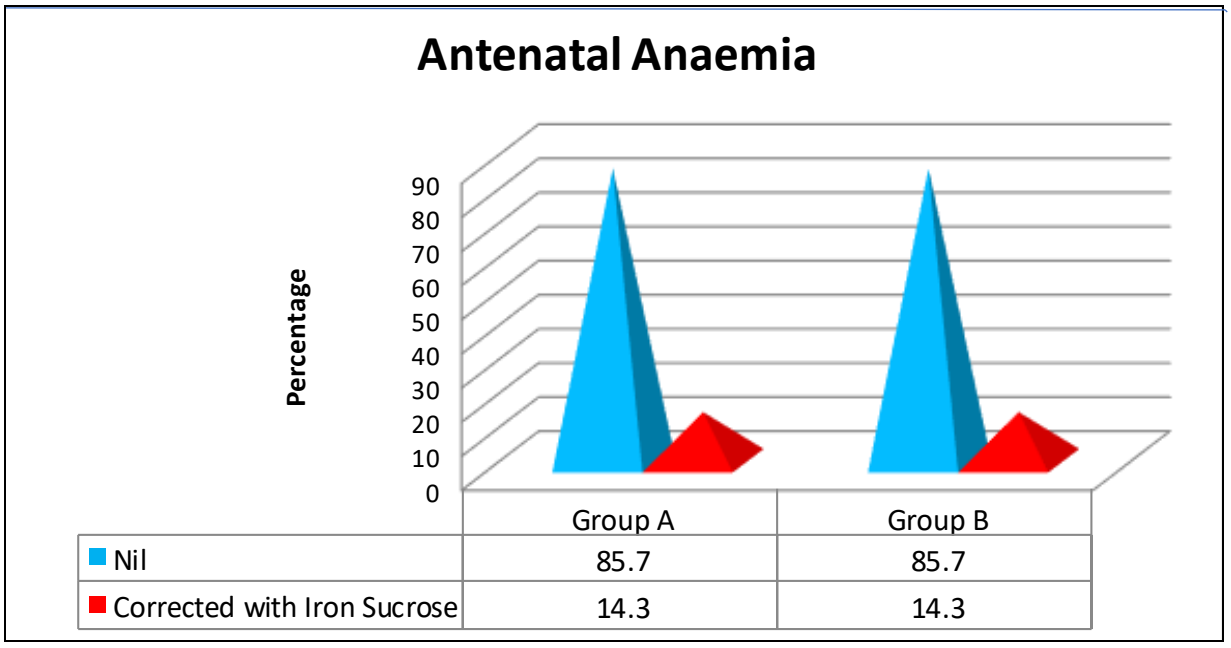


Table 9: Parity wise comparison between IS group and FCM group

Parity	Group A		Group B		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
1st Child	7	33.3	16	38.09	0.839
2nd Child	10	47.6	21	50.0	
3rd Child	3	14.2	4	9.52	
>3	1	4.8	1	2.4	
Total	**21**	**100.0**	**42**	**100.0**	

Table 9 shows that in Iron sucrose group, majority 14(66.7%) were multipara and 7 women (33.3%) were primipara. In FCM group, 26(61.9%) were multipara and 16 women (38.1%) were primipara. There was no statistical difference between the two groups related to parity (p= 0.839).

Figure 17

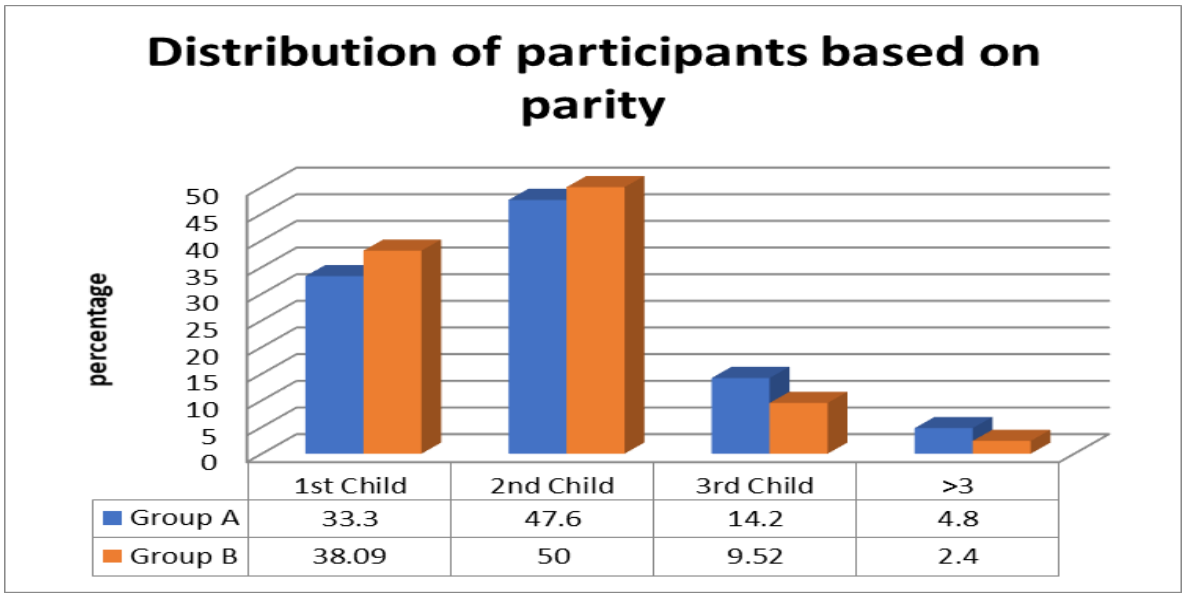


Table 10: Comparison of mode of delivery between IS group and FCM group

Mode of Delivery	Group A		Group B		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
Normal Vaginal Delivery	11	52.4	21	50.0	0.859
LSCS	10	47.6	21	50.0	
Total	**21**	**100.0**	**42**	**100.0**	

Mode of delivery between the two groups was compared and it is shown in Table 10. The caesarean delivery rate was 47.6% and 50% in Iron sucrose and FCM group respectively and it was statistically not significant (p=0.859).

Figure: 18

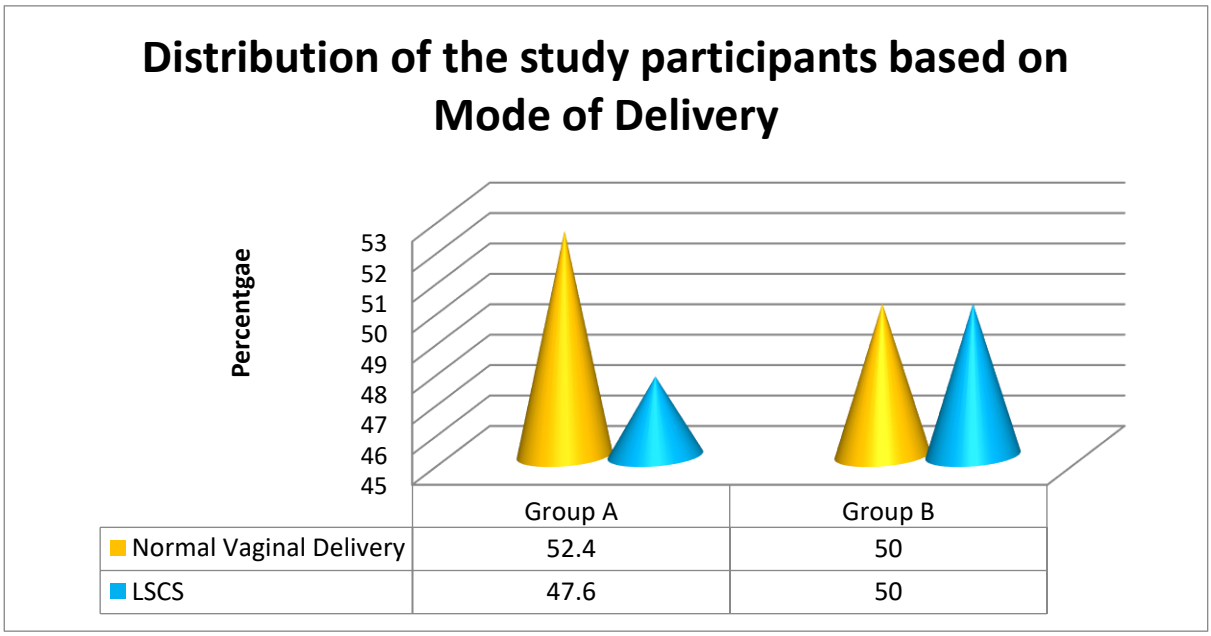


Table 11: Comparison of haemoglobin level between IS group and FCM group

Comparison of Group Vs Haemoglobin Level		N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	7.6	9.0	8.44	0.40
	Group B	42	7.2	9.0	8.37	0.48
At the end of 4 weeks	Group A	21	9.8	11.5	10.56	0.47
	Group B	42	9.8	12.3	11.09	0.58
At the end of 12 weeks	Group A	21	10.1	11.9	10.99	0.53
	Group B	42	10.2	12.6	11.51	0.54

Table 11 shows the comparison of haemoglobin increase following IS and FCM infusion. In IS group, mean haemoglobin raise at the end of 4weeks and 12 weeks was 10.56 g/dl and 10.99 g/dl respectively. In FCM group, mean haemoglobin raise at 4weeks and 12 weeks was 11.09 g/dl and 11.51 g/dl respectively. Comparatively higher haemoglobin rise was observed in FCM group at the end of 4weeks and 12 weeks of therapy.

Figure: 19

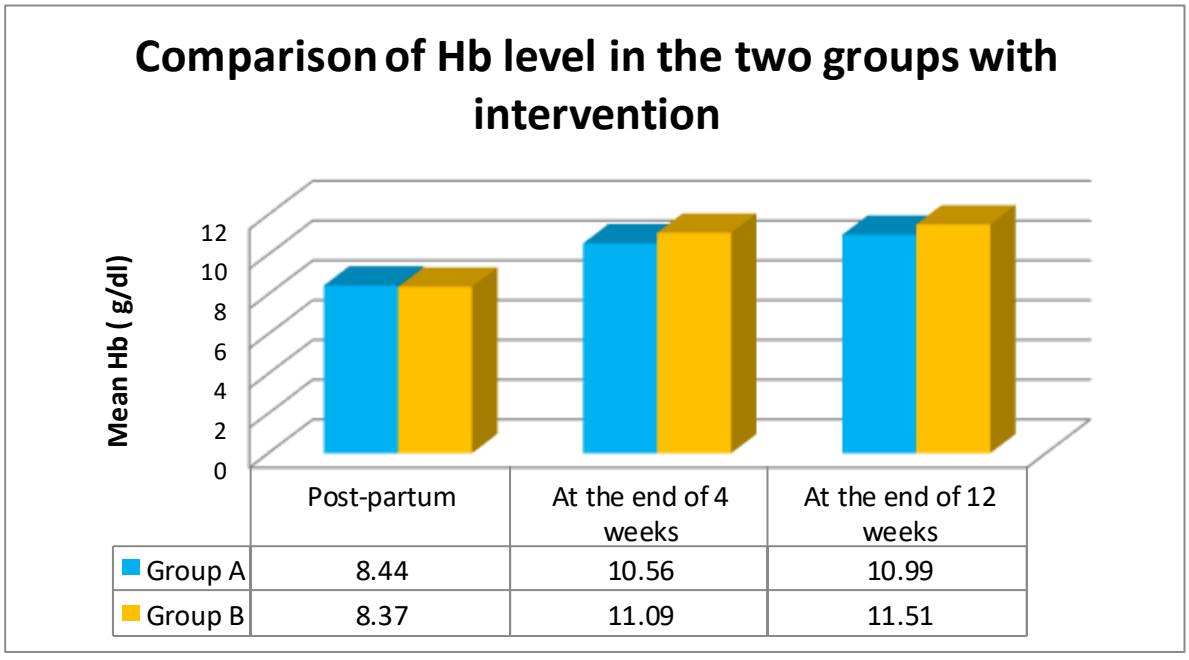


Table 12: Comparison of rise in haemoglobin between IS group and FCM group

Group	Hb level Initially		Hb level at the end of 12 weeks of intervention		Difference in the Hb level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	8.44	0.40	10.99	0.53	2.55	0.28	<0.001
Group B	8.37	0.48	11.51	0.54	3.13	0.36	

There was a raise in Hb level when measured at the end of 12 weeks among participants of both the groups. The mean raise in haemoglobin was higher in FCM group (3.13g/dl) compared to 2.55 g/dl in IS group and the difference was statistically significant (p =0.000).

