"COMPARISON OF INTRAVENOUS FERRIC CARBOXYMALTOSE, INTRAVENOUS IRON SUCROSE AND INTRAMUSCULAR IRON SORBITOL IN ANEMIA IN PREGNANCY: A RANDOMISED CONTROLLED TRIAL"

By

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Dissertation submitted to BLDE University, Vijayapur.

In partial fulfillment of the requirements for the degree of

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IN

OBSTETRICS AND GYNAECOLOGY

Under the guidance of

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LIST OF ABBREVIATIONS

- Hb - Hemoglobin
- PCV- Packed Cell Volume
- MCV- Mean Corpuscular Volume
- MCHC- Mean Corpuscular Haemoglobin Concentration
- MCH- Mean Corpuscular Haemoglobin
- LMP- Last Menstrual Period
- EDD- Expected Date of Delivery
- FCM- Ferric Carboxymaltose
- CRH- Corticotropin Releasing Hormone
- sTfR- Soluble Transferrin Receptor
- EPO- Erythropoietin
- WHO- World Health Organization

ABSTRACT

OBJECTIVES:

The objective is to compare the efficacy and side effects of Ferric carboxymaltose (FCM), iron sucrose and iron sorbitol and the improvement in blood parameters in anemic women in pregnancy.

MATERIALS AND METHODS:

Pregnant women from 24 weeks to 34 weeks of gestation undergoing antenatal care with hemoglobin levels between 6.5 gm% to < 9.0 gm%, with no prior iron therapy or iron therapy received more than 6 weeks ago are included in the study.

Cases are subjected for blood investigations (Complete blood count, Peripheral smear, Reticulocyte count, Serum Ferritin). Cases are then divided into three groups: Group A- Ferric Carboxymaltose, Group B- Iron Sucrose, Group C- Iron Sorbitol. Equal number of cases are divided into three groups according to randomization table (seed no. 21185).

Cases are followed up after 2 weeks and 6 weeks after drug administartion for blood parameters (Complete blood count, Serum Ferritin, Reticulocyte count).

Primary observation is to compare the improvement in Complete Blood Count (CBC) parameters and Serum Ferritin levels and the time taken for the improvement by the iron preparations being studied. Secondary observation is to compare cost effectiveness and the side effects of these three drugs.

RESULTS:

Ferric carboxymaltose has found to be the most effective and the fastest drug in correction of anemia compared to iron sucrose and iron sorbitol as it increases the Hb levels by 1.86gm/dl by 2 weeks and 4.02gm/dl in 6 weeks. Iron Sorbitol cuases

an average increase in Hb of 2.08 gm/dl and Serum Ferritin of 43.51ng/ml at 6 weeks and considered to be less effective drug among the three drugs.

CONCLUSION:

In cases where there time is the limiting factor FCM would be the drug of choice for getting the fastest rise in Hb levels but at the cost of increased expenses. Iron Sorbitol is significantly poor in improvement in blood parameters when compared to the other two drugs, but where there is no other option, either due to non availability or due to prohibitive costs, it gives a satisfactory improvement in patient profile than with no therapy alone.

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INTRODUCTION

Prevalence of anemia in all the groups is higher in India as compared to other developing countries. Prevalence of anemia in South Asian countries is among the highest in the world. According to WHO, India has the highest prevalence of anemia among the South Asian countries.[1]

Anemia is widely prevalent in developing countries like India. The most common affected group is pregnant women. Estimates show that nearly two-thirds of all pregnant women are anemic.[2] The main cause of anemia in pregnancy is iron deficiency anemia, i.e. about 95%.[3]

Anemia is the most common nutritional deficiency disorder in the world. The prevalence of IDA, as per WHO, is about 18 percent in developed countries and 35-75 percent (average 56%) in developing countries[4]. Globally, the prevalence of iron deficiency anaemia is 55.9 percent with variations between developed and developing countries. In India, prevalence for IDA ranges between 33-89 percent[5]. About half of the global maternal deaths due to anaemia, occur in South Asian countries, among which India contributes to about 80 percent of this mortality ratio.[6]

WHO defines iron deficiency anaemia as haemoglobin (Hb) <11 g %.[4] In India, the ICMR classification of iron deficiency anaemia is: Hb 8-11 g% as mild, Hb 5-8 g % as moderate and Hb <5 g% as severe anaemia. Serum ferritin <12-15 µg/l in absence of interfering factors is considered as iron deficiency[1].

The CDC (Centers for Disease Control and Prevention- 1998) defined anemia in iron supplemented pregnant women using cutoff of 5th percentile- 11g/dL in the first trimester and third trimester, and 10.5 g/dL in the second trimester.[7]

Pregnancy complicated by anemia becomes a high risk pregnancy with potentially life threatening complications for the mother. Anemia is a major

contributory factor for maternal and fetal morbidity and mortality in developing countries like India.[8] Poor outcomes for the fetus and infant include: preterm birth, fetal growth restriction, intrauterine fetal death, low Apgar scores and infection.[9]

Added to that, especially in the developing countries, anemia may be detected late because of poor follow up and antenatal care, poor drug absorption, poor drug compliance and inconsistent deworming practices. Late detection of anemia further puts the pregnant lady at risk of life threatening complications. Hence there is a need to develop more and more methods of effective, safe and most of all, fast acting anemia treatment for these women. Hence the entry of newer drugs in the market which claim superiority over the others for anemia management in pregnancy.

Surveys like [National Family Health Survey (NFHS), District Level Household Survey (DLHS), Indian Council of Medical Research (ICMR) Micronutrient Survey] have been conducted to calculate the prevalence of anaemia in India. During 10th Five Year Plan (2002-2007)[1], a study conducted by ICMR[10] shows that the prevalence of anaemia was highest among pregnant women (50-90%) and that of moderate (<8 g%) and severe anaemia (<5 g%) was persistently high. Prevalence of anemia was high in all states of the country, with considerable variations in moderate to severe anaemia[11]. Other factors that are responsible for high incidence of anaemia in our country include early marriage, multiple pregnancies, less birth spacing, teenage pregnancy, phytate rich Indian diet, low iron and folic acid intake and high incidence of worm infections in Indian population[12].

The causes of anemia in pregnancy and their frequency are dependent on multiple factors such as ethnicity, geography, nutritional status, preexisting iron status and prenantal iron supplementation. Other factors are socioeconomic status and anemia is more prevalent among indigent women (ACOG, 2013a)[7].

AIMS AND OBJECTIVES

PRIMARY OBJECTIVES:

To compare the efficacy of IV Ferric carboxymaltose (FCM), iron sucrose and iron sorbitol in terms of:

1. Comparative improvement in Complete Blood Count (CBC) Parameters.
2. Comparative improvement in Serum Ferritin levels.
3. Time taken for the improvement by the iron preparations being studied.

SECONDARY OBJECTIVES:

1. To compare cost effectiveness
2. To compare the side effects of these three drugs.

REVIEW OF LITERATURE:

In a study conducted by Dhanani Jatin V. et al[13], 60 pregnant women were included in the study according to selection criteria and randomly assigned into one of the two groups, i.e. iron sucrose group (*n* = 30) or iron sorbitol citric acid group(*n* = 30) and follow up was taken at 14 days and 28 days. All laboratory parameter levels increased significantly after both the iron sucrose and iron sorbitol citric acid therapy. The rise in hemoglobin was found to be slightly more in the iron sucrose group as compared to the iron sorbitol citric acid therapy after the second week. There was no other significant difference in the efficacy of both the groups in anemia therapy in pregnant women.

In a study conducted by Bernd Froessler et al[14], 65 pregnant women with anemia between gestational age 24 to 40 weeks were administered ferric carboxymaltose and followed up at 3, 6 and 8 weeks post-infusion. There was a significant increase in haemoglobin levels from 3 to 6 weeks post-infusion (average increase 12 g/dl). By 8 weeks post-infusion, these values had returned back to levels comparable with those observed at 3 weeks post-infusion, which were still significantly higher than pre-infusion levels. The study concluded that ferric carboxymaltose administration in the second and third trimester of pregnancy is likely to be safe and effective and ferric carboxymaltose successfully corrected IDA prior to delivery.

In a study conducted by Patricia Christoph et al[15], in 206 pregnant women, of whom, 103 received Ferric Carboxymaltose and 103 received Iron Sucrose. Demographic data did not show any significant difference between the two groups. There was a statistically highly significant difference among the two groups in the need for repeated administration. Patients in the ferric carboxymaltose group received,

on the average, the double dose of iron weekly. More patients in the iron sucrose group received repetitive doses of iron intravenously. These differences correspond to the recommended treatment schemes of ferric carboxymaltose and iron sucrose, respectively; ferric carboxymaltose can be administered in much higher single dose than iron sucrose.

In a study conducted by Patel J et al[16], in 30 pregnant women and 30 post partum women comparing intravenous iron sucrose and ferric carboxymaltose therapy, the mean rise of hemoglobin value was 5.2 g/L for ferric carboxymaltose and 4.1 g/L for iron sucrose in pregnant women and for postpartum women mean rise of hemoglobin was 4.9g/L on the 15th day of treatment. The study concluded that Intravenous ferric carboxymaltose administration increases the hemoglobin level more rapidly as compared to iron sucrose in women with iron deficiency anemia in the pregnancy and postnatal period. It also stores iron more rapidly. Ferric carboxymaltose is well tolerated and is a safe and effective alternative to blood transfusion in the treatment of iron deficiency anemia in the postpartum period.

In a study conducted by Singh Subhadra et al[17], Intravenous iron sucrose therapy is safe, convenient, more effective, and faster acting than intramuscular iron sorbitol therapy for the treatment of moderate to severe anemia during pregnancy.

In a study conducted by Lomte DB et al[18], the potency, safety, effectiveness and mechanism of action of Intravenous iron sucrose therapy was higher than intramuscular iron sorbitol therapy for the treatment of moderate to severe anemia during pregnancy.

In a study conducted by Seid MH et al[19], FCM -treated subjects were significantly more likely to: (a) achieve a hemoglobin greater than 12 g/dL in a shorter time period with a sustained hemoglobin greater than 12 g/dL at day 42, (b)

achieve hemoglobin rise 3 g/dL or greater more quickly, and (c) attain higher serum transferrin saturation and ferritin levels. Drug-related adverse events occurred less frequently with FCM. Intravenous FCM was safe and well tolerated with an efficacy superior to oral ferrous sulphate in the treatment of postpartum iron deficiency anemia.

In a study conducted by Breymann C et al[20], Ferric carboxymaltose was as effective as oral iron sulphate in changing hemoglobin, despite the much shorter treatment period (2 weeks vs 12 weeks). Ferritin levels were significantly higher. Except for injection site burning, iron carboxymaltose was better tolerated than ferrous sulphate, mainly concerning gastrointestinal side effects. There were no safety concerns identified in breast-fed infants. Parenteral iron carboxymaltose was found to be a safe and effective treatment option for postpartum anemia, with advantages of a shorter treatment period, better compliance, rapid normalization of iron storages, and lower incidence of gastrointestinal side effects.