Figure: 20

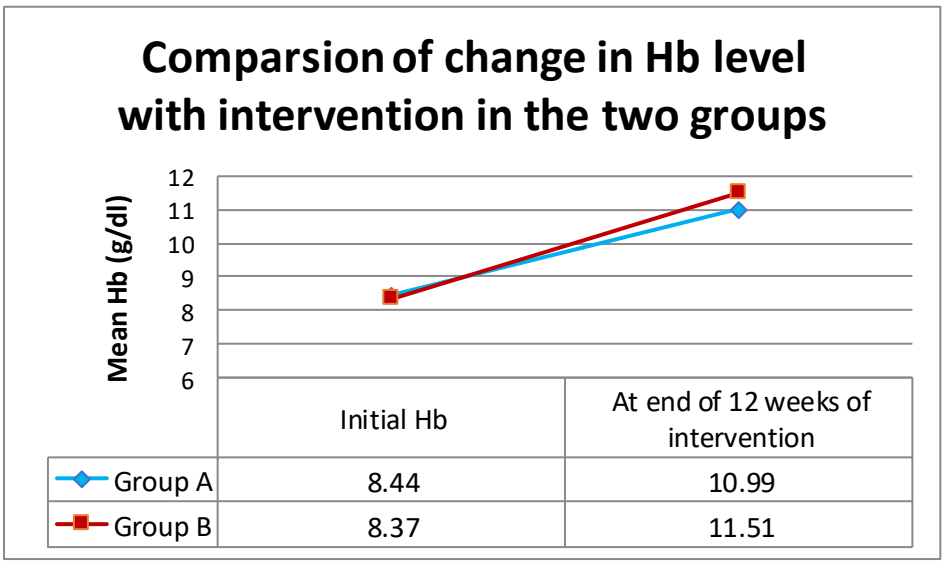
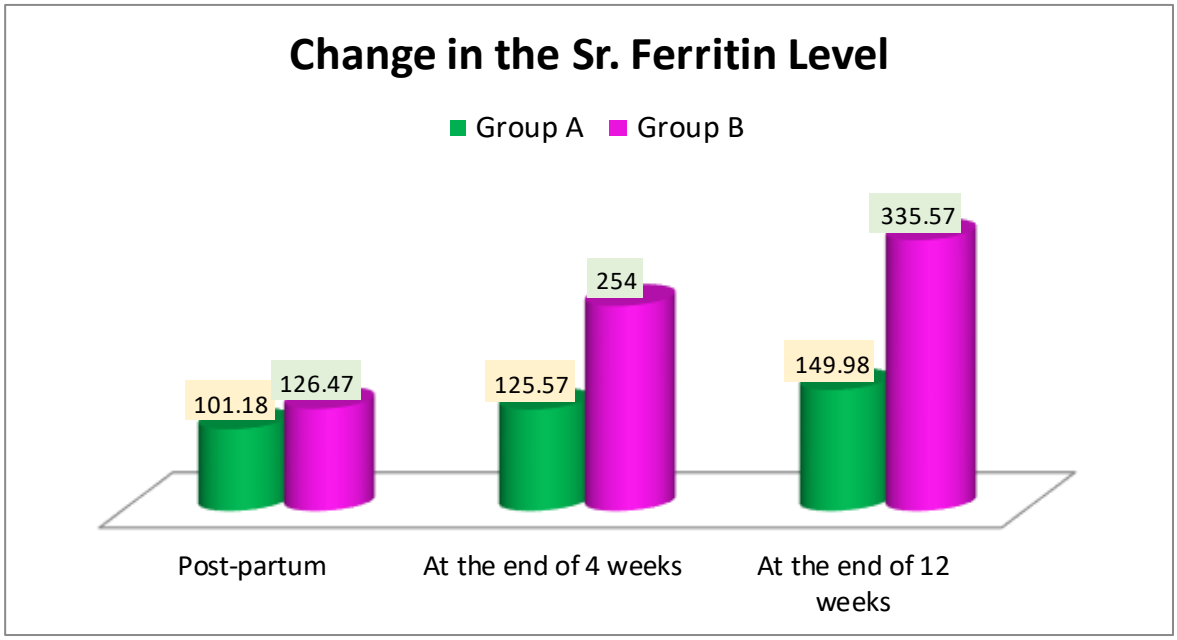


Table 13: Comparison of Ferritin between IS group and FCM group

Comparison of Group Vs Sr. Ferritin		N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	12.8	211.0	101.18	59.44
	Group B	42	12.6	465.0	126.47	100.60
At the end of 4 weeks	Group A	21	45.6	225.0	125.57	55.23
	Group B	42	98.0	550.0	254.00	111.45
At the end of 12 weeks	Group A	21	75.3	248.0	149.98	51.29
	Group B	42	179.0	655.0	335.57	107.34

Table 13 shows the improvement in ferritin levels following IS and FCM therapy when measured at 4 weeks and 12 weeks of therapy.

Figure: 20



The above figure depicts comparatively higher raise of ferritin level in FCM group than IS group.

Table 14: Comparison of rise in serum ferritin between IS group and FCM group

Group	Sr. Ferritin level Initially		Sr. Ferritin level at the end of 12 weeks of intervention		Difference in the Sr. Ferritin level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	101.18	59.44	149.98	51.29	48.80	14.74	<0.001
Group B	126.47	100.60	335.57	107.34	209.10	73.26	

Table 14 describes the increase in ferritin levels at the end of 12weeks between both forms of iron therapy. The mean ferritin value was higher in FCM group (335.57µg/L) compared to 149.98 µg/L in IS group (p= 0.000).

Figure: 22

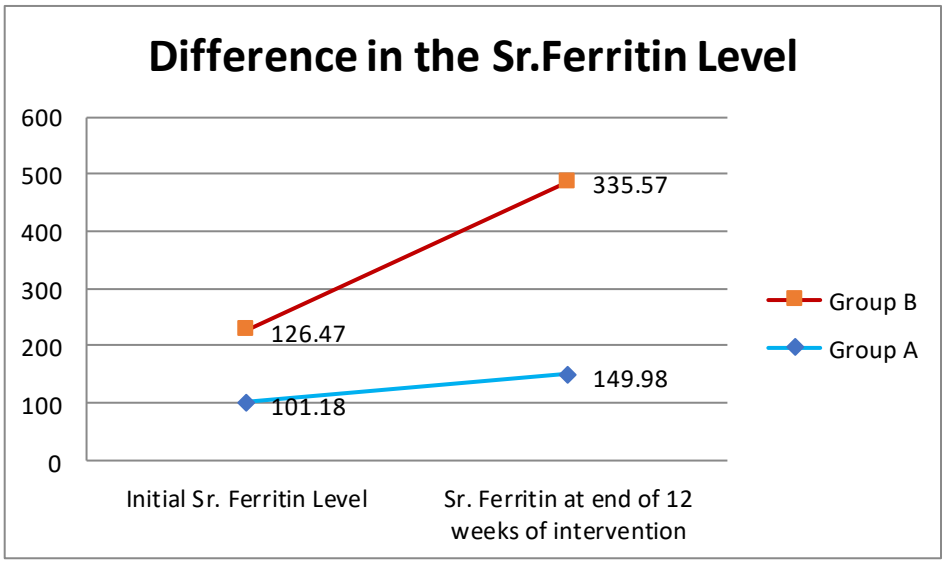


Table 15: Comparison of PCV between IS group and FCM group

Comparison of Group vs PCV		N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	26.2	32.8	29.65	1.94
	Group B	42	22.9	34.8	27.30	2.60
At the end of 4 weeks	Group A	21	28.3	36.2	32.62	2.17
	Group B	42	24.6	35.4	28.83	2.36
At the end of 12 weeks	Group A	21	33.6	39.5	36.40	1.87
	Group B	42	32.6	46.3	39.23	3.35

Table 15 shows the increase in PCV among the two groups. The mean raise in PCV values of IS group was 32.62%, 36.40% at four weeks and twelve weeks of therapy. Corresponding values of FCM group was 28.83% and 39.23%.

Figure: 23

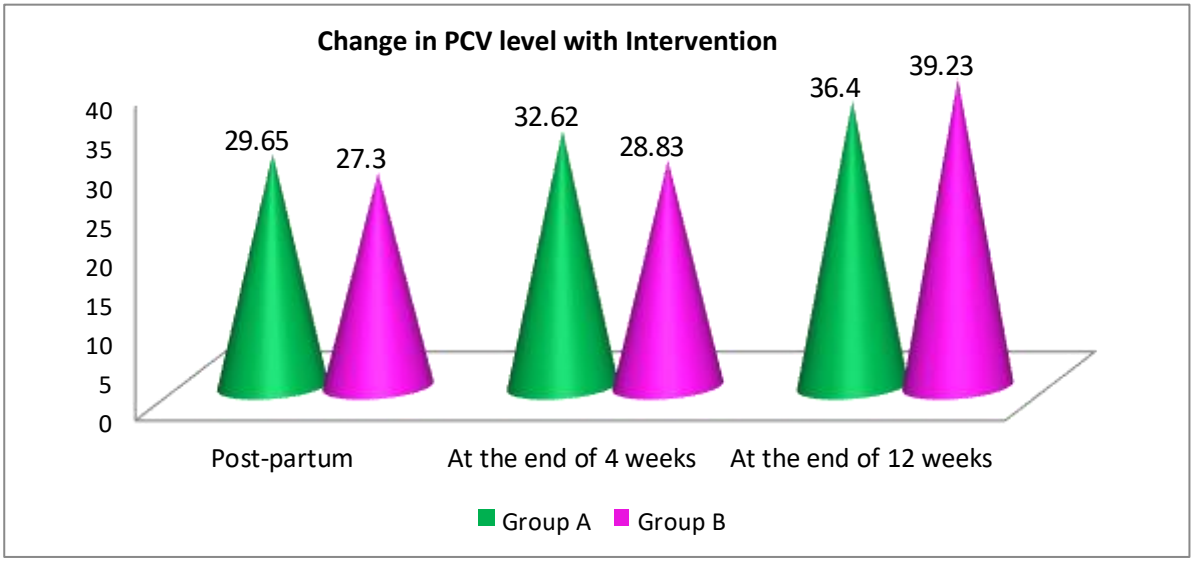


Table 16: Comparison of rise in PCV between IS group and FCM group

Group	PCV level Initially		PCV level at the end of 12 weeks of intervention		Difference in the PCV level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	29.65	1.94	36.41	1.87	6.75	1.32	**<0.001**
Group B	27.30	2.61	39.23	3.35	11.93	4.43	

Table 16 shows the PCV rise at the end of 12 weeks following parenteral iron therapy. In IS group, mean increase was 36.41% in Iron sucrose group. In FCM group, the value was 39.23%. The PCV rise was higher in FCM group which was statistically significant group (p=0.000).

Figure: 24

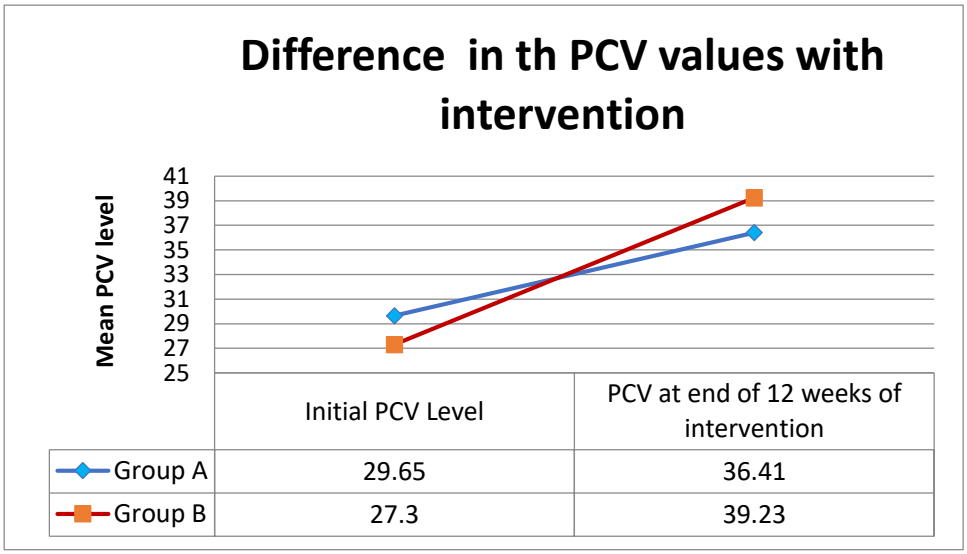


Table 17: Comparison of MCV between IS group and FCM group

Comparison of Group vs MCV		N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	66.8	75.2	70.98	2.35
	Group B	42	63.9	78.4	70.07	3.69
At the end of 4 weeks	Group A	21	77.4	86.7	82.11	3.11
	Group B	42	72.4	92.4	81.92	4.46
At the end of 12 weeks	Group A	21	83.5	96.0	88.80	3.47
	Group B	42	86.2	98.6	92.15	3.26

Table 17 shows the increase in MCV among the two groups following parenteral iron therapy. In IS group, the maximum increase of MCV value at the end of 4 weeks and 12 weeks was 86.7 fl and 96 fl. The corresponding values in FCM group was 92.4fl and 98.6fl.

Figure: 25

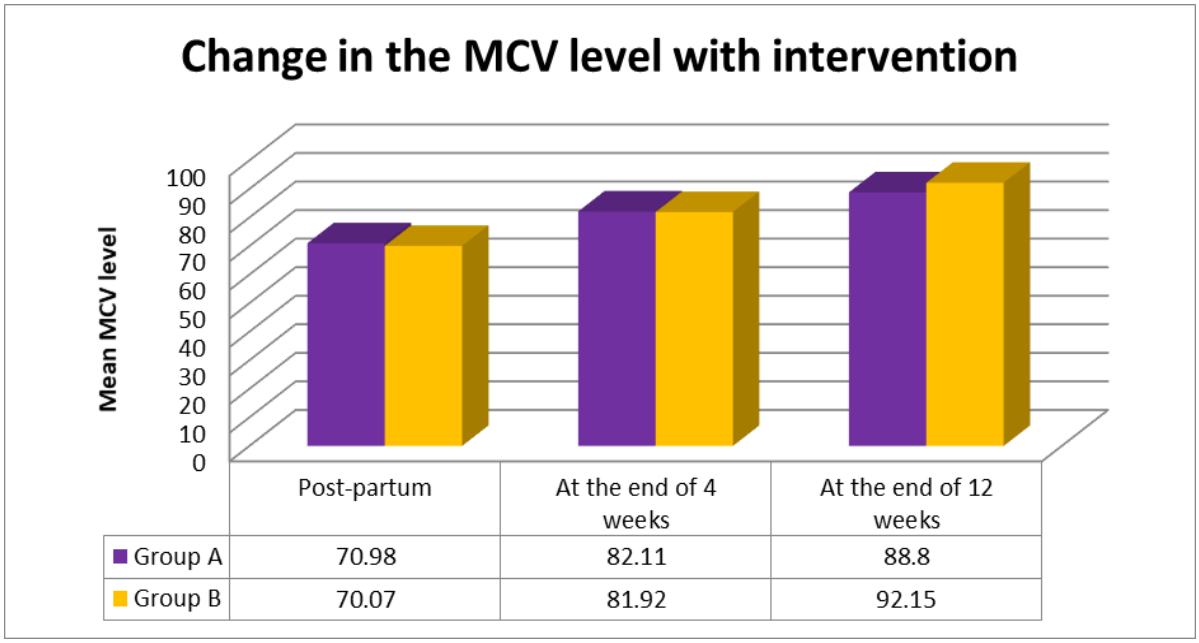


Table 18: Comparison of rise in MCV between IS group and FCM group

Group	MCV level Initially		MCV level at the end of 12 weeks of intervention		Difference in the MCV level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	70.98	2.35	88.80	3.47	17.81	2.34	**<0.001**
Group B	70.07	3.69	92.15	3.26	22.08	3.95	

Table 18 shows the increase in MCV level among the two groups when measured at 12 weeks of therapy. The values were 17.81 fl in IS group and 22.08fl in FCM group, comparatively higher in FCM group. The difference was statistically significant (p=0.000).

Figure: 26

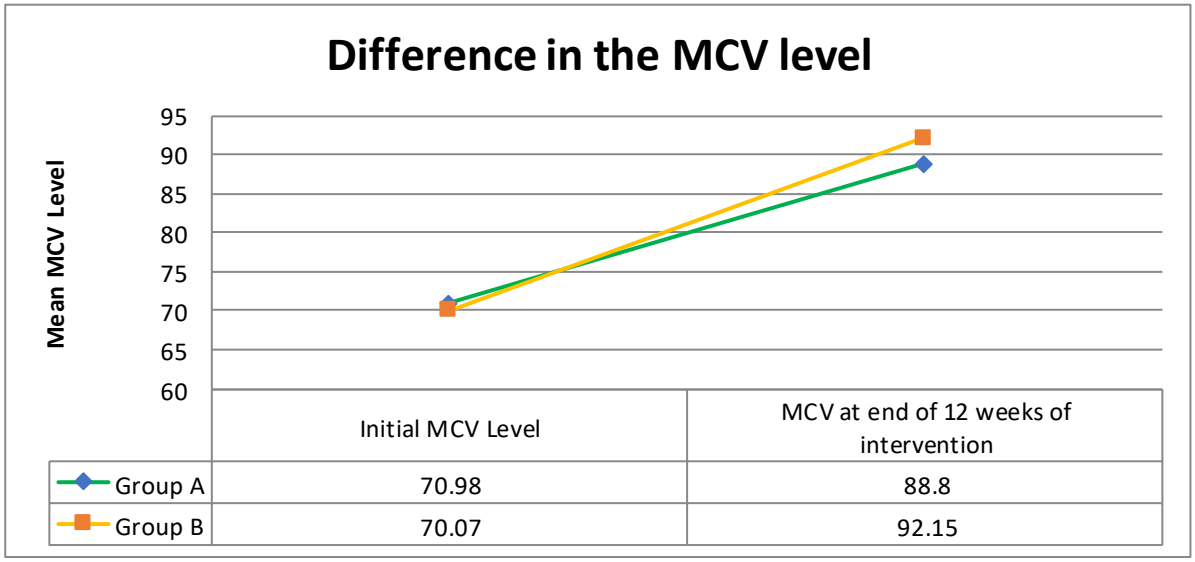


Table 19: Comparison of MCHC between IS group and FCM group

Comparison of Group vs MCHC		N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	23.9	30.7	27.59	1.67
	Group B	42	21.9	32.5	26.13	2.87
At the end of 4 weeks	Group A	21	25.6	33.2	29.95	2.05
	Group B	42	24.6	33.1	28.31	2.22
At the end of 12 weeks	Group A	21	28.4	36.7	32.87	2.17
	Group B	42	27.9	34.6	30.67	1.89

Table 19 shows the increase in MCHC following parenteral iron therapy. The maximum increase in MCHC values at 4 weeks and 12 weeks was 33.2% and 36.7% in IS group. The corresponding values were 33.1% and 34.6% in FCM group.

Figure: 27

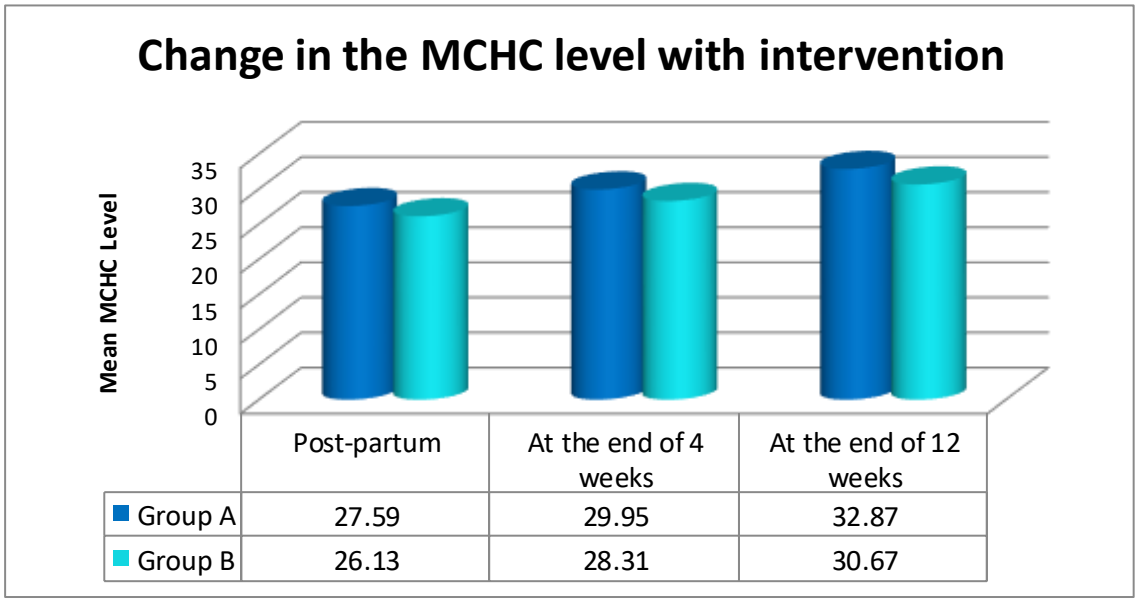


Table 20: Comparison of rise in MCHC between IS group and FCM group

Group	MCHC level Initially		MCHC level at the end of 12 weeks of intervention		Difference in the MCHC level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	26.13	2.87	30.67	1.89	4.53	1.58	**0.05**
Group B	27.59	1.67	32.87	2.17	5.28	0.79	

Table 20 shows the difference in MCHC level at the end of 12 weeks of therapy. The mean increase in MCHC value was 4.53% in IS and 5.28% in FCM group and the difference was statistically just significant (p =0.05).