According to the 10th five-year plan (ICMR), oral iron in therapeutic doses should be administered to pregnant women with mild anemia. However, for moderate to severe anemias parentral therapy should be started as the first line.[21]

Ferric carboxymaltose (FCM) is the newest drug to be introduced to facilitate effective treatment of IDA as well as rapid replacement of iron stores. Ferric carboxymaltose is a newer dextran-free iron formulation having near neutral pH, physiological osmolarity and increased bioavailability which allows for single dose, short 15 minute infusion time and higher dosing (up to 1000 mg).

FCM comprises of a macro molecular iron hydroxide complex of polynuclear iron (III) hydroxide in a carbohydrate shell. The complex has a molecular weight of around 1,50,000 Daltons.

Once in the body, iron is released gradually, avoiding the toxicity of many other iron compounds but allowing large amounts of iron to be delivered which results in much better therapeutic window. Due to stability of the complex, FCM does not release ionic iron under physiological conditions. The iron hydroxide is tightly bound within a carbohydrate cage. Therefore, iron hydroxide core with its carbohydrate shell is taken up by macrophages and enters the lysosomes where Fe3+ can be converted to Fe2+ as required. The Fe2+ is released by divalent metal transporter (DMT1) then by ferroportin and taken up by transferrin after oxidation by ceruloplasmin. The release rate of iron from polynuclear iron hydroxide carbohydrate complexes is inversely related to molecular weight of complex.

FCM has no mutagenic potential does not damage chromosomes and is not associated with bone marrow cell toxicity. At high doses, there were no signs of embryonal, fetal or maternal toxicity in experimental animals, no effects on fertility or embryonic development.[22] However its use in pregnancy is approved for second and third trimester only.[23]

Iron Sucrose is a recently introduced parenteral iron therapy with the advantage of intravenous administration in two to three divided doses with almost nil side effects. Compared to oral iron in pregnancy iron sucrose is superior with respect to the rate of both haemoglobin increase and iron store replenishment, along with a good safety profile.[24, 25, 26] Some of the studies show that iron sucrose, is safe and effective for the management of anemia and can be administered without a test dose.[27]

In each infusion, the maximum total dose administered is 200 mg elemental iron in 50/100 mL 0.9% NaCl, infused in 20–30 minutes, or as intravenous bolus administration. No test dose is given. It is claimed to raise the haemoglobin levels

within 2 weeks of administration. Total dose was administered over 5 days and maximum daily dose administered was 400 mg elemental iron.[28]

Iron Sorbitol is an age old parenteral drug for the treatment of IDA which is available in the form of iron sorbitol citric acid, which is administered intramuscularly in divided doses (i.e. 75 mg daily). Because the iron sorbitol citric acid is highly dialyzable, 30–35% of elemental iron is excreted directly just after its administration[13]. However, the time taken to raise the Hb levels is 4-6 weeks, equivalent to that of oral iron therapy.

The molecular weight of sorbitol is of the order of 5000. It has a pH of 7.5, is stable in human serum, does not cause hemolysis and does not affect the clotting mechanism. After intramuscular injection, rapid absorption takes place from the site, two-thirds of the injected dose being removed within three hours and 80-85% in 12 hours. The majority of the injected iron is absorbed directly into capillaries, although some passes into the regional lymphatic drainage. Thirty per cent is excreted by the kidneys within 24 hours.[29]

Iron metabolism during pregnancy

Pregnancy causes changes in iron metabolism which includes cessation of menstruation, expansion of red cell mass, deposition of iron in fetus and placenta and increased intestinal absorption of dietary iron.

Increased erythropoiesis

Iron requirements during pregnancy depend on iron metabolism which varies with period of gestation. During the first trimester of pregnancy, iron requirements decrease as a result of cessation of menstruation. Maternal blood volume expands at around 16 weeks of gestation so that iron requirements are increased. Expansion of maternal blood volume peaks at 20 to 25 weeks of gestation, the need for iron

increases until the end of pregnancy. In the third trimester, there is increase in iron uptake and fetal erythropoiesis.[30]

The mechanism for the increase of erythropoiesis during pregnancy have not been fully elucidated. Erythropoietin is the hormone that stimulates erythropoiesis, and human placental hormones including lactogen, estrogen and progesterone are elevated and are thought to influence red cell mass expansion.[30]

Total haemoglobin (Hb) mass expansion during pregnancy is proportionally smaller than the expansion of plasma volume leading to dilutional or physiological anemia. As pregnancy progresses, this gap between the rate of plasma volume expansion and red blood cell mass becomes greater, causing a fall in Hb and hematocrit.

Increased in iron absorption

Compared to nonpregnant women, in women in the first trimester of pregnancy the intestinal iron absorption is lower because of the decreased iron needs. To meet the needs of the increased erythropoiesis, absorption of iron increases after the first trimester.

Using stable isotope methods, Barrett et al[31] found much higher absorption rates in non-iron-deficient pregnant women at the same interval of pregnancy relative to absorption rates 16 – 24 weeks after delivery and concluded that iron requirements can be met with diet alone. However, these high absorption rates should be confirmed by other studies before they are accepted.

Estimated needs of iron in normal pregnancy

The total iron requirement for a normal pregnant woman is approximately 1 gm.[32] Iron requirements vary by the period of gestation and are increased greatly especially after the first trimester. Iron is required for requirements of mother, fetal

growth, placenta, and blood volume expansion. The extra need for iron is met by increased mobilization of iron stores and increased intestinal absorption. Estimates of iron utilization and losses during pregnancy and losses are presented in Table 1.

Table 1 Estimates of iron needs during pregnancy [32]

SOURCE	IRON NEED (mg/pregnancy)
Maternal basal requirement	220mg
Fetal deposition	290mg
Placenta	25mg
Expansion of red cell mass	500mg
Total needs	1035mg

In developing countries, diets are low in iron absorption promoters and high in inhibitors. In such diets it has been estimated that only 5% or 10% of dietary iron is available for absorption. In this case, 20 – 40 mg of elemental iron per day would be needed to meet the fixed iron requirements of a normal pregnancy (excluding red cell mass expansion). An equal amount of iron will be needed to provide Hb and tissue expansion.[33] These requirements are very difficult to meet in the great majority of women in developing as well as developed countries.[30] Therefore, iron supplementation is preferred especially in women who enter pregnancy in an iron deficient state.

Anemia and iron deficiency

Anemia is characterized by a reduction in Hb concentrations leading to decrease in the oxygen-carrying capacity of the blood. WHO defines anemia as Hb < 11.0g/dl for pregnant women.[34]

Iron is stored mainly in the liver and the stores are used when insufficient iron is absorbed. This occurs when dietary intake of iron is less or when bioavailability is low. IDA occurs in stages[34]

1. **Depleted iron stores**. During this stage the Hb remains above the anemia cut off value and serum iron is normal, but the body iron stores are absent. A low serum ferritin (< 12 µg/L), is indicative of depleted iron stores.
2. **Iron-deficient erythropoiesis.** In this stage, also called iron deficiency without anemia, Hb concentration remains above the anemia cutoff value, but the transport of iron is decreased and iron-deficiency erythropoiesis develops. This stage is characterized by low serum iron, increased free protoporphyrin in red blood cells and an increase in the soluble transferrin receptor concentrations.
3. **Iron deficiency anemia**. This is the most severe form of iron deficiency characterized by absence of iron stores and decreased transport of iron. Iron supply for Hb synthesis is inadequate and consequently, Hb falls below the established cutoff levels.

Causes of anemia and iron deficiency during pregnancy

Not all people with iron deficiency are anemic and not all people with anemia are iron deficient. Anemia is the most severe manifestation of iron deficiency. In locations where iron deficiency is the major cause of anemia, more people are iron-deficient than being anemic. Additionally, where anemia is caused by factors other than iron deficiency, iron deficiency still is a significant cause of anemia.[35]

Anemia is caused by low production of red blood cells or by destruction or shortened life span of red blood cells. In developing countries, many other factors, in addition to iron deficiency, occur and contribute to the high prevalence of anemia.

These factors include other nutritional deficiencies, malaria, hookworm infestation and infections.[36]

Poor intake and/or bioavailability of dietary iron

In developing countries poor intake of iron, especially heme iron from animal sources, is very common where the traditional diet could be vegetarian and largely comprised of cereal and pulses-based foods. The pregnant women is at a higher risk for iron deficiency due to decreased intake and bioavailability of iron, coupled with the increased demand for iron.

Hookworm and other helminth infections

Helminth infections are common in developing countries with a poor water supply and sanitation. Every year, more than 1000 million people are infected with Ascaris lumbricoides, Trichuris trichiura, and hookworm.[37] Two species, Ancylostoma duodenale and Necator americanus, are endemic in human populations. The only mechanism by which hookworm contribute to IDA is chronic blood loss. Hookworms are contracted when the parasite enters the skin through the feet, as people walk barefoot on feces-contaminated soils.[38] Both the worm load and the fecal egg count are correlated with the amount of blood loss, and the severity of IDA. Infection is especially disastrous to iron status during pregnancy because of the increased demand for iron during pregnancy. The WHO recommends using anti-helminthic drugs, such as albendazole, during second or third trimester of pregnancy as a part of strategies aimed to improve IDA.[39]

Malaria

Malaria contributes to anemia throughout life as well as during pregnancy. Malarial parasites destroy red blood cells and suppress the production of red blood cells.[36] Plasmodium falciparum (P. falciparum) is the main cause of severe clinical

malaria. Among pregnant women living in areas where P. falciparum malaria is endemic, the attributable risk that accounts for the prevalence of anemia ranged between 2 – 15% and that of low birth weight (LBW) ranged between 8 – 14%.[40] Treatment of malaria during pregnancy has been effective in reducing anemia and risk of LBW infants.[40]

Iron supplementation, alongwith vitamin A should be coupled with antimalarial treatment for anemia and LBW prevention during pregnancy.[41, 42, 43]

Other infections/chronic inflammation

Helicobacter pylori causes anemia by increasing blood loss and reducing stomach acid, resulting in poor iron absorption. Bacterial diarrhea may also cause anemia when chronic and characterized by bloody stools. Chronic diarrhea causes malabsorption and undernutrition, decreasing the red blood cell production. Chronic disease due to inflammation make anemia more severe by increasing metabolism and iron requirements.[36]

The same occurs in women infected with HIV; the requirements for iron is high. Their risk for anemia increases due to several factors including poor diet, presence of other infections and decreased appetite.

Other nutritional deficiencies – Folate, vitamin B12 and vitamin A

Relatively few studies have assessed nutritional factors, other than iron deficiency, responsible for anemia in pregnancy. Key nutrients needed for production of red cells are folate, vitamin B12, and vitamin A.[44]

Folate deficiency causes megaloblastic anemia and is second in occurrence as a cause for nutritional deficiency anemia after IDA.[44]

More critical is folate deficiency during conception because of the risk of neural tube and other developmental defects in the fetus. Due to the increased rate of

cell division during pregnancy and the role of folate in cell reproduction, folate supplementation is recommended during pregnancy. Vitamin B12 deficiency also causes megaloblastic anemia. Since vitamin B12 is only present in animal products, pregnant women following a vegetarian diet or whose intake of animal products is minimal, are at risk for vitamin B12 deficiency.

Vitamin A deficiency (VAD) is more prevalent in parts of the developing world especially in South East Asia.[45] Vitamin A is essential for hematopoiesis. In addition, antenatal supplementation with both iron and vitamin A has shown to reduce anemia prevalence among pregnant women. The mechanisms of vitamin A that exerts its effect on hematopoiesis have not been fully elucidated.