Figure: 28

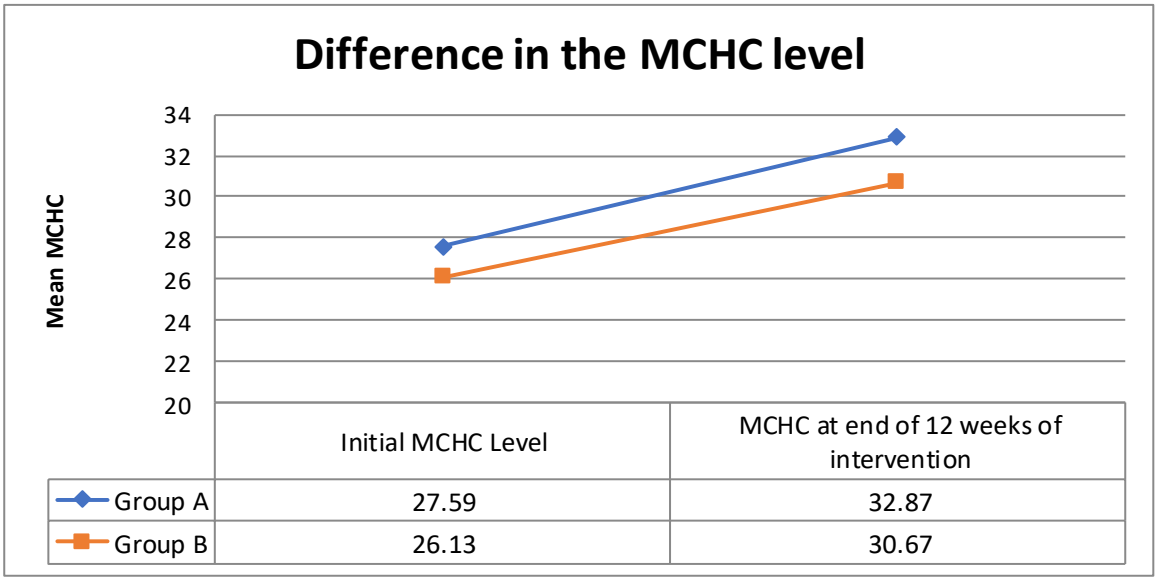


Table 21: **Comparison of MCH between IS group and FCM group**

Group	MCH	N	Minimum	Maximum	Mean	SD
Post-partum	Group A	21	0	29	26.03	6.08
	Group B	42	23	30	26.81	1.98
At the end of 4 weeks	Group A	21	27.3	32.7	29.92	1.64
	Group B	42	25.7	33.1	29.22	1.83
At the end of 12 weeks	Group A	21	30.5	34.9	33.18	1.34
	Group B	42	27.4	34.5	31.28	1.92

Table 21 shows the increase in MCH levels among the two groups. The mean increased MCH values for IS group at the end of 4 weeks and 12 weeks was 29.92 pg and 33.18 pg. The corresponding values were 29.22 pg and 31.28 pg in FCM group.

Figure: 29

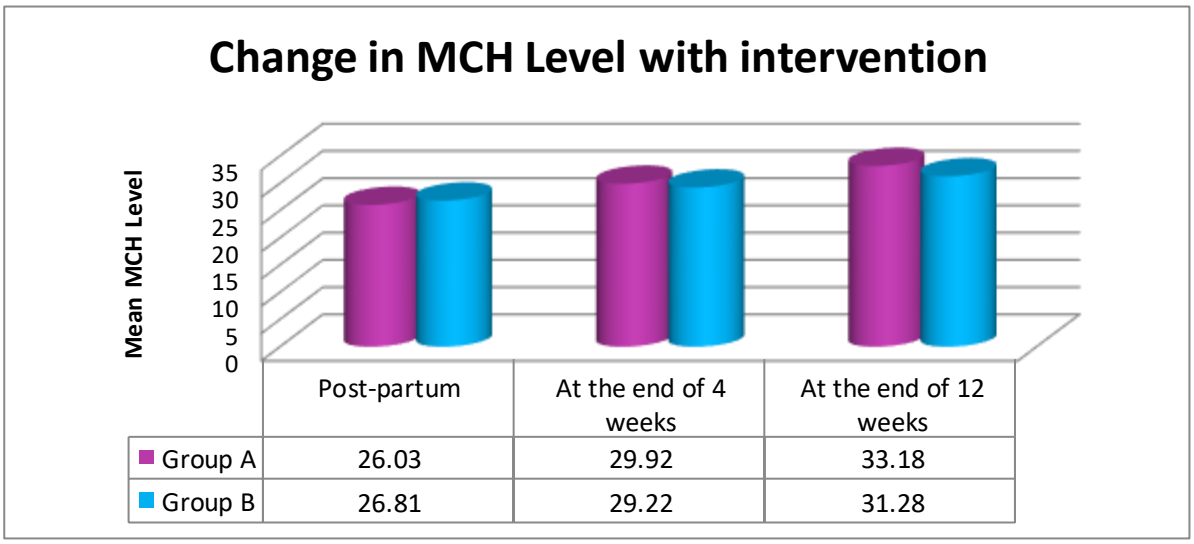


Table 22: Comparison of rise in MCH between IS group and FCM group

Group	MCH level Initially		MCH level at the end of 12 weeks of intervention		Difference in the MCH level		p value (unpaired t test)
	Mean	SD	Mean	SD	Mean	SD	
Group A	26.03	6.08	33.18	1.34	7.15	0.87	**<0.001**
Group B	26.81	1.98	31.28	1.92	4.47	1.23	

Table 22 shows the improvement in MCH values at the end of 12 weeks at the end of 12 weeks of parenteral iron therapy. The mean increase in MCH value was 33.18 pg in IS group and 31.28 pg in FCM group. The increased MCH value in IS group was statistically significant (p value =0.000).

Figure: 30

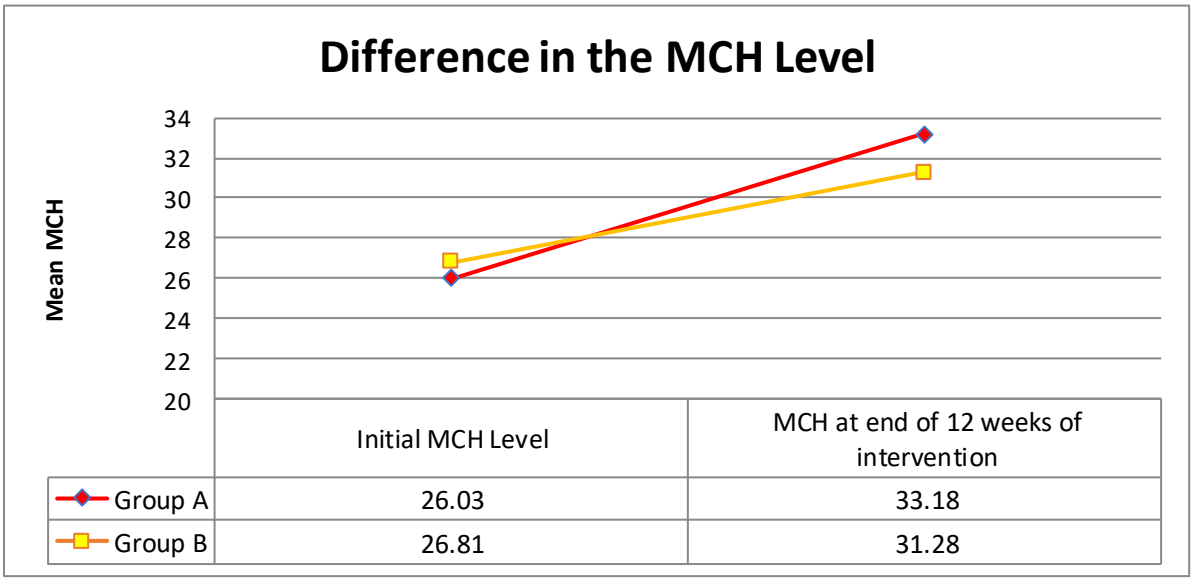
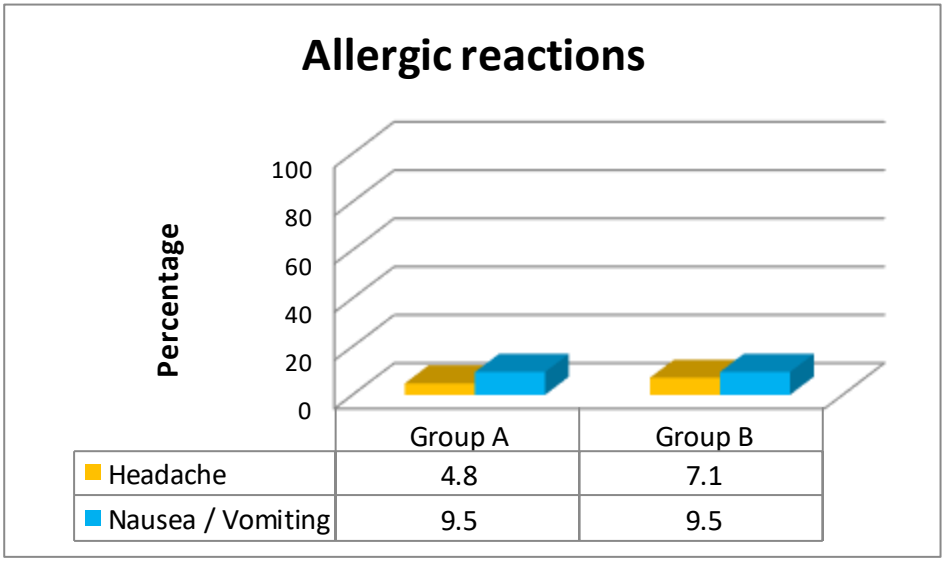


Table 23: **Comparison of adverse reactions between IS group and FCM group**

Allergic Reactions	Group A		Group B		p value (unpaired t test)
	Frequency	Percentage	Frequency	Percentage	
Nil	17	81.0	35	83.3	
Itching and rash	1	4.8	0	-	
Headache	1	4.8	3	7.1	
Nausea / Vomiting	2	9.5	4	9.5	0.54
Total	**21**	**100.0**	**42**	**100.0**	

The allergic reactions following the parenteral iron therapy among the two groups was compared. Only 4 women in IS group and 7 in FCM group had one or the other reactions which was statistically not significant. Nil anaphylactic reactions observed among both groups.

Figure: 31



DISCUSSION

DISCUSSION

Postpartum anaemia is a major public health problem and is observed in 65% of women in India. Postpartum anaemia imposes a substantial disease burden during the critical period of maternal infant interactions.[2]

In India, early age of marriage and childbearing is more prevalent in rural and economically backward areas. Low socioeconomic status causes poor maternal health because of illiteracy, customs and beliefs, refusal to accept nutritional and health benefits provided by government.[4]

WHO recommends oral iron supplementation to postpartum women. Anaemic women who have a longer average length of hospital stay, are more likely to receive a blood transfusion if not corrected in time and incur higher hospitalization costs.[9] Use of oral iron is hindered by gastrointestinal side effects and poor patient compliance whereas second generation preparations such as iron dextran are associated with risk of anaphylactic reactions.

In addition, inflammatory reaction secondary to surgically assisted deliveries leads to sequestration of iron in macrophages and decrease of intestinal absorption. So that administered iron is not available for erythropoiesis. To overcome this problem parenteral iron preparations were used. Due to limitations of older parenteral iron preparation, search of novel drug resulted in iron sucrose and latest is FCM. Blood transfusions are usually reserved for most severe cases and life threatening situations.

In our study the most common affected age was 18-30 years among both the groups and it was not statistically significant between the two groups ($p = 0.603$). This is similar with a study conducted by Joshi et al where the most common age group

affected was 18-25 years.[77] Lunagariya et al also observed that most common age group affected was 20-25 years.[78]

In our study, postpartum anaemia was more commonly observed in multiparous women. This is similar with Sethu et al study where 68% of postpartum anemic women were multipara. [56]

On comparing the educational status of the study participants among two groups, 74% women in IS group and 78% women in FCM group completed high school education. This is similar with findings of Pfenninger et al, who observed 60-70% had completed high school education.[62]

In our study, 3 women (14.3%) of IS group and 6 women (14.3%) of FCM group had antenatal anaemia correction. The need for antenatal anaemia correction between both groups was statistically not significant (p=1.0). This was also replicated in a study conducted by Rathod et al and they reported around 20% had antenatal anemia correction.[64]

In the present study, the overall mean increase in Hb at the end of 12 weeks was 2.55 g/dl and 3.13 g/dl in IS and FCM group respectively. The mean increase in ferritin was 48.80 µ/L and 209.10 µ/L in IS and FCM groups respectively and it was statistically significant. The reported increase in hemoglobin and ferritin levels by various authors is shown in the table 24:

Table 24: Comparison of raise in hemoglobin and ferritin levels in various studies

	Rise In Hb (g/dl)	Rise In S.ferritin (µg/L)
SETHU [56] IS FCM	 3.35 4.58	 64 106
PFENNIGNER [62] IS FCM	 2.2 2.8	 56 114
RATHOD [64] IS FCM	 3.4 4.4	 164 406.7
CALVET [66] IS FCM	 2.9 3.6	 108.5 224
GARG [69] IS FCM	 3.32 3.95	 146 314
HOL KKV [70] IS FCM	 2.30 2.52	 43.65 44.40
AGGARWAL [75] IS FCM	 3.4 4.4	 64 106.7
SINGH [76] IS FCM	 2.8 3.4	 148 256
LUNAGARIYA [78] IS FCM	 3.1 4.2	 48 124
Current study (ESIC medical college & PGIMSR) IS FCM	 **2.55** **3.13**	 **48.80** **209.10**

INCREASE IN HEMOGLOBIN

In our study, the mean rise of Hb was 2.55g/dl in IS and 3.13g/dl in FCM groups (p=0.000). This is in similar with findings observed by Singh et al among 200 postpartum anaemic patients. They observed mean rise of Hb was 2.8 g/dl for IS group and 3.4 g/dl for FCM group.[80]

A retrospective study by Pfenninger et al [62] in 2012 compared the safety and efficacy of high dose FCM with IS for the treatment of postpartum anaemia among 210 inpatients. Rapid administration of FCM was as safe as IS in the management of PPA despite five times of higher dosage. FCM was as effective as IS in changing Hb levels from the baseline. In present study, the mean rise in Hb is comparatively higher in FCM group with minimal side effects (p= 0.000). This is also replicated in a study conducted by Patel et al [71] where the mean rise of hemoglobin value was 3.8 g/dl for FCM and 2.7 g/dl for IS.

INCREASE IN FERRITIN

In our study, the mean improvement of serum ferritin in IS group at 12 weeks was 149.98 µg/L from the baseline value of 101.18 µg/L. In FCM group, the corresponding value was 335.57 µg/L from the baseline value of 100.60 µg/L (p=0.000).

Calvet et al [66] reported that ferritin level increase in 6 weeks was about 224 µg/L in FCM group and 108.5 µg/L in IS group. Singh et al [76] observed increase in serum ferritin from baseline value of 39.9 µg/L to 256 µg/L at 12 weeks in FCM group. In Iron Sucrose group the increase was up to 148 µg/L from the baseline value of 32.4

µg/L (p=0.001). Garg et al [69] showed the statistically significant increase in mean value of serum ferritin level at 12 weeks of about 146 µg/L in IS group and 314 µg/L in FCM group. Thus, present study has proved restoration of iron stores by rapid rise in ferritin levels following FCM similar to findings observed in other studies.

INCREASE IN MCV, MCH AND MCHC

In our study, the mean improvement in MCV value after 12 weeks following IS therapy was 88.80fl. The corresponding value following FCM therapy was 92.15fl which was statistically significant (p=0.000). Also mean increase in MCHC value was 4.53% in IS group and 5.28% in FCM group which was statistically just significant (p =0.05). Above findings are similar to observations by Van Wyck et al [63] and Dev S M et al [82] and they found significant increase in MCV after FCM therapy.

In our study, mean increase in MCH values following IS therapy (33.18pg) was slightly higher than FCM therapy (31.28pg). This is in contrast to Lunagariya et al [78] study where they reported the increase in MCH was higher in FCM group compared to IS group. This could be attributable to lesser sample size taken in our study.

ADVERSE REACTIONS

Commonly occurring adverse drug reactions in ferric carboxy maltose recipients include nausea, headache, dizziness, hypertension and injection-site reactions. In our study, FCM was well tolerated, only 7 (16.6%) patients developed mild adverse events like headache and nausea. In IS group, 4 (19.1%) patients developed adverse events. The occurrence of adverse events was statistically not significant (p= 0.54). This was comparable to study by Garg et al [69] where 16% participants in FCM group and 20% in IS group had adverse events.

But, in studies by Rathod [64] and Damineni et al [65] FCM was very well tolerated with reported adverse events rate of lesser than 1%. Joshi et al [77] in their comparative study observed minor adverse effects which was more common in IS group (7.2%) when compared to FCM group (3.3%), which was statistically significant. The statistical insignificance in the present study could be attributable to lesser sample size.

In the present study women who received FCM expressed better overall satisfaction to administration of treatment due to single prick and very mild reversible adverse reactions. No serious adverse reactions observed between both groups.

SUMMARY

SUMMARY

- Postpartum women with Hb between 7 to 9 g/dl were included in the study.
- The anaemia occurrence was more common in younger age group (18-28 years) and multiparous women.
- 14.3% women had antenatal anaemia correction for mild and moderate degree which was statistically not significant between both groups (p=1.0).
- Majority of participants belong to lower middle class between both groups.
- In FCM group, 50% had vaginal delivery and 50% had caesarean delivery. Corresponding figures for IS group was 52.4% and 47.6%. The modes of delivery was comparable and statistically not significant (p=0.859).
- Majority (70%) of the participants had postpartum baseline hemoglobin value of 8 to 9 g/dl.
- The mean increase in hemoglobin value was 2.55 g/dl in IS group whereas it was 3.13 g/dl in FCM group after 12 weeks of therapy (p=0.000).
- Effective rise of ferritin was observed at the end of 12 weeks. In IS group the mean increase in serum ferritin was149.98 µg/L at 12 weeks from baseline value of 101.18 µg/L. But the improvement was higher among FCM group where the mean increase in serum ferritin was 335.57 µg/L at 12 weeks from the baseline value of 126.47 µg/L (p=0.000).
- There was significant rise in PCV value in FCM group compared to IS group at the end of 12 weeks. The mean increase of PCV value was 6.75% in IS group compared to 11.93% in FCM group (p=0.000).

- There was a significant increase in MCV values in FCM group compared to IS group when measured at the end of 12 weeks (p=0.0001). The raise in MCH value was slightly higher in IS group compared to FCM group.
- Milder adverse reactions like nausea, vomiting, headache and itching were observed in 19.1% (n=4) of IS group and 16.6% (n=7) of FCM group (p=0.54). No anaphylactic reactions noted in both groups.
- The only limiting factor was high cost of FCM but this was very well compensated when the number of days or visits in hospital was less in FCM group. Also single venous access has reduced the risks of infection by single prick.

CONCLUSION

CONCLUSION

- The present study observation showed raise in haemoglobin, serum ferritin and blood indices in both iron sucrose and ferric carboxy maltose group. However, the improvement was better and rapid in ferric carboxy maltose group. Also, use of single 1000mg dose of ferric carboxy maltose reduces the number of infusions, enabling the possibility of cost reductions compared to multiple administrations of iron sucrose.
- The overall satisfaction reported by the postpartum women was better with ferric carboxy maltose as they received the drug with minimum hospital stay in a single dose (within 15 minutes). It decreases bed occupancy and burden on health facility in developing country like India.
- Ferric carboxy maltose lacks dextran and less immunogenic with minimal adverse reactions.
- The ability to deliver a high dose of iron within a short time and less side effects makes ferric carboxy maltose suitable for patients requiring quicker restoration of iron stores. Our study further strengthens the clinical trial findings of good safety and efficacy of ferric carboxy maltose in patients with postpartum anaemia in real-world clinical practice.

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ANNEXURES

PROFORMA

NAME: AGE:

IP.NO:

SOCIOECONOMIC STATUS: BOOKED: YES / NO

MENSTRUAL: Regular / Irregular

Heavy flow / Normal flow.

--------/----------

MARIETAL HISTORY: MARRIED / UNMARRIED

PAST OBSTETRIC HISTORY: G P L A / Prev.

LCB/Abortion:

MODE OF DELIVERY: SVD PERINEAL TEAR [I/II/III]

Instrumental [forceps/vacuum]

LSCS [Emergency/Elective]

TIME & DATE:

HISTORY OF PPH: YES / NO

PERSONAL HISTORY

☐ Smoker Alcoholic Mixed diet

AWARE OF IRON RICH DIET: YES / NO

H/O. BLOOD TRASFUSION: YES / NO

RENAL/HEPATIC DISEASE: YES / NO

PREV IRON INJECTION: YES / NO

BRONCHIAL ASTHMA/HEART DISEASE: YES / NO

ALLERGY TO IRON FORMULATIONS: YES / NO

COMPLIANCE TO ORAL IRON IN ANTENATAL PERIOD: GOOD / BAD

POST DELIVERY

HEMOGLOBIN:

S. FERRITIN:

PCV, MCV, MCHC, MCH

IRON REQUIREMENT = [2.4 X PRE.PREGNANCY WEIGHT X (Hb DEFICIT)] + 500

=

=

PARENTERAL IRON GIVEN: ON PND-

DOSAGE SCHEDULE:

ALLERGIC REACTIONS:

REPEAT INVESTIGATIONS AFTER 4 WEEKS AND 12 WEEKS

BASELINE VALUES

HEMOGLOBIN:

S. FERRITIN:

PCV :

MCV :

MCHC :

MCH :

INCREASE IN HEMOGLOBIN:

INCREASE IN FERRITIN:

PCV :

MCV :

MCHC :

MCH :

CODING

EDUCATION:

1. Primary
2. High School
3. Higher Secondary
4. Graduate
5. Illiterate

SES:

1. upper
2. middle upper
3. middle lower
4. lower upper
5. lower

ANTENATAL ANEMIA:

1. Nil
2. Corrected with Iron Sucrose
3. Corrected with Blood transfusion

AGE:

1. 18-25
2. 26-30
3. 32-35
4. 36-40

PARITY:

1. 1ST Child
2. 2nd Child
3. 3rd Child
4. >3

MODE OF DELIVERY:

1. SVD
2. LSCS

ALLERGIC REACTIONS:

1. Nil
2. Pain at injection site
3. Itching and rash
4. Abdominal pain
5. Headache
6. Nausea / Vomiting

INFORMATION SHEET

Title of study:

"Comparative study of efficacy and safety of intravenous iron sucrose versus ferric carboxymaltose in the treatment of postpartum iron deficiency anaemia"

Name of principal investigator:

Dr. M. REVATHY

Designation and Institutional Affiliation:

FINAL YEAR PG
M.S (OG)
DEPARMENT OF OBSTETRICS AND GYNAECOLOGY
ESIC Medical College & PGIMSR
K.K. Nagar, Chennai.