Maternal hematological status and pregnancy outcomes

According to WHO (2002 report) [46], iron deficiency was among the top 10 risk factors after underweight, tobacco use and unsafe water and sanitation. Anemia among women decreases work productivity and makes it difficult to carry out daily tasks and to care for children. It results in weakeness during pregnancy and delivery. Additionally, anemia has adverse birth outcomes such as LBW and premature birth.

Effect of anemia on maternal mortality and morbidity:

In developing countries, where clinical information is incomplete, it is difficult to establish the cause of death. Hence, available data on the association between anemia in pregnancy and maternal mortality are limited and methodologies that are used to measure this association are flawed.[47] However, maternal mortality and morbidity may also be related to the underlying causes of anemia such as malaria, HIV, haemorrhage, etc. About 600,000 women die each year as a result of pregnancy complications and childbirth and 99% of deaths occur in developing countries.[48] In developing countries the risk of dying in pregnancy and childbirth is 50 – 100 times

greater than in developed countries. The difference is primarily in availability and adequacy of antenatal care and timely access to obstetric care. The risk of death is greatly increased with severe anemia by factor of 3.5 and there is little evidence of increased risk associated with mild or moderate anemia.[47]

Decreased work output and physical performance associated with increased risk for infection have been reported as a result of anemia.[36]

Maternal anemia and birth outcomes

Inconsistent results exist in the literature regarding the relationship between maternal anemia and adverse birth outcomes: In several studies, anemia in pregnancy is associated with increased risks for LBW and premature labor. Both LBW and preterm delivery are most common in developing countries and contribute to perinatal mortality.[49]

Proposed mechanisms through which IDA contributes to adverse pregnancy outcomes include:

- A decrease in oxygen supply to the fetus, caused by low circulating Hb, stimulates a stress response resulting in increase in corticotropin-releasing hormone (CRH).[50] CRH is shown to be a major risk factor for preterm labor[51], intrauterine growth retardation (IUGR)[52] and preeclampsia[53].
- An increase in serum norepinephrine concentrations and risk of maternal infections as a result of iron deficiency, independently of anemia, which might also increase CRH.[54]
- An increase in oxidative damage to erythrocytes and the fetoplacental unit is caused by iron deficiency.[55,56]

In addition, studies have suggested a differential effect of trimester-specific Hb level on birth outcome and no association between third-trimester severe anemia and LBW or preterm birth has been reported.[57, 58]

It may be difficult to differentiate between dilutional or physiological anemia and true anemia, during the third trimester when blood volume expansion is at its peak.

High hemoglobin levels during pregnancy and birth outcomes

Failure of blood volume to expand properly also could lead to pregnancy complications and this decrease in blood volume expansion leads to decreased transport of oxygen and nutrients to the fetus through the placenta and as result restrict fetal growth.[59]

High Hb level (> 14.4 g/dl), during the first and the second trimester, was associated with small for gestational age but not preterm birth.[57]

Similarly, risk for LBW was increased by Hb > 12 g/dl during the second and third trimester. Based on certain studies, high Hb or hematocrit during pregnancy are regarded as a signal for possible pregnancy complications.[42]

Clinical and laboratory assessment for indicators of iron and anemia status

Different laboratory tests exist for the evaluation of iron status and anemia status. However, in a developing country while conducting research, one must keep in mind the logistics involved in sample collection and processing when choosing the indicator and the method to be used. The method should be field-friendly, simple, inexpensive and easy to use. It also has to be reliable in order to provide accurate information on which public health policies and intervention programs are based.

Hemoglobin. The WHO defines anemia during pregnancy as Hb < 11.0 g/dl in the first trimester and third trimester of pregnancy or when the trimester is

unknown and < 10.5 g/dl in the second trimester of pregnancy.[34] These values have been adjusted for the expansion in plasma volume that causes the Hb to be diluted. Anemia in pregnancy is further subdivided into mild anemia (Hb 10.0 – 10.9 g/dl), moderate anemia (Hb 7.0 – 9.9 g/dl) and severe anemia (Hb < 7.0 g/dl).[34] Hb measurement during pregnancy is usually carried out by automated (Coulter) counter. However, in developing countries, a portable Hb photometer (HemoCue) has been widely used as a simple and accurate alternative.[44] Hb is measured with a finger-prick sample of whole blood drawn up directly into a disposable microcuvette by capillary action and inserted into a HemoCue photometer and this Hb photometer has been found to have a sensitivity of between 80% and 97% and a specificity between 79% and 99%, depending on the cut off points for Hb used.[60, 61] Where a Hemocue is not available, detection of anemia depends on conjunctival inspection in pregnant women, which has low sensitivity[44] and therefore is insufficient.

Iron status

Laboratory tests used in the clinical assessment of IDA are Hb, hematocrit, serum iron, total iron binding capacity, EPO, free erythrocyte protoporphyrin, bone marrow aspirates, ferritin, and soluble transferrin receptor (sTfR). These markers of iron deficiency tend to be less reliable and not sensitive enough during pregnancy as they are altered by gestation, expansion of plasma volume and infection, independent of iron status. Some investigators recommended that since ferritin reflects iron stores and sTfR reflects cellular iron, the combined use of these two measurements allow accurate definition of the entire spectrum of body iron status during pregnancy.[62]

MATERIALS AND METHODS

METHODS OF COLLECTION OF DATA:

SOURCE OF DATA:

Pregnant women from 24 weeks to 34 weeks of gestation undergoing Antenatal care at the OBG OPD/IPD in BLDE UNIVERSITY'S, Shri B. M. Patil Medical College, Hospital and Research Centre, Bijapur with Haemoglobin levels between 6.5 gm% to < 9.0 gm%, with no prior iron therapy or iron therapy received more than 6 weeks ago.

PERIOD OF STUDY:

October 2013 - June 2015

SAMPLE SIZE:

Determination of Sample Size (n)

Ferric Carboxymaltose:

The sample size n for the desired estimators from the study " Intravenous iron treatment in pregnancy: comparison of high-dose ferric carboxymaltose vs. iron sucrose" may be calculated by the following formula with the following assumptions.

Standard deviation of resistance index $\sigma = 9.9$

Z $\alpha/2 = 1.96$ at 5% level of significance.

The permissible error e = 2.74414

$$n = \frac{Z\ \alpha/2^{2}\ \sigma^{2}}{e^{2}}$$

$$= \frac{(1.96)^{2} \text{ x } (9.9)^{2}}{(2.74414)^{2}}$$

$$= 50$$

Iron Sucrose:

The sample size n for the desired estimators of the study" Intravenous iron treatment in pregnancy: comparison of high-dose ferric carboxymaltose vs. iron sucrose" may be calculated by the following formula, with the following assumptions.

Standard deviation of resistance index $\sigma = 4.9$

Z $\alpha/2 = 1.96$ at 5% level of significance.

The permissible error e = 1.358211

$$n = \frac{Z\ \alpha/2^{2}\ \sigma^{2}}{e^{2}}$$

$$= \frac{(1.96)^{2} \text{ x } (4.9)^{2}}{(1.358211)^{2}}$$

$$= 50$$

Iron Sorbitol:

The sample size n for the desired estimators of the study "Comparison of efficacy and safety of two parenteral iron preparations in pregnant women" may be calculated by the following formula with the following assumptions.

Standard deviation of resistance index $\sigma = 4.9$

$Z\ \alpha/2 = 1.96$ at 5% level of significance.

The permissible error $e = 1.358211$

$$n = \frac{Z\ \alpha/2^{2}\ \sigma^{2}}{e^{2}}$$

$$= \frac{(1.96)^{2} \text{ x } (4.9)^{2}}{(1.358211)^{2}}$$

$$= 50$$

INCLUSION CRITERIA:

1. Pregnant women with IDA.
2. Period of gestation between 24-34 weeks (confirmed by dates and USG).
3. Level of Hb between 6.5gm% < 9gm%

EXCLUSION CRITERIA:

1. Anemia not linked to iron deficiency
2. Intolerance to iron derivatives.
3. History of asthma, thromboembolism, seizures or drug abuse.
4. Women with evidence of renal or hepatic dysfunction.
5. Women who have received any form of iron therapy in the past 6 weeks.

Detailed history of all the patients recorded according to the proforma and complete examination done.

After having met all the inclusion and exclusion criteria and obtaining written informed consent participants are to be enrolled in the study group.

Procedure:

Among the pregnant women coming for Antenatal follow up in the OBG OPD in BLDE Hospital, Vijayapur, consenting for the study and fulfilling the inclusion criteria,will be randomized into three groups by a computer generated randomized table (SEED NO. 21185).

GROUP A (FCM) : Will receive **:**

Single dose infusion of 1000mg over 15 minutes in 100 ml Normal Saline.

GROUP B (IRON SUCROSE) :

Infusion of 200mg/day over 20 minutes in 100ml Normal Saline for 5 days (total 1000mg)

GROUP C (IRON SORBITOL) :

Test dose of 0.5ml deep im given on Day 1

Intramuscular administration of 75mg/day for subsequent 13 days.(total 1000mg- including 1ml of previous days ampoule).

OBSERVATIONS:

Immediate:

- Any adverse effects

Following Visits (At 2 weeks & 6 weeks) :

- Any delayed adverse effects
- Amelioration of symptoms of Anemia.

Investigations:

Baseline:

- Peripheral Blood Film
- CBC (Hb, platelet count, RBC, PCV, MCH, MCV, MCHC)
- Reticulocyte Count

- Serum Ferritin levels

At 2 weeks & 6weeks:

- CBC (Hb, platelet count, RBC, PCV, MCH, MCV, MCHC)
- Reticulocyte Count
- Serum Ferritin Levels

Statistical Analysis:

Data will be analysed using-

- Diagrams
- Mean and Standard Deviation
- Paired and Unpaired t-test
- Anova Test

RESULTS AND OBSERVATION

Table 2) The age distribution of the cases studied across three study groups.

Age Group (Years)	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
<20	3 (6.0)	2 (4.0)	2 (4.0)	0.947^{NS}	0.840^{NS}	0.855^{NS}
20 – 24	15 (30.0)	15 (30.0)	19 (38.0)			
25 – 29	26 (52.0)	28 (56.0)	24 (48.0)			
>30	6 (12.0)	5 (10.0)	5 (10.0)			
Total	**50 (100.0)**	**50 (100.0)**	**50 (100.0)**			

Values are n (% of cases). P-values by Chi-Square test. P-value<0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) The mean ± standard error or mean (SEM) of age of the cases from Group A, Group B and Group C was 25.8 ± 0.52, 25.7 ± 0.49 and 24.9 ± 0.47years respectively.
2) The age distribution did not differ significantly between groups A and B P-value>0.05. The age distribution did not differ significantly between intervention groups A and C (P-value>0.05). The age distribution did not differ significantly between intervention groups B and C (P-value>0.05).

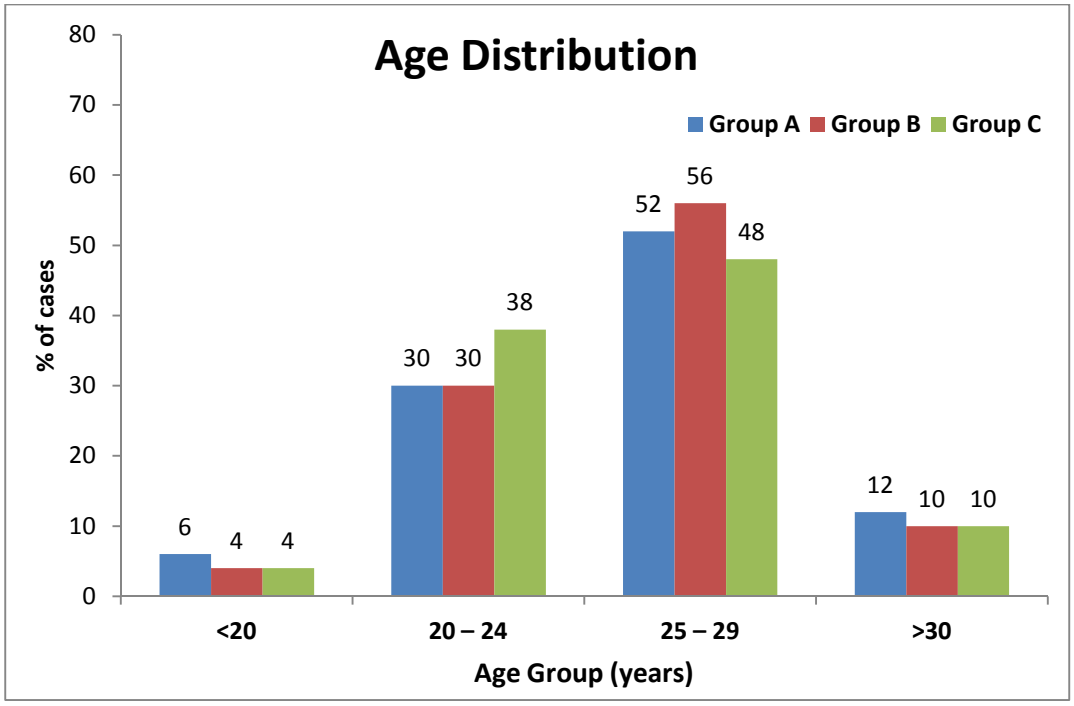

Figure 1) The age distribution of the cases studied across three study groups.

Table 3) The inter-group and intra-group comparison of hemoglobin measurements across three study groups.

Hemoglobin (g%)	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	7.84 ± 0.09	7.95 ± 0.09	8.08 ± 0.11	0.999^{NS}	0.221^{NS}	0.999^{NS}
2-Weeks	9.70 ± 0.09	9.19 ± 0.09	8.92 ± 0.11	0.001^{***}	0.001^{***}	0.001^{***}
6-Weeks	11.86 ± 0.11	10.83 ± 0.09	10.16 ± 0.11	0.001^{***}	0.001^{***}	0.001^{***}
% change at 6-Weeks	51.7%	36.5%	26.1%	0.001^{***}	0.001^{***}	0.001^{***}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**

    a. The average baseline hemoglobin did not differ significantly across three study groups (P-value>0.05 for all).

    b. The average 2-weeks post-treatment hemoglobin is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 2-weeks post-treatment hemoglobin is significantly higher in group B compared to group C (P-value<0.001).

    c. The average 6-weeks post-treatment hemoglobin is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 6-weeks post-treatment hemoglobin is significantly higher in group B compared to group C (P-value<0.001).

    d. The average 6-weeks post-treatment % change in hemoglobin is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 6-weeks post-treatment % change in hemoglobin is significantly higher in group B compared to group C (P-value<0.001).

2) **Intra-Group Comparison:**

    a. In Group A, the average 2-weeks and 6-weeks post-treatment hemoglobin is significantly higher compared to baseline hemoglobin (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment hemoglobin is significantly higher compared to 2-weeks post-treatment hemoglobin (P-value<0.001).

    b. In Group B, the average 2-weeks and 6-weeks post-treatment hemoglobin is significantly higher compared to baseline hemoglobin

(P-value<0.001 for both). Similarly, the average 6-weeks post-treatment hemoglobin is significantly higher compared to 2-weeks post-treatment hemoglobin (P-value<0.001).

c. In Group C, the average 2-weeks and 6-weeks post-treatment hemoglobin is significantly higher compared to baseline hemoglobin (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment hemoglobin is significantly higher compared to 2-weeks post-treatment hemoglobin (P-value<0.001).

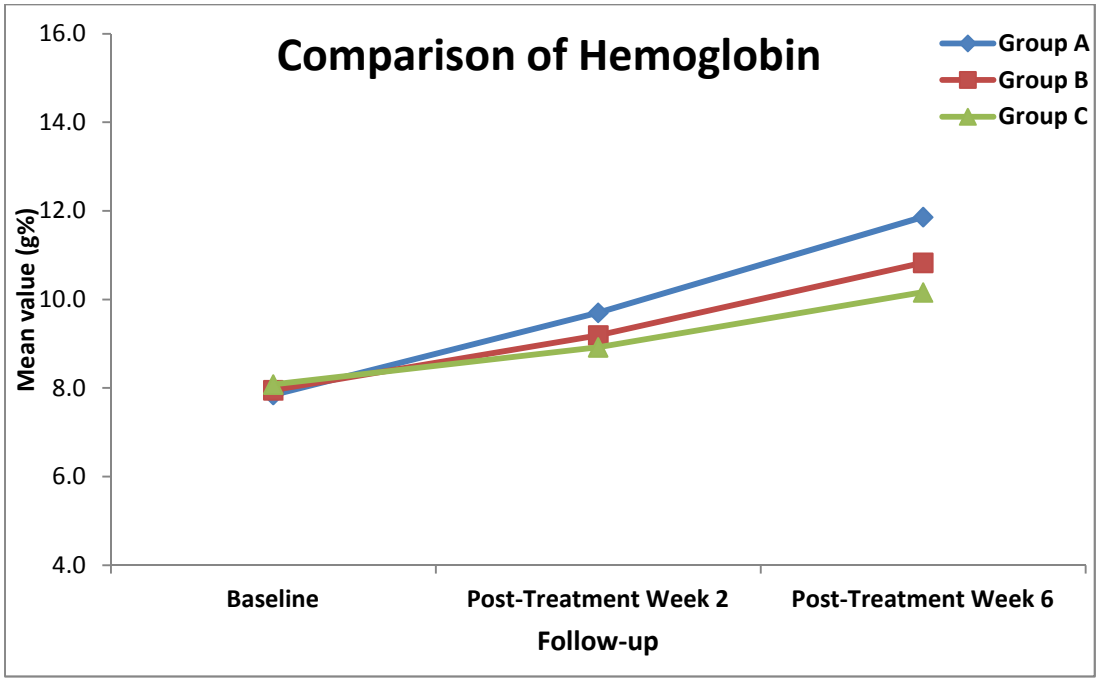

Figure 2a) The inter-group and intra-group comparison of hemoglobin measurements across three study groups.

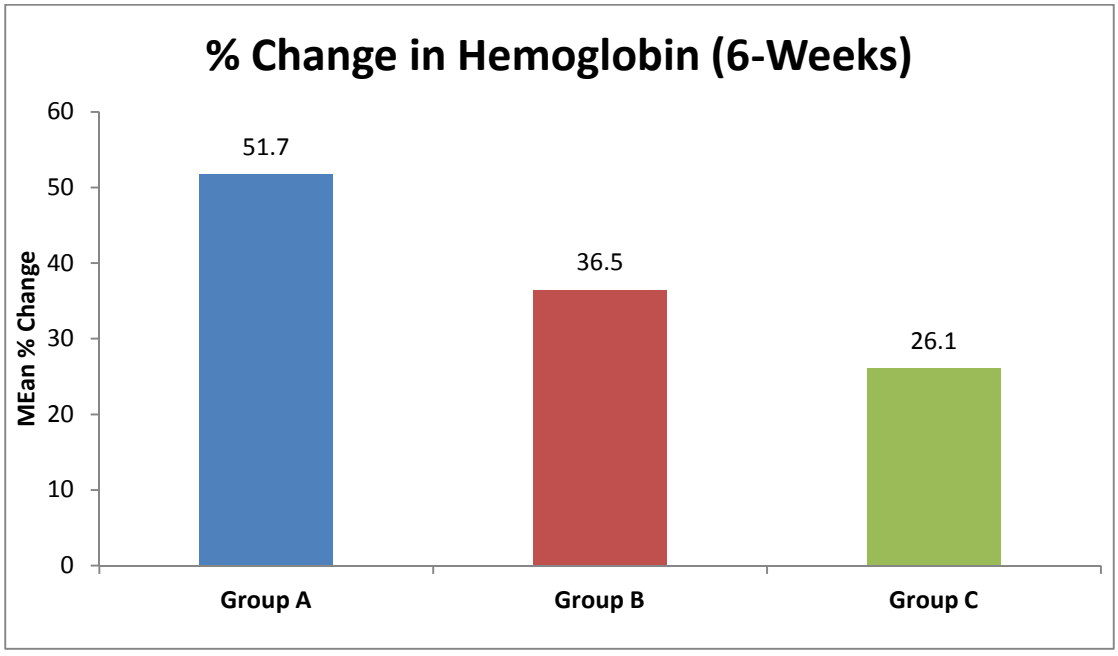

Figure 2b) The inter-group comparison of % change in hemoglobin at 6-weeks across three study groups.

Table 4) The inter-group and intra-group comparison of Platelet count measurements across three study groups.

Platelet count	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	2.80 ± 0.11	3.06 ± 0.12	2.78 ± 0.10	0.344^{NS}	0.999^{NS}	0.281^{NS}
2-Weeks	2.91 ± 0.08	2.68 ± 0.09	2.84 ± 0.12	0.262^{NS}	0.999^{NS}	0.673^{NS}
6-Weeks	2.74 ± 0.09	2.86 ± 0.08	2.86 ± 0.10	0.999^{NS}	0.069^{NS}	0.461^{NS}
% change at 6-Weeks	9.1%	2.4%	2.9%	0.999^{NS}	0.999^{NS}	0.264^{NS}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.423^{NS}	0.723^{NS}	0.185^{NS}			
Baseline v 6-Weeks	0.096^{NS}	0.167^{NS}	0.149^{NS}			
2-Weeks v 6-Weeks	0.635^{NS}	0.073^{NS}	0.846^{NS}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline platelet did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average 2-weeks and 6-weeks post-treatment platelet did not differ significantly across three study groups (P-value>0.05 for all).
    c. The average 6-weeks post-treatment % change in platelet did not differ significantly across three study groups (P-value>0.05 for all).
2) **Intra-Group Comparison:**
    a. In Group A, the average 2-weeks and 6-weeks post-treatment platelet did not differ significantly compared to baseline platelet (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment platelet did not differ significantly compared to 2-weeks platelet (P-value>0.05).
    b. In Group B, the average 2-weeks and 6-weeks post-treatment platelet did not differ significantly compared to baseline platelet (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment platelet did not differ significantly compared to 2-weeks platelet (P-value>0.05).
    c. In Group C, the average 2-weeks and 6-weeks post-treatment platelet did not differ significantly compared to baseline platelet (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment platelet did not differ significantly compared to 2-weeks platelet (P-value>0.05).