BACKGROUND:

Childbirth should be a joyous event. However, unforeseen medical problems such as postpartum haemorrhage or postpartum anaemia can develop and make this time very difficult. Postpartum anaemia is observed in up to 27% of women. It is a major contributable factor and indirect cause of maternal death. Iron deficiency is the commonest treatable cause of postpartum anaemia. Parental iron therapy results faster and higher replenishment of iron stores and correction of Hb levels with better compliance.

OBJECTIVE:

The objective of this study was to compare the safety and efficiency of intravenous iron sucrose and intravenous ferric carboxymaltose in treating postpartum iron deficiency anaemia.

METHODS:

For all postpartum women in ESIC during the study period, Hb%, serum ferritin and PCV will be done after 24 hours of delivery. 63 Patients with Hb 7 to 9 g/dl are

taken for the study. Iron requirement calculated according to their Body weight and Haemoglobin deficiency. 63 women of postpartum iron deficiency anaemia in ESIC hospital will be allocated randomly into two groups.

Group A: In Iron sucrose group, subjects are given iron sucrose in multiple doses, max 200 mg/day in alternate days till the required dosage completed.

Group B: In Ferric carboxymaltose group, subjects are given FCM as maximum 1000mg single dose.

Both groups Hb%, serum ferritin and hematocrit will be done after 4 weeks and 12 weeks from the last dose of parenteral iron. Side effects and compliance are noted.

Only the investigators are blinded in this study.

RISKS:

Previously registered adverse events are all mild and quickly reversible and mostly restricted to local reactions at the infusion site. Minor reactions like diarrhoea, Nausea, Vomiting, Constipation, injection site reactions, Headache, skin discolouration may be noted.No major adverse reactions/anaphylaxis documented previously.

BENEFITS:

Parenteral iron therapy replenishes the Hb and iron stores faster and reduces the risk of postpartum anxiety, depression, lactation failure, cognitive impairment, secondary haemorrhage and longer hospital stays. This improves mother baby relationships and quality of life.

Thus it adds value to the society.

The finding of the study may be analyzed statistically and presented in conferences/workshops/published in research papers and journals. The individual identifying information will be kept confidential. The participation is voluntary, and the participants may withdraw at any time without giving reasons. Refusal to participate in the study will not adversely affect their treatment.

CONTACT DETAILS OF INVESTIGATOR:

Mobile NO: 9942950548

Email ID: revs.murugan@gmail.com

CONSENT SHEET

Title of study:

"Comparative study of efficacy and safety of intravenous iron sucrose Versus ferric carboxymaltose in the treatment of postpartum iron deficiency anaemia"

I Mrs. _____ Of age____ years have been informed in detail in my own language by the investigator regarding the purpose of the study. The title of the study is **"comparative study of efficacy and safety of intravenous iron sucrose Versus ferric carboxymaltose in the treatment of postpartum iron deficiency anaemia"**. Being a prospective interventional study the primary objective of the study is to compare the rise in Hb, iron stores and adverse events following intravenous iron sucrose Versus ferric caxboxymaltose administration in postpartum iron deficient women in ESIC Medical college hospital & PGIMSR, K.K. Nagar, Chennai.

Postpartum anaemia is associated with longer hospital stays, depression, anxiety, persistent ill health and lactation failure in mother and delayed development in infants. Adequate and early treatment of anaemia in postpartum period will have improved life quality in women in child bearing age group parenteral iron therapy found to replenish the iron stores faster than oral iron. So, two iv drugs for iron therapy are compared here for their efficacy and safety. The results are obtained from blood investigations before and after the therapy. Research results may help in knowing the iron therapy with better efficacy, less side effects and better compliance and hence adds valuable benefits to the society. No serious adverse effects previously noted in the administration of the above drugs.

I understand that I can withdraw at any time without giving reasons. I consent to the access and the use of this research data by the researchers, and Institutional Ethics committee for research presentation, writing and monitoring purposes.

There will be no financial burden on me. I willingly adhere to the protocol of the study and give consent to the proposed study voluntarily.

Signature of Investigator

Signature of Participant

Witness signature
in case of illiterate

Dr. M. REVATHY
Final year PG
Department of Obstetrics and Gynaecology
ESIC Medical College & PGIMSR
K.K. Nagar
Chennai-600078

Date:
Place:

தகவல் தாள்

ஆய்வின் தலைப்பு:

"பிரசவத்திற்குப் பிந்தைய இரும்புச்சத்து குறைபாடு இரத்த சோகை சிகிச்சையில் நரம்பு இரும்பு சுக்ரோஸ் மற்றும் ஃபெரிக் கார்பாக்சிமால்டோஸின் செயல்திறன் மற்றும் பாதுகாப்பு பற்றிய ஒப்பீட்டு ஆய்வு"

முதன்மை புலனாய்வாளரின் பெயர்:

டாக்டர் எம்.ரேவதி

பதவி மற்றும் நிறுவன இணைப்பு:

I YEAR PG
M.S (OG)
மகப்பேறியல் மற்றும் பெண்ணோயியல் துறை
ESIC மருத்துவக் கல்லூரி & PGIMSR
கே.கே.நகர்,
சென்னை-600078.

பின்னணி:

பிரசவம் ஒரு மகிழ்ச்சியான நிகழ்வாக இருக்க வேண்டும். இருப்பினும், மகப்பேற்றுக்கு பின் ஏற்படும் ரத்தக்கசிவு அல்லது பிரசவத்திற்குப் பிறகான இரத்த சோகை போன்ற எதிர்பாராத மருத்துவ பிரச்சினைகள் உருவாகி இந்த நேரத்தை மிகவும் கடினமாக்குகின்றன. மகப்பேற்றுக்கு பிறகான இரத்த சோகை 27% பெண்களில் காணப்படுகிறது. இது ஒரு முக்கிய பங்களிப்பு காரணி மற்றும் தாய்வழி பங்களிப்பு மரணத்திற்கு மறைமுக காரணம். பிரசவத்திற்குப் பிறகான இரத்த சோகைக்கு இரும்புச்சத்து குறைபாடு பொதுவான சிகிச்சையாகும். நரம்பு இரும்பு சிகிச்சையானது எச்.பி மற்றும் இரும்புச் சத்தை விரைவாகவும் அதிகமாகவும் நிரப்புவதோடு சிறந்த இணக்கத்துடன் செயல்படுகிறது.

நோக்கம்:

இந்த ஆய்வின் நோக்கம், பிரசவத்திற்குப் பிறகான இரும்புச்சத்து குறைபாடு இரத்த சோகைக்கு சிகிச்சையளிப்பதில் நரம்பு இரும்பு சுக்ரோஸ் மற்றும் iv ஃபெரிக் கார்பாக்சிமால்டோஸின் செயல்திறனை மற்றும் பாதுகாப்பை ஒப்பிடுவதாகும்.

முறைகள்:

ஆய்வுக் காலத்தின் ESIC இல் உள்ள அனைத்து மகப்பேற்றுக்கு பிறகான பெண்களுக்கும், Hb%, சீரம் ஃபெரிடின் மற்றும் பி.சி.வி ஆகியவை 24 மணி நேர பிரசவத்திற்குப் பிறகு செய்யப்படும். இவற்றுல் Hb 7 முதல் 10 g / dl உள்ள நோயாளிகள் 60 பேர் ஆய்வுக்கு அழைத்துச் செல்லப்படுகிறார்கள். இரும்புச் சத்து தேவையை

அவர்களின் உடல் எடை மற்றும் ஹீமோகுளோபின் குறைபாட்டின் படி கணக்கிடப்படுகிறது. அவ்வாறு இரத்த சோகை உள்ள 60 பெண்கள் தோராயமாக இரண்டு குழுக்களாக பிரிக்கப்படுவர்.

குழு A: இரும்பு சுக்ரோஸ் குழுவில், பெண்களுக்கு இரும்பு சுக்ரோஸ் பல அளவுகளில் வழங்கப்படும். தேவையான அளவு முடிவடையும் வரை மாற்று நாட்களில் அதிகபட்சம் 200 மி.கி / நாள்.

குழு B: ஃபெரிக் கார்பாக்சிமால்டோஸ் குழுவில், பெண்களுக்கு அதிகபட்சம் 1000 மி.கி ஒற்றை டோஸாக FCM வழங்கப்படும்.

மருந்து செலுத்திய பின் ஒரு மணி நேரத்திற்கு பக்கவிளைவிற்காக கண்காணிக்கப்பட்டு சிகிச்சை அளிக்கப்படுவர்.

Hb%, சீரம் ஃபெரிடின் மற்றும் ஹெமாடோக்ரிட் ஆகிய ஆய்வுகள் இரு குழுக்களும், நரம்பு இரும்பின் கடைசி டோஸிலிருந்து 15 ஆம் நாள் மற்றும் 30 ஆம் நாளில் செய்யப்படும். பக்க விளைவுகள் மற்றும் இணக்கம் குறித்து ஆராயப்படும்.

பக்கவிளைவுகள்:

முன்னர் பதிவுசெய்யப்பட்ட பாதகமான நிகழ்வுகள் அனைத்தும் லேசானவை மற்றும் விரைவாக மீளக்கூடியவை. வயிற்றுப்போக்கு, குமட்டல், வாந்தி, மலச்சிக்கல், ஊசி தள எதிர்வினைகள், தலைவலி, தோல் நிறமாற்றம் போன்ற சிறிய எதிர்வினைகள் கவனிக்கப்படலாம்.

பெரிய ஆவணப்படுத்தப்பட்ட எதிர்வினைகள் / அனாபிலாக்ஸிஸ் முன்னர் ஆவணப்படுத்தப்படவில்லை.

நன்மைகள்:

நரம்பு ஐ.வி இரும்பு சிகிச்சையானது எச்.பி. மற்றும் நரம்பு இரும்புச் சத்தை விரைவாக நிரப்புகிறது. பிரசவத்திற்குப் பிறகான கவலை, மனச்சோர்வு, பாலூட்டுதல் தோல்வி, அறிவாற்றல் குறைபாடு, இரண்டாம் நிலை ரத்தக்கசிவு மற்றும் நீண்ட காலமாக மருத்துவமனையில் தங்குவதற்கான அபாயத்தை குறைக்கிறது. இது தாய் குழந்தை உறவுகளையும் வாழ்க்கைத் தரத்தையும் மேம்படுத்துகிறது.

இதனால் அது சமூகத்திற்கு மதிப்பு சேர்க்கிறது.

ஆய்வின் கண்டுபிடிப்பு புள்ளிவிவர ரீதியாக பகுப்பாய்வு செய்யப்பட்டு மாநாடுகள் / ஆய்வுப் பயிற்சி / ஆராய்ச்சி ஆவணங்கள் மற்றும் பத்திரிகைகளில் வெளியிடப்படலாம். தனிப்பட்ட அடையாளம் காணும் தகவல் ரகசியமாக வைக்கப்படும். பங்கேற்பு தன்னார்வமானது, மேலும் பங்கேற்பாளர்கள் எந்த

நேரத்திலும் காரணங்களை தெரிவிக்காமல் திரும்பப் பெறலாம். ஆய்வில் பங்கேற்க மறுப்பது அவர்களின் சிகிச்சையை எந்தவிதத்திலும் பாதிக்காது.

<u>முதன்மை ஆய்வாளர் தொடர்பு விவரங்கள்:</u>

தொலைபேசி எண்: **9942950548**

7708243203

மின்னஞ்சல் முகவரி: <u>revs.murugan@gmail.com</u>

இந்த ஆய்வில் ஏதேனும் சந்தேகம் இருப்பின் மேற்கண்ட தொலைபேசி எண்ணை அழைக்கலாம்.

<u>ஒப்புதல் தாள்</u>

<u>ஆய்வின் தலைப்பு:</u>

"பிரசவத்திற்குப் பிந்தைய இரும்புச்சத்து குறைபாடு இரத்த சோகை சிகிச்சையில் நரம்பு இரும்பு சுக்ரோஸ் மற்றும் ஃபெரிக் கார்பாக்சிமால்டோஸின் செயல்திறன் மற்றும் பாதுகாப்பு பற்றிய ஒப்பீட்டு ஆய்வு"

திருமதி. _____, _____ வயதாகிய எனக்கு, எனது சொந்த மொழியில் ஆய்வாளரால் ஆய்வின் நோக்கம் குறித்த விவரங்கள் விரிவாக தெரிவிக்கப்பட்டுள்ளது. ஆய்வின் தலைப்பு **"பிரசவத்திற்குப் பிந்தைய இரும்புச்சத்து குறைபாடு இரத்த சோகை சிகிச்சையில் நரம்பு இரும்பு சுக்ரோஸ் மற்றும் ஃபெரிக் கார்பாக்சிமால்டோஸின் செயல்திறன் மற்றும் பாதுகாப்பு பற்றிய ஒப்பீட்டு ஆய்வு".** ஆய்வின் முதன்மை நோக்கம், நரம்பு இரும்பு சுக்ரோஸ் மற்றும் ஃபெரிக் கார்பாக்சிமால்டோஸ் செலுத்தியபின் ஹெச்.பி., உடல் இரும்புச் சத்தின் முன்னேற்றம் மற்றும் அவற்றை செலுத்தும்போது ஏற்படும் பாதகமான நிகழ்வுகளை ஒப்பிடுவது.

பிரசவத்திற்குப் பிறகான இரத்த சோகை, நீண்ட காலமாக மருத்துவமனையில் தங்கியிருத்தல், மனச்சோர்வு, பதட்டம், தாயின் தொடர்ச்சியான உடல்நலக்குறைவு, பாலூட்டுதல் தோல்வி மற்றும் குழந்தைகளின் வளர்ச்சியை தாமதப்படுத்துதல் ஆகியவற்றுடன் தொடர்புடையது. பிரசவத்திற்குப் பிந்தைய காலத்தில் இரத்த சோகைக்கு போதுமான மற்றும் முன்கூட்டியே சிகிச்சையளிப்பது குழந்தை தாங்கும் வயதிற்குட்பட்ட பெண்களின் வாழ்க்கைத் தரத்தை மேம்படுத்தும். நரம்பு இரும்பு சிகிச்சை வாய்வழி இரும்பை விட உடல் இரும்புச் சத்தை விரைவாக அதிகரிக்கிறது. எனவே, நரம்பு இரும்பு சிகிச்சைக்கான இரண்டு iv மருந்துகள், அவற்றின் செயல்திறன் மற்றும் பாதுகாப்பிற்காக இங்கே ஒப்பிடப்படுகின்றன. சிகிச்சைக்கு முன்னும் பின்னும் இரத்த பரிசோதனையிலுருந்து முடிவுகள் பெறப்படுகின்றன. இந்த ஆய்வின் மூலம் சிறந்த செயல்திறன், குறைந்த பக்க விளைவுகள் மற்றும் சிறந்த இணக்கத்துடன் கூடிய மருந்தை அறிந்து கொள்ள ஆராய்ச்சி முடிவுகள் உதவக்கூடும். எனவே சமூகத்திற்கு மதிப்புமிக்க நன்மைகளை சேர்க்கிறது. மேற்கூறிய மருந்துகளின் நிர்வாகத்தில் முன்னர் குறிப்பிடப்பட்ட பாதகமான விளைவுகள் எதுவும் இல்லை.

காரணங்களை தெரிவிக்காமல் எந்த நேரத்திலும் நான் திரும்பப் பெற முடியும் என்பதை நான் புரிந்துகொள்கிறேன். ஆராய்ச்சியாளர்களால் இந்த ஆராய்ச்சி தரவை அணுகுவதற்கும் பயன்படுத்துவதற்கும் மற்றும் ஆராய்ச்சி விளக்கக்காட்சி, எழுதுதல், கண்காணிப்பு நோக்கங்களுக்கும் நான் ஒப்புக்கொள்கிறேன்.

எனக்கு எந்த நிதிச் சுமையும் இருக்காது. ஆய்வின் நெறிமுறையை நான் விருப்பத்துடன் கடைப்பிடித்து, முன்மொழியப்பட்ட ஆய்வுக்கு தானாக முன்வந்து ஒப்புதல் அளிக்கிறேன்.

புலனாய்வாளரின் கையொப்பம் பங்கேற்பாளரின் கையொப்பம்

சாட்சி கையொப்பம்
கல்வியறிவற்ற நிலையில்

டாக்டர் எம்.ரேவதி
I YEAR PG
மகப்பேறியல் மற்றும் பெண்ணோயியல் துறை

ESIC மருத்துவக் கல்லூரி & PGIMSR,
K.K.Nagar,
சென்னை-600078

நாள்:

இடம்:

MASTER CHART

S.No	Age	Education	SES	Antenatal Anemia	PARITY	MODE OF DELIVERY	PP																						ALLERGIC REACTIONS
							Hemoglobin				S. Ferritin				PCV				MCV				MCHC				MCH				
							PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	
A1	23	2	3	1	2	1	7.6	9.8	10.3	2.7	18.5	52.8	75.3	56.8	26.7	28.3	33.6	6.9	69.5	78.5	85.6	16.1	24.6	27.5	28.7	4.1	27.3	29.6	32.8	5.5	1
A2	28	2	5	1	1	1	8.2	10.1	10.4	2.2	76.5	96.3	112.6	36.1	28.9	30.5	34.5	5.6	70.6	82.6	88.5	17.9	27.4	28.6	31.5	4.1	26.3	28.3	31.5	5.2	1
A3	31	3	3	1	2	1	8.9	10.9	11.6	2.7	114	146	187	73	32.5	34.9	38.2	5.7	74	86.7	92.5	18.5	28.7	30.5	33.4	4.7	27.9	30.5	33.4	5.5	1
A4	32	4	4	1	1	1	8.5	10.8	11.2	2.7	85	98.6	126	41	29.3	33.4	37.5	8.2	72.3	85.6	91.8	19.5	27.6	29.7	32.8	5.2	25.6	27.9	30.8	5.2	3
A5	21	3	3	2	1	2	7.9	10.5	10.7	2.8	145	180.5	205.7	60.7	26.2	28.9	34.6	8.4	66.8	79.2	90.5	23.7	23.9	25.6	28.4	4.5	24.8	28.4	33.5	8.7	1
A6	24	4	3	1	1	2	8.8	10.2	11.1	2.3	97	126	152.6	55.6	28.3	32.4	38.5	10.2	73.4	84.6	89.4	16	28.4	32.4	34.6	6.2	25.6	27.6	30.5	4.9	1
A7	29	4	3	1	1	1	9	10.8	11.9	2.9	23.6	72.5	98.3	74.7	32.5	36.2	39.5	7	75.2	86.7	96	20.8	29.5	32.7	34.8	5.3	28.6	32.1	34.7	6.1	1
A8	26	3	2	2	2	1	8.5	11.1	11.3	2.8	168	186	198	30	31.2	34.6	37.8	6.6	68.7	78.9	85.7	17	28.6	31.9	35.7	7.1	28.7	30.9	33.7	5	1
A9	24	1	4	1	2	1	8.7	10.8	11.4	2.7	211	225	248	37	30.6	33.4	37	6.4	69.3	79.5	90.2	20.9	26.8	28.4	32.6	5.8	27.3	31.6	34.7	7.4	1
A10	23	1	3	1	1	2	8.2	10.5	10.9	2.7	149	165.9	182	33	31.7	34.5	38.2	6.5	71.6	83.6	89.3	17.7	27.6	29.5	33.2	5.6	28.2	32.7	34.9	6.7	1
A11	31	3	5	1	2	2	7.7	9.8	10.1	2.4	12.8	64.7	85	72.2	28.6	31.9	34.6	6	67.2	78.3	85.2	18	24.7	26.8	29.4	4.7	24.9	27.3	31.5	6.6	1
A12	30	3	3	1	1	2	8.4	10.9	11.2	2.8	67	92.7	119.4	52.4	30.9	33.5	38.4	7.5	69.5	79.6	84.6	15.1	28.7	31.6	34.9	6.2	28.4	32.1	34.7	6.3	5
A13	27	5	4	1	1	2	8.4	10.2	10.6	2.2	124	148	173.5	49.5	31.4	34.2	37.9	6.5	68.4	77.4	83.5	15.1	29.6	32.4	34.5	4.9	27.7	29.8	33.5	5.8	1
A14	35	3	3	1	3	1	9	11.5	11.7	2.7	184.5	198	212.5	28	32.8	35.8	37.5	4.7	74.5	86.7	93.7	19.2	30.7	33.2	36.7	6	29.1	32.7	34.8	5.7	1
A15	23	2	4	1	2	1	8.7	10.8	11.3	2.6	68.7	87.2	124.6	55.9	30.2	33.5	38.1	7.9	73.6	85.4	92.5	18.9	27.2	30.5	32.6	5.4	27.6	29.6	33.9	6.3	1
A16	26	2	5	1	1	1	8.9	11.2	11.8	2.9	45.9	62.8	97.3	51.4	27.6	29.9	34.5	6.9	72.9	83.7	89.6	16.7	28.4	31.4	34.5	6.1	26.8	28.6	31.6	4.8	6
A17	27	4	3	1	1	1	8.2	10.5	10.7	2.5	156	186	192.4	36.4	28.8	32.6	35	6.2	70.5	82	85.3	14.8	27.8	29.7	31.8	4	28.3	30.8	33.4	5.1	1
A18	36	3	4	1	3	2	8.1	9.8	10.2	2.1	179	185	205.6	26.6	28.1	32.5	35.5	7.4	69.7	78.6	83.9	14.2	26.3	28.9	31.7	5.4	27.4	29.7	33.9	6.5	1
A19	24	2	4	2	2	2	8.6	10.9	11.2	2.6	108.3	145	169	60.7	29.7	31.7	33.8	4.1	71.3	83.7	91.2	19.9	26.9	28.6	31.9	5	27.1	29.8	32.5	5.4	1
A20	26	3	3	1	2	2	8.3	10.5	10.8	2.5	54.8	72.4	97.9	43.1	27.3	29.8	34.6	7.3	70.4	81.7	87.5	17.1	27.9	28.4	32.9	5	28.4	29.6	33.8	5.4	1
A21	39	2	4	1	4	2	8.7	10.2	10.5	1.8	36.2	45.6	86.9	50.7	29.4	32.7	35.2	5.8	71.2	81.5	88.3	17.1	28.1	30.8	33.7	5.6	26.9	28.9	32.7	5.8	6