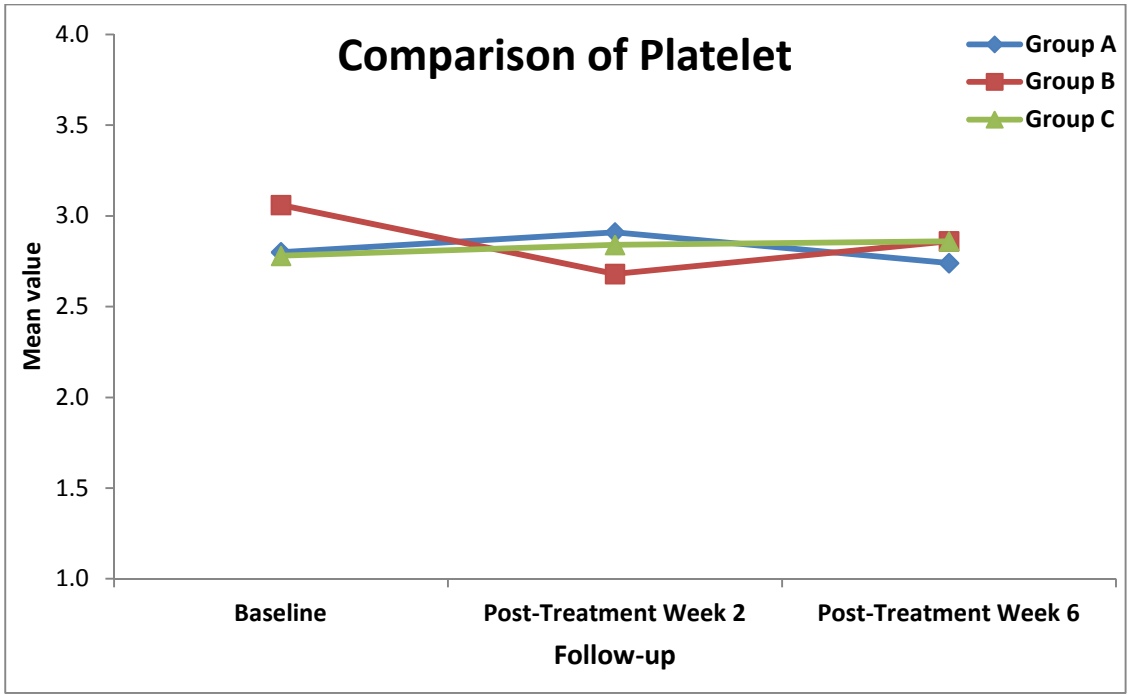

Figure 3a) The inter-group and intra-group comparison of Platelet measurements across three study groups.

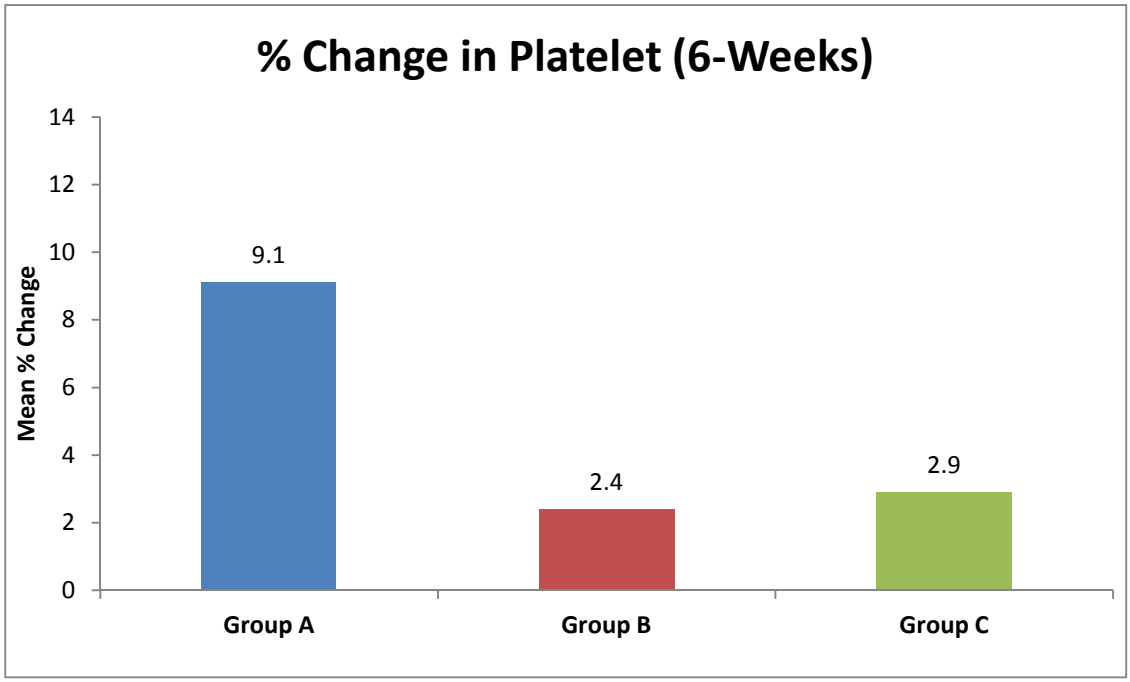

Figure 3b) The inter-group comparison of % change in Platelet at 6-weeks across three study groups.

Table 5) The inter-group and intra-group comparison of RBC measurements across three study groups.

RBC	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	3.60 ± 0.07	3.65 ± 0.06	3.76 ± 0.09	0.999^{NS}	0.238^{NS}	0.736^{NS}
2-Weeks	4.14 ± 0.07	4.13 ± 0.06	3.96 ± 0.10	0.999^{NS}	0.085^{NS}	0.060^{NS}
6-Weeks	4.58 ± 0.09	4.36 ± 0.10	4.19 ± 0.11	0.214^{NS}	0.097^{NS}	0.266^{NS}
% change at 6-Weeks	29.0%	21.4%	12.6%	0.714^{NS}	0.098^{NS}	0.167^{NS}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.221^{NS}	0.133^{NS}	0.197^{NS}			
Baseline v 6-Weeks	0.094^{NS}	0.082^{NS}	0.123^{NS}			
2-Weeks v 6-Weeks	0.110^{NS}	0.122^{NS}	0.345^{NS}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline RBC did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average 2-weeks and 6-weeks post-treatment RBC did not differ significantly across three study groups (P-value>0.05 for all).
    c. The average 6-weeks post-treatment % change in RBC did not differ significantly across three study groups (P-value>0.05 for all).
2) **Intra-Group Comparison:**
    a. In Group A, the average 2-weeks and 6-weeks post-treatment RBC did not differ significantly compared to baseline RBC (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment RBC did not differ significantly compared to 2-weeks RBC (P-value>0.05).
    b. In Group B, the average 2-weeks and 6-weeks post-treatment RBC did not differ significantly compared to baseline RBC (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment RBC did not differ significantly compared to 2-weeks RBC (P-value>0.05).
    c. In Group C, the average 2-weeks and 6-weeks post-treatment RBC did not differ significantly compared to baseline RBC (P-value>0.05 for both). Similarly, the average 6-weeks post-treatment RBC did not differ significantly compared to 2-weeks RBC (P-value>0.05).

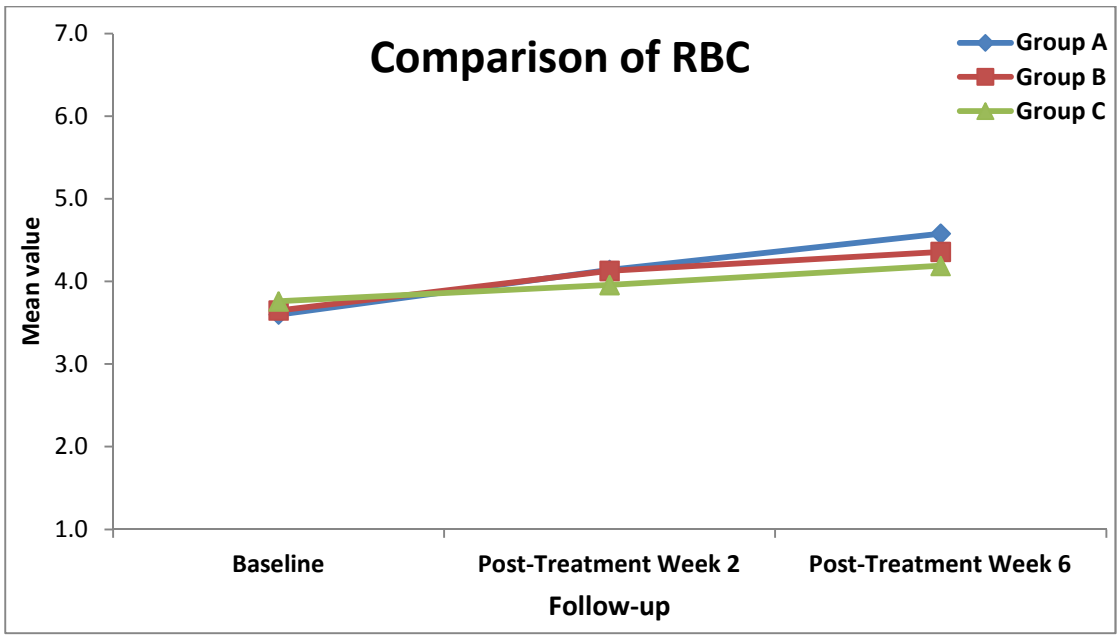

Figure 4a) The inter-group and intra-group comparison of RBC measurements across three study groups.

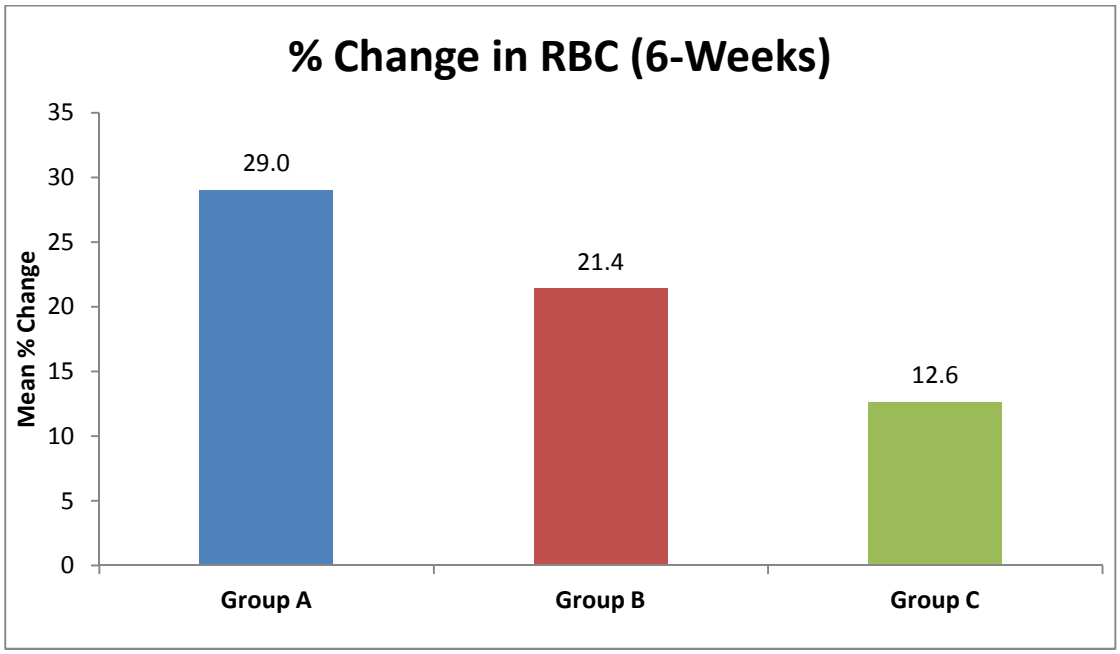

Figure 4b) The inter-group comparison of % change in RBC at 6-weeks across three study groups.

Table 6) The inter-group and intra-group comparison of PCV measurements across three study groups.

PCV	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	23.69 ± 0.28	23.93 ± 0.26	24.19 ± 0.35	0.999^{NS}	0.699^{NS}	0.999^{NS}
2-Weeks	27.89 ± 0.25	27.48 ± 0.29	27.16 ± 0.33	0.966^{NS}	0.914^{NS}	0.909^{NS}
6-Weeks	33.48 ± 0.29	32.51 ± 0.23	30.77 ± 0.29	0.311^{NS}	0.146^{NS}	0.347^{NS}
% change at 6-Weeks	42.1%	35.9%	27.2%	0.552^{NS}	0.096^{NS}	0.223^{NS}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline PCV did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average 2-weeks and 6-weeks post-treatment PCV did not differ significantly across three study groups (P-value>0.05 for all).
    c. The average 6-weeks post-treatment % change in PCV did not differ significantly across three study groups (P-value>0.05 for all).
2) **Intra-Group Comparison:**
    a. In Group A, the average 2-weeks and 6-weeks post-treatment PCV is significantly higher compared to baseline PCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment PCV is significantly higher compared to 2-weeks post-treatment PCV (P-value<0.001).
    b. In Group B, the average 2-weeks and 6-weeks post-treatment PCV is significantly higher compared to baseline PCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment PCV is significantly higher compared to 2-weeks post-treatment PCV (P-value<0.001).
    c. In Group C, the average 2-weeks and 6-weeks post-treatment PCV is significantly higher compared to baseline PCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment PCV is significantly higher compared to 2-weeks post-treatment PCV (P-value<0.001).

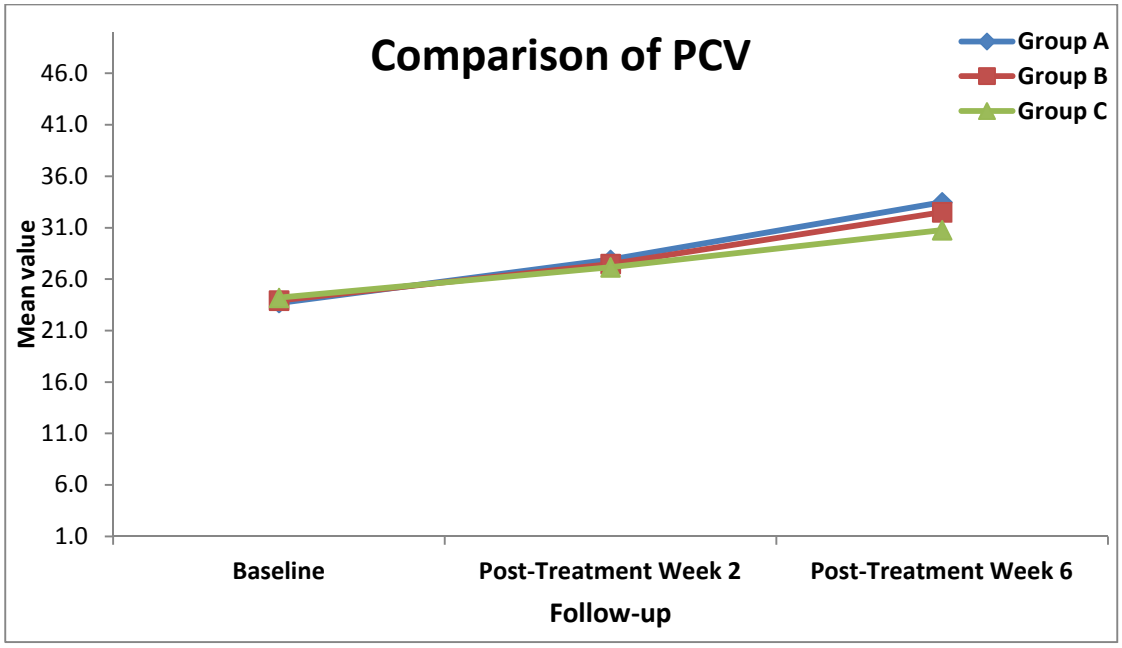

Figure 5a) The inter-group and intra-group comparison of PCV measurements across three study groups.

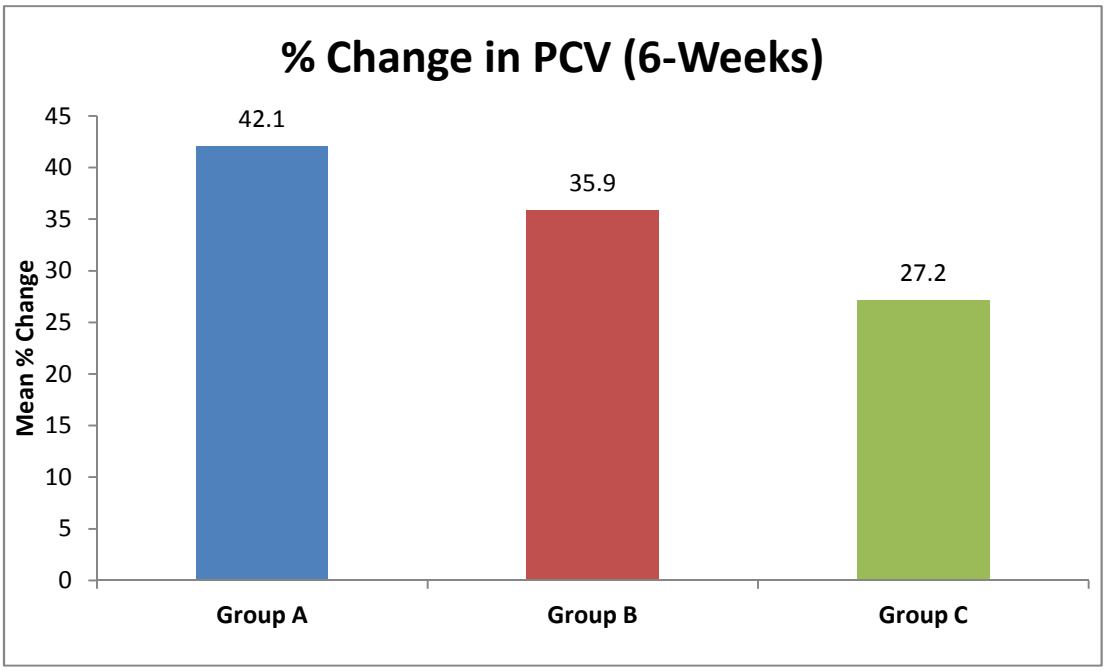

Figure 5b) The inter-group comparison of % change in PCV at 6-weeks across three study groups.

Table 7) The inter-group and intra-group comparison of MCV measurements across three study groups.

MCV	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	70.48 ± 0.75	68.94 ± 0.95	68.49 ± 1.12	0.760^{NS}	0.422^{NS}	0.999^{NS}
2-Weeks	80.60 ± 0.59	79.13 ± 0.74	77.59 ± 0.95	0.641^{NS}	0.510^{NS}	0.823^{NS}
6-Weeks	88.21 ± 0.31	86.98 ± 0.49	83.43 ± 0.75	0.600^{NS}	0.242^{NS}	0.569^{NS}
% change at 6-Weeks	25.7%	27.1%	22.7%	0.999^{NS}	0.313^{NS}	0.057^{NS}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**

    a. The average baseline MCV did not differ significantly across three study groups (P-value>0.05 for all).

    b. The average 2-weeks and 6-weeks post-treatment MCV did not differ significantly across three study groups (P-value>0.05 for all).

    c. The average 6-weeks post-treatment % change in MCV did not differ significantly across three study groups (P-value>0.05 for all).

2) **Intra-Group Comparison:**

    a. In Group A, the average 2-weeks and 6-weeks post-treatment MCV is significantly higher compared to baseline MCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCV is significantly higher compared to 2-weeks post-treatment MCV (P-value<0.001).

    b. In Group B, the average 2-weeks and 6-weeks post-treatment MCV is significantly higher compared to baseline MCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCV is significantly higher compared to 2-weeks post-treatment MCV (P-value<0.001).

    c. In Group C, the average 2-weeks and 6-weeks post-treatment MCV is significantly higher compared to baseline MCV (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCV is significantly higher compared to 2-weeks post-treatment MCV (P-value<0.001).

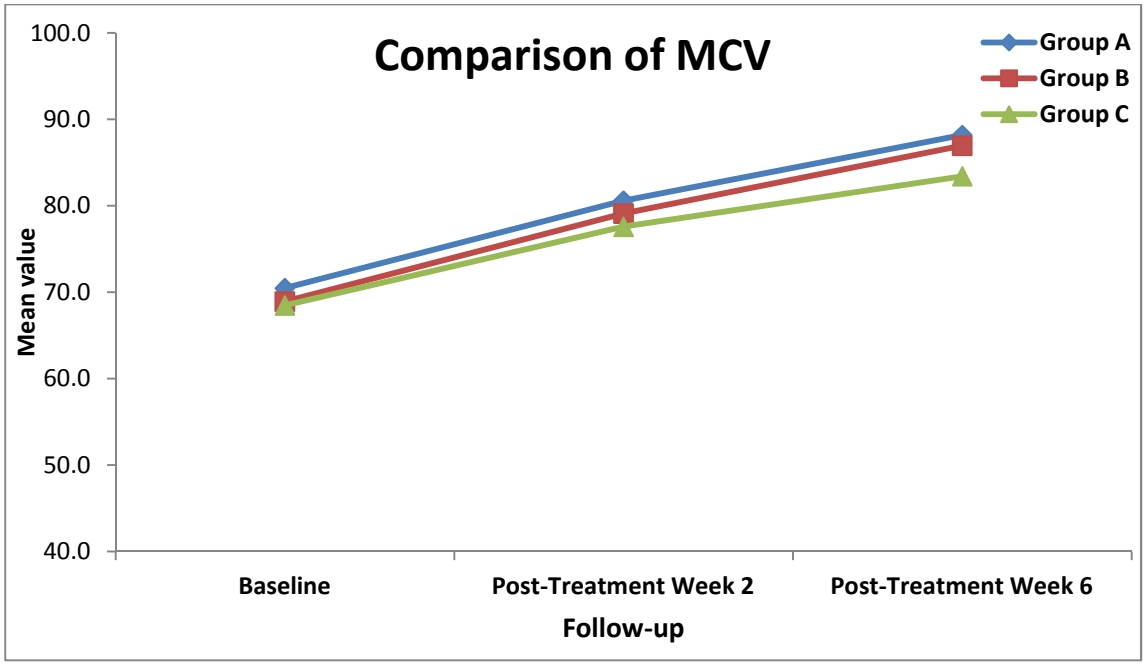

Figure 6a) The inter-group and intra-group comparison of MCV measurements across three study groups.