S.NO	Age	Education	SES	Antenatal Anemia	PARITY	MODE OF DELIVERY	PP																														ALLERGIC REACTIONS
							Hemoglobin				S. Ferritin				PCV				MCV				MCH				MCHC										
							PP	1 month	3month	Difference	PP	1 month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference	PP	1month	3month	Difference							
B1	32	3	2	1	1	1	8.6	11.2	11.6	3	347.4	550	655	307.6	27.9	30.4	35.5	7.6	69	72.4	92.6	23.2	29.5	31.2	32.4	2.9	25.3	26.5	31.5	6.2							1
B2	30	3	4	1	1	1	8.6	10.3	11.2	2.6	169.2	330	452	282.8	26.8	28.9	38.5	11.7	67	78.4	89.9	22.5	22.4	25.6	28.6	6.2	27.6	27.9	31.2	3.6							1
B3	27	2	5	1	1	1	8.6	10.8	11.5	2.9	194.3	450	546	351.7	27.8	28.9	36.5	8.7	72	77.6	86.2	13.8	25.6	27.2	31.4	5.8	27.5	29.5	33.1	5.6							1
B4	23	3	3	1	1	1	9	11.9	12.4	3.4	98.6	230	280	181.4	28.4	29.4	34.8	6.4	75	84.5	96.5	22	27.6	28.3	32.4	4.8	29.4	30.5	34.2	4.8							1
B5	24	4	4	1	2	2	8.7	11.4	11.5	2.8	112.8	356	425	312.2	34.8	35.4	39.6	4.8	73	86.3	94.5	21.6	22.9	24.6	28.6	5.7	25.3	27.6	30.2	4.9							1
B6	28	3	3	1	1	2	9	12.3	12.6	3.6	130.3	336	365	234.7	28.6	29.6	35.8	7.2	68	74.5	86.4	18.5	23.8	27.6	29.8	6	24.3	25.9	28.9	4.6							1
B7	24	3	3	2	1	1	7.6	9.8	10.2	2.6	17.8	150	350	332.2	23.5	24.6	34.5	11	68	79.5	90.1	21.7	27.2	28.7	30.4	3.2	29.3	31.2	34.2	4.9							1
B8	27	2	4	1	1	2	8.9	11.5	11.7	2.8	51.2	250	280	228.8	27.9	28.5	38.2	10.3	68	79.5	93.2	25.4	21.9	24.9	28.3	6.4	25.1	29	30.9	5.8							1
B9	29	1	3	2	1	1	8.2	10.8	11.4	3.2	81.9	285	320	238.1	27.2	28.6	40.5	13.3	69	79.8	94.5	25.9	23.8	28.3	31.5	7.7	24.6	28.2	32.6	8							1
B10	23	4	4	2	1	1	9	11.7	12.2	3.2	86.4	152	254	167.6	25.2	27.9	42.9	17.7	72	86.4	96	24.4	28.6	29.8	32.6	4	26.3	29.8	32.4	6.1							5
B11	26	3	3	2	3	2	8.9	11.8	12.2	3.3	146.3	250	326	179.7	29.3	30.5	46.3	17	73	87.6	91.4	18.9	32.5	33.1	34.6	2.1	30.4	33.1	34.5	4.1							1
B12	29	2	4	1	4	2	8.7	11	11.5	2.8	376.4	390	456	79.6	31.2	32.4	43.5	12.3	71	82.3	89.2	18.7	30.8	31.4	33.5	2.7	28.5	29.5	33.8	5.3							1
B13	32	4	3	1	2	2	8.9	11.5	12.1	3.2	465	524	560	95	32.8	33.5	34.8	2	73	84.5	87.6	15.1	29.8	30.9	32.5	2.7	29.1	29.5	32.8	3.7							6
B14	22	3	4	1	1	2	8.7	11.2	11.9	3.2	76.8	254	369	292.2	31.7	32.5	33.8	2.1	75	86.9	94.2	19.6	30.5	31.6	33.4	2.9	29.8	32.5	33.6	3.8							1
B15	27	3	5	1	2	1	8.7	11.2	11.5	2.8	45.7	326	390	344.3	32.4	33.5	34.9	2.5	69	79.9	90.5	22	25.6	27.3	30.5	4.9	26.5	28.4	32.9	6.4							1
B16	26	2	4	1	1	1	8.1	10.6	11.3	3.2	49.9	256	356	306.1	23.8	24.9	32.6	8.8	64	78	92.5	28.2	23.6	26.9	29.8	6.2	27.5	28.9	32.4	4.9							1
B17	28	2	3	1	2	2	9	11	12.5	3.5	88.7	280	345	256.3	25.9	27.5	38.6	12.7	65	77.2	89.2	23.8	24.9	26.4	29.5	4.6	27.3	30.4	33.5	6.2							6
B18	30	3	4	1	2	1	8.6	10.9	11.4	2.8	89	189	248	159	26.5	27.6	39.2	12.7	66	76.9	92.5	26.1	26.7	29.3	33.5	6.8	27.1	29.5	32.1	5							1
B19	31	3	2	1	2	1	8	11.2	11.4	3.4	97.4	260	356	258.6	27.5	28.6	37.9	10.4	69	82.4	94.2	25.7	26.7	28.7	32.4	5.7	28.4	29.9	30.4	2							6
B20	40	5	3	1	2	2	8.3	11.2	11.5	3.2	356	425	482	126	24.6	26.5	39.5	14.9	67	85.4	95.6	28.4	28.5	29.8	33.5	5	27.9	31.5	32.5	4.6							1
B21	21	4	3	1	1	1	8.2	10.8	11.1	2.9	98	125	284	186	28.6	29.5	42	13.4	69	84.6	96.3	27.8	23.9	25.6	28.7	4.8	25.4	28.4	29.9	4.5							1
B22	26	2	5	1	1	1	8.9	12	12.3	3.4	246.8	365	415	168.2	27.5	28.9	43.6	16.1	68	81.9	93.7	25.8	24.5	27.7	29.3	4.8	25.3	28.7	29.7	4.4							6
B23	31	3	4	1	2	2	7.7	10.6	11	3.3	106.4	326	452	345.6	28.6	29.8	41.9	13.3	69	82.1	91.8	22.5	22.7	25.7	28.6	5.9	24.9	26.9	28.6	3.7							1
B24	28	3	3	1	2	2	8.6	10.8	11.2	2.6	195	297	354	159	27.9	29.5	36.8	8.9	69	87	94.6	25.9	23.9	28.4	30.8	6.9	25.6	27.9	28.9	3.3							1
B25	28	3	4	1	1	2	7.9	10	10.5	2.6	123.8	289	365	241.2	25.4	27.5	35.9	10.5	64	81.6	92.4	28.5	22.7	26.4	29.3	6.6	24.3	25.7	27.4	3.1							5
B26	30	3	3	1	2	2	7.7	10.4	10.9	3.2	92	148	225	133	27.9	28.5	38.4	10.5	73	92.4	98.6	26	28.6	30.5	32.5	3.9	26.4	29.2	31.2	4.8							1
B27	33	1	3	1	2	2	8.2	11	11.4	3.2	146	239	317	171	28.3	29.6	41.8	13.5	75	86.5	97.5	22.7	29.7	31.2	33.2	3.5	28.5	30.5	31.8	3.3							1
B28	29	4	4	1	1	2	8.9	11.2	11.4	2.5	88	190	269	181	25.6	26.8	43.2	17.6	76	86.7	96.2	20.3	30.1	32.4	32.6	2.5	27.9	29.8	30.8	2.9							1
B29	27	3	4	1	2	2	8.2	10.6	11.7	3.5	114	258	369	255	23.8	25.6	44.6	20.8	65	79.5	89.3	24	24.6	27.9	29.4	4.8	25.4	27.6	29.6	4.2							1
B30	24	4	3	1	2	2	7.4	10.9	11.2	3.8	96	118	258	162	25.8	26.7	42.7	16.9	77	89.4	96.7	19.9	29.8	31.5	32.6	2.8	29.4	30.5	31.7	2.3							1
B31	22	2	5	2	1	1	8.3	10.4	10.8	2.5	192	356	421	229	22.9	24.9	39.5	16.6	69	76.5	88.2	19.3	23.5	26.8	28.5	5	24.6	27.8	28.7	4.1							1
B32	25	4	3	1	2	1	8.7	10.8	11.2	2.5	84	169	264	180	25.6	28.6	38.9	13.3	77	84.6	92.8	15.6	28.6	29.8	30.7	2.1	26.3	28.4	29.9	3.6							1
B33	24	3	5	1	1	1	7.2	10.2	10.4	3.2	56	154	225	169	27.3	29	37.6	10.3	70	78.5	89.3	19.8	24.8	27.4	28.9	4.1	28.1	30.5	32.5	4.4							1
B34	23	1	4	1	2	2	7.8	10.9	11.2	3.4	74	180	276	202	28	29.8	40.1	12.1	69	74.6	86.7	18	27.5	28.7	29.5	2	28.4	32.4	33.1	4.7							1
B35	20	2	3	1	1	1	8.1	11	11.5	3.4	82.9	119	285	202.1	29.2	31.2	42.6	13.4	65	79.2	89.6	24.2	22.6	25.8	27.9	5.3	24.6	28.4	28.6	4							1
B36	27	3	3	2	1	1	8.6	11.2	11.5	2.9	74.3	234	289	214.7	24.9	26	44.5	19.6	67	75.4	86.4	19.2	23.5	25.9	28.4	4.9	23.8	27.3	28.6	4.8							1
B37	32	3	3	1	1	1	8.3	11.4	11.8	3.5	12.6	125	198	185.4	27.7	29.4	39.8	12.1	69	82.4	92.6	23.7	21.9	24.7	28.7	6.8	22.9	25.9	27.6	4.7							1
B38	23	2	4	1	1	1	8.3	11.8	12	3.7	24.6	98	179	154.4	24.9	28.6	36.8	11.9	66	83.6	93.2	26.9	24.9	26.5	28	3.1	23.5	28.6	30.5	7							1
B39	38	2	3	1	3	1	7.8	11	11.2	3.4	124	156	218	94	26.8	27.6	37.6	10.8	76	86.3	94.5	18.6	28.3	29.5	30.5	2.2	28.4	29.8	31.3	2.9							1
B40	33	1	4	1	2	2	7.7	11.2	11.4	3.7	156	220	245	89	27.6	29.9	41.8	14.2	78	84.2	91.5	13.1	27.4	29.2	31.2	3.8	29.1	31.7	32.6	3.5							1
B41	29	2	3	1	2	2	8.5	12.2	12	3.5	26.5	153	192	165.5	24.8	25.6	42.5	17.7	73	83.7	92.8	20.3	27.6	29.3	30.2	2.6	29.5	32.4	33.4	3.9							1
B42	29	3	3	1	2	2	8.7	12.3	12.2	3.5	17.8	106	179	161.2	23.8	28.2	37.5	13.7	69	80.1	89	19.8	23.8	26.7	29.5	5.7	26.4	29.6	29.9	3.5							5