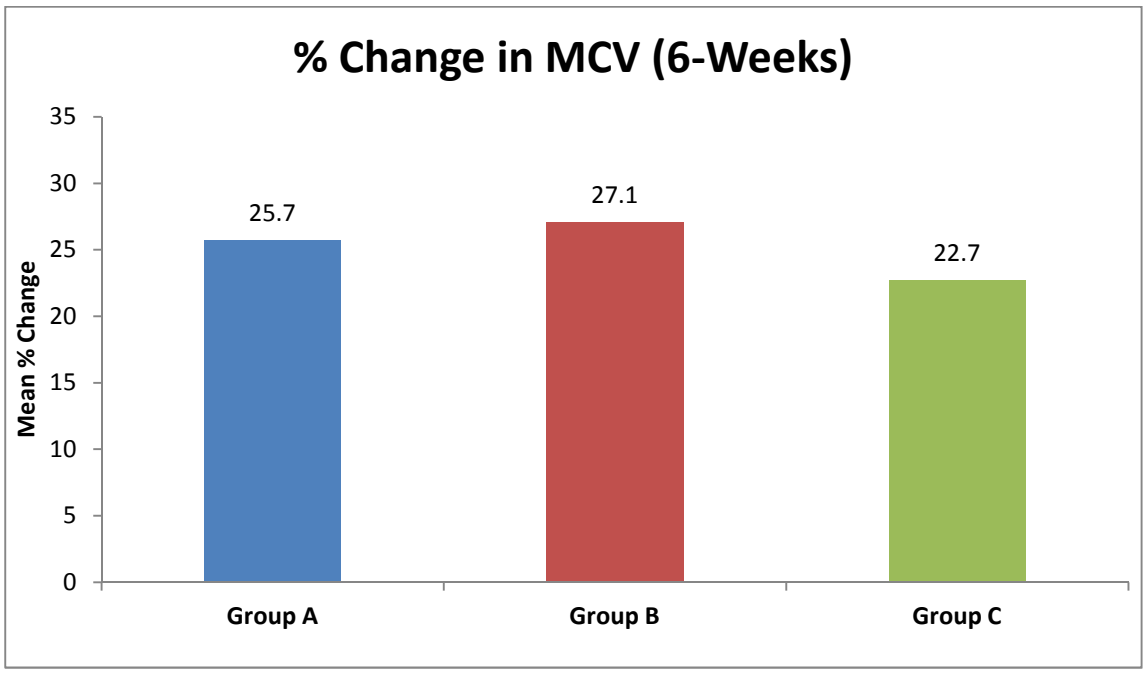

Figure 6b) The inter-group comparison of % change in MCV at 6-weeks across three study groups.

Table 8) The inter-group and intra-group comparison of MCH measurements across three study groups.

MCH	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	21.09 ± 0.29	21.16 ± 0.25	21.18 ± 0.29	0.999^{NS}	0.999^{NS}	0.999^{NS}
2-Weeks	23.49 ± 0.26	22.57 ± 0.24	22.08 ± 0.29	0.048^{*}	0.002^{**}	0.035^{*}
6-Weeks	32.37 ± 0.31	28.95 ± 0.21	26.51 ± 0.27	0.001^{***}	0.001^{***}	0.001^{***}
% change at 6-Weeks	54.4%	37.6%	25.7%	0.001^{***}	0.001^{***}	0.001^{***}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline MCH did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average 2-weeks post-treatment MCH is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 2-weeks post-treatment MCH is significantly higher in group B compared to group C (P-value<0.05).
    c. The average 6-weeks post-treatment MCH is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment MCH is significantly higher in group B compared to group C (P-value<0.05).
    d. The average 6-weeks post-treatment % change in MCH is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment % change in MCH is significantly higher in group B compared to group C (P-value<0.05).
2) **Intra-Group Comparison:**
    a. In Group A, the average 2-weeks and 6-weeks post-treatment MCH is significantly higher compared to baseline MCH (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCH is significantly higher compared to 2-weeks post-treatment MCH (P-value<0.001).
    b. In Group B, the average 2-weeks and 6-weeks post-treatment MCH is significantly higher compared to baseline MCH (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCH is

significantly higher compared to 2-weeks post-treatment MCH (P-value<0.001).

c. In Group C, the average 2-weeks and 6-weeks post-treatment MCH is significantly higher compared to baseline MCH (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCH is significantly higher compared to 2-weeks post-treatment MCH (P-value<0.001).

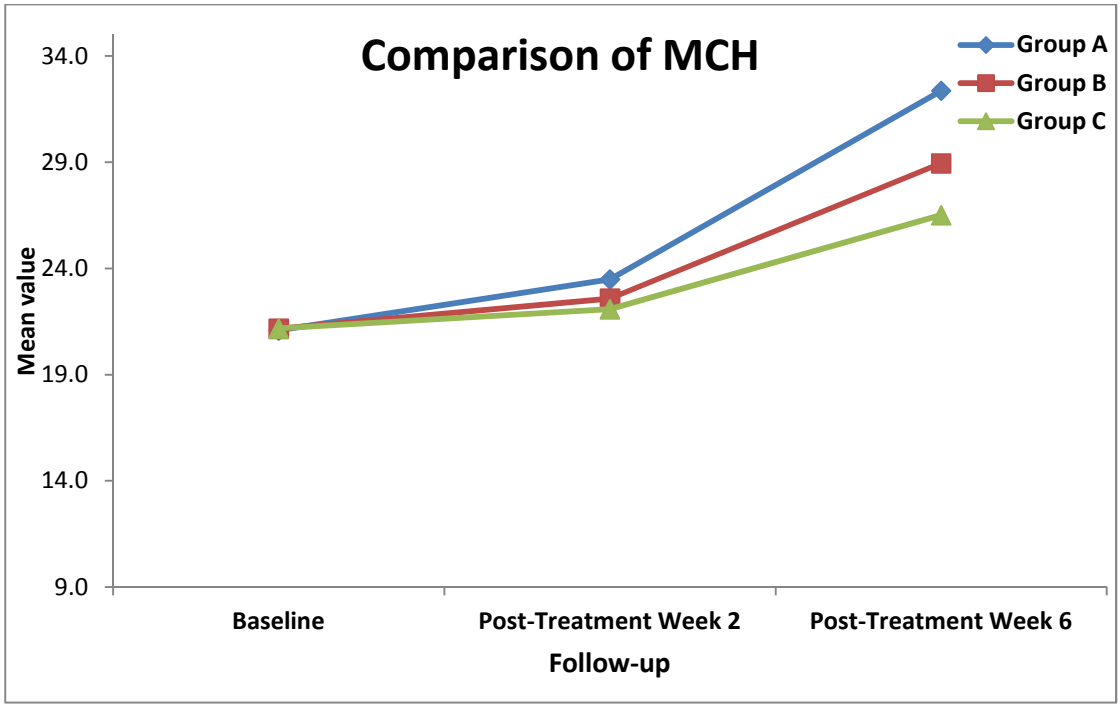

Figure 7a) The inter-group and intra-group comparison of MCH measurements across three study groups.

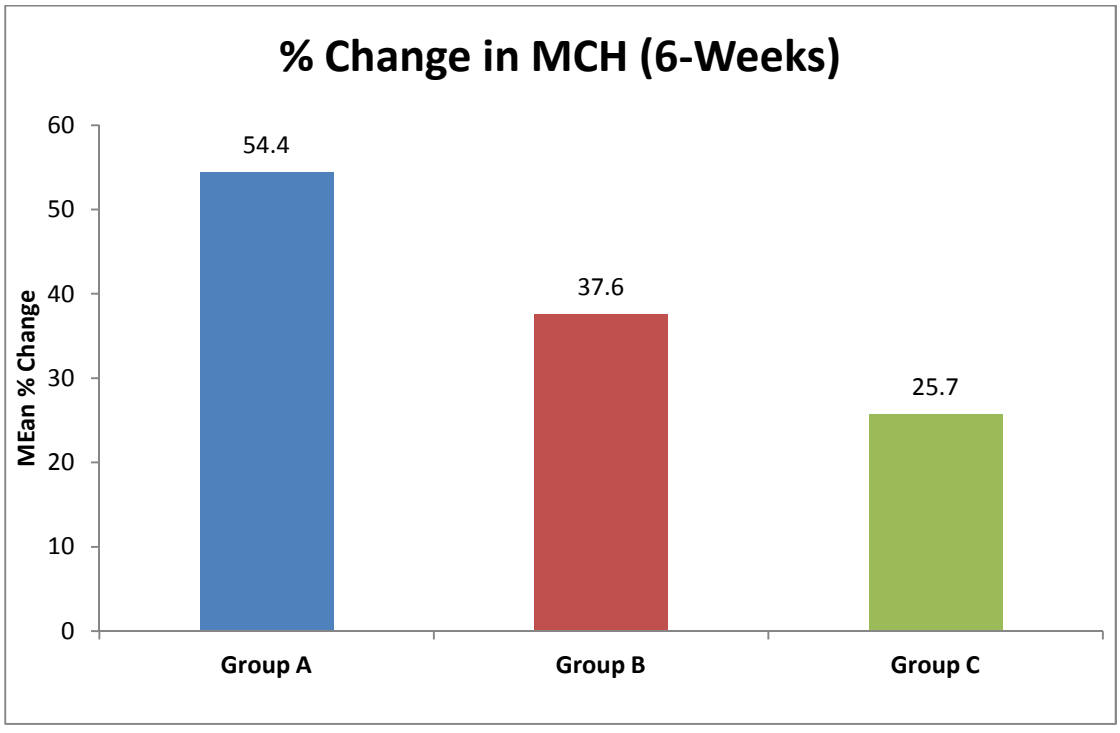

Figure 7b) The inter-group comparison of % change in MCH at 6-weeks across three study groups.

Table 9) The inter-group and intra-group comparison of MCHC measurements across three study groups.

MCHC	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	26.00 ± 0.30	25.91 ± 0.32	25.96 ± 0.30	0.999^{NS}	0.999^{NS}	0.999^{NS}
2-Weeks	29.94 ± 0.26	28.77 ± 0.33	27.58 ± 0.32	0.023^{*}	0.001^{***}	0.022^{*}
6-Weeks	32.87 ± 0.20	31.59 ± 0.23	30.54 ± 0.32	0.002^{**}	0.001^{***}	0.012^{*}
% change at 6-Weeks	29.2%	22.6%	17.9%	0.041^{*}	0.001^{***}	0.048^{*}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**

    a. The average baseline MCHC did not differ significantly across three study groups (P-value>0.05 for all).

    b. The average 2-weeks post-treatment MCHC is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 2-weeks post-treatment MCHC is significantly higher in group B compared to group C (P-value<0.05).

    c. The average 6-weeks post-treatment MCHC is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment MCHC is significantly higher in group B compared to group C (P-value<0.05).

    d. The average 6-weeks post-treatment % change in MCHC is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment % change in MCHC is significantly higher in group B compared to group C (P-value<0.05).

2) **Intra-Group Comparison:**

    a. In Group A, the average 2-weeks and 6-weeks post-treatment MCHC is significantly higher compared to baseline MCHC (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCHC is significantly higher compared to 2-weeks post-treatment MCHC (P-value<0.001).

    b. In Group B, the average 2-weeks and 6-weeks post-treatment MCHC is significantly higher compared to baseline MCHC (P-value<0.001 for

both). Similarly, the average 6-weeks post-treatment MCHC is significantly higher compared to 2-weeks post-treatment MCHC (P-value<0.001).

c. In Group C, the average 2-weeks and 6-weeks post-treatment MCHC is significantly higher compared to baseline MCHC (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment MCHC is significantly higher compared to 2-weeks post-treatment MCHC (P-value<0.001).

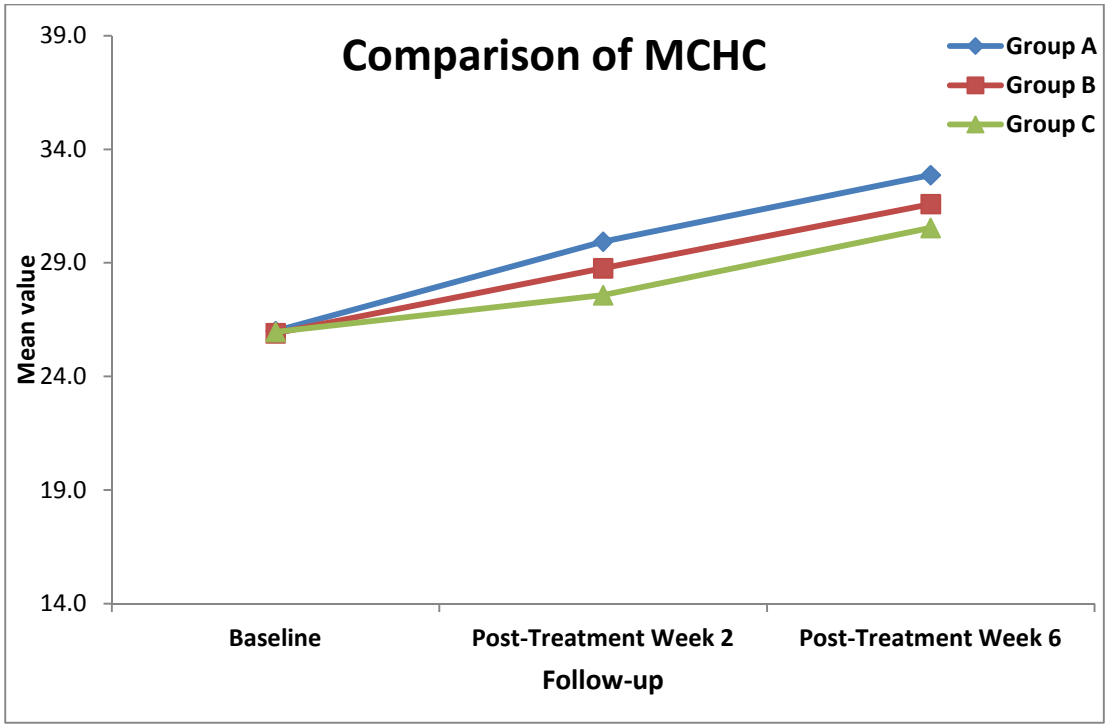

Figure 8a) The inter-group and intra-group comparison of MCHC measurements across three study groups.

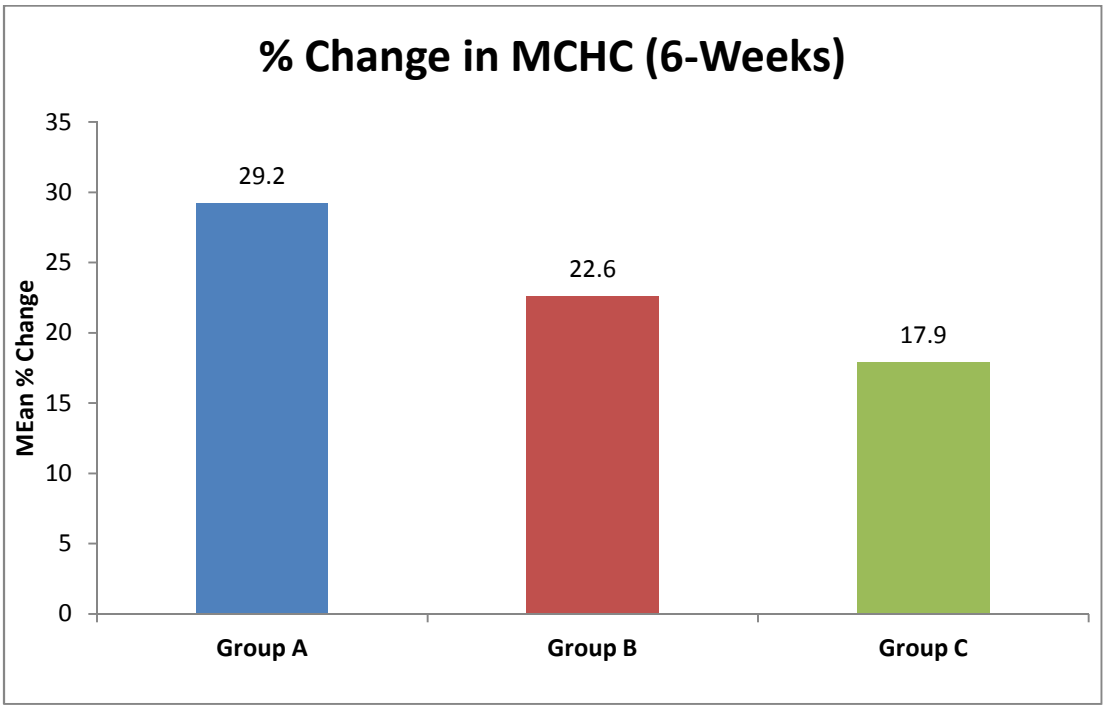

Figure 8b) The inter-group comparison of % change in MCHC at 6-weeks across three study groups.

Table 10) The inter-group and intra-group comparison of RETICULOCUTE measurements across three study groups.

RETICULOCYTE	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	1.35 ± 0.03	1.40 ± 0.03	1.46 ± 0.04	0.852^{NS}	0.066^{NS}	0.650^{NS}
2-Weeks	2.20 ± 0.03	1.91 ± 0.03	1.66 ± 0.04	0.001^{***}	0.001^{***}	0.001^{***}
6-Weeks	3.30 ± 0.04	2.92 ± 0.05	2.25 ± 0.05	0.001^{***}	0.001^{***}	0.001^{***}
% change at 6-Weeks	147.4%	110.3%	56.7%	0.001^{***}	0.001^{***}	0.001^{***}
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			
2-Weeks v 6-Weeks	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**

    a. The average baseline RETICULOCYTE did not differ significantly across three study groups (P-value>0.05 for all).

    b. The average 2-weeks post-treatment RETICULOCYTE is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 2-weeks post-treatment RETICULOCYTE is significantly higher in group B compared to group C (P-value<0.001).

    c. The average 6-weeks post-treatment RETICULOCYTE is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 6-weeks post-treatment RETICULOCYTE is significantly higher in group B compared to group C (P-value<0.001).

    d. The average 6-weeks post-treatment % change in RETICULOCYTE is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment % change in RETICULOCYTE is significantly higher in group B compared to group C (P-value<0.05).

2) **Intra-Group Comparison:**

    a. In Group A, the average 2-weeks and 6-weeks post-treatment RETICULOCYTE is significantly higher compared to baseline RETICULOCYTE (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment RETICULOCYTE is significantly higher compared to 2-weeks post-treatment RETICULOCYTE (P-value<0.001).

b. In Group B, the average 2-weeks and 6-weeks post-treatment RETICULOCYTE is significantly higher compared to baseline RETICULOCYTE (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment RETICULOCYTE is significantly higher compared to 2-weeks post-treatment RETICULOCYTE (P-value<0.001).

c. In Group C, the average 2-weeks and 6-weeks post-treatment RETICULOCYTE is significantly higher compared to baseline RETICULOCYTE (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment RETICULOCYTE is significantly higher compared to 2-weeks post-treatment RETICULOCYTE (P-value<0.001).

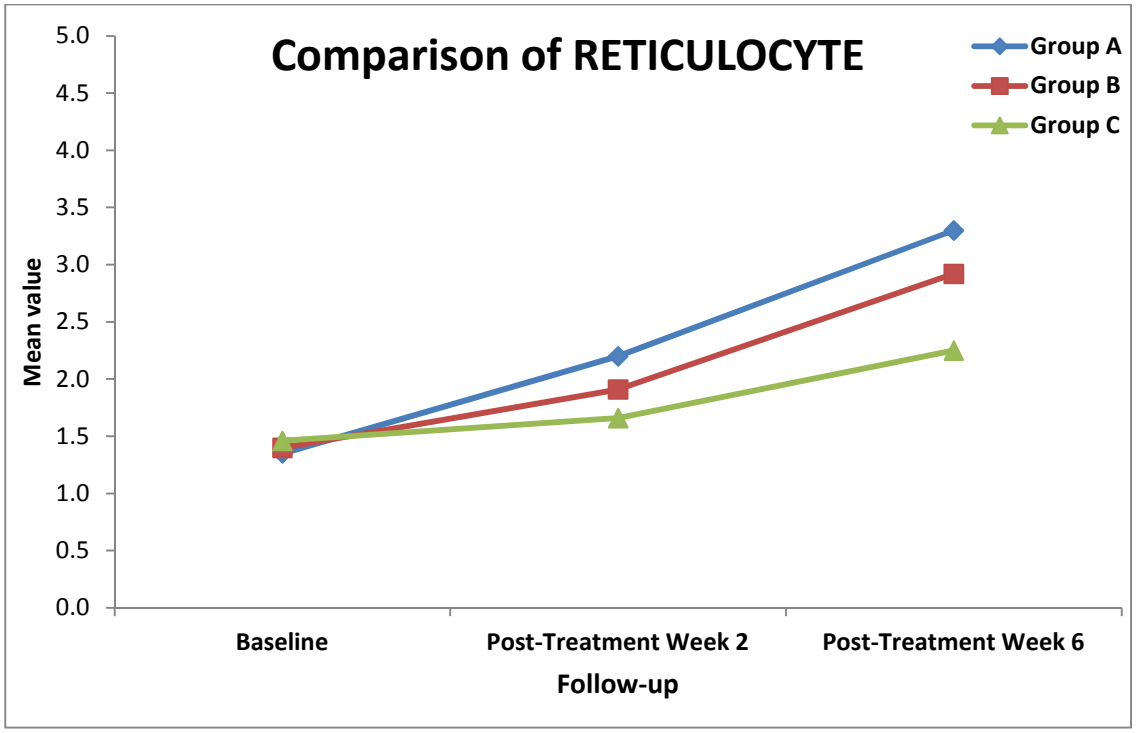

Figure 9a) The inter-group and intra-group comparison of RETICULOCYTE measurements across three study groups.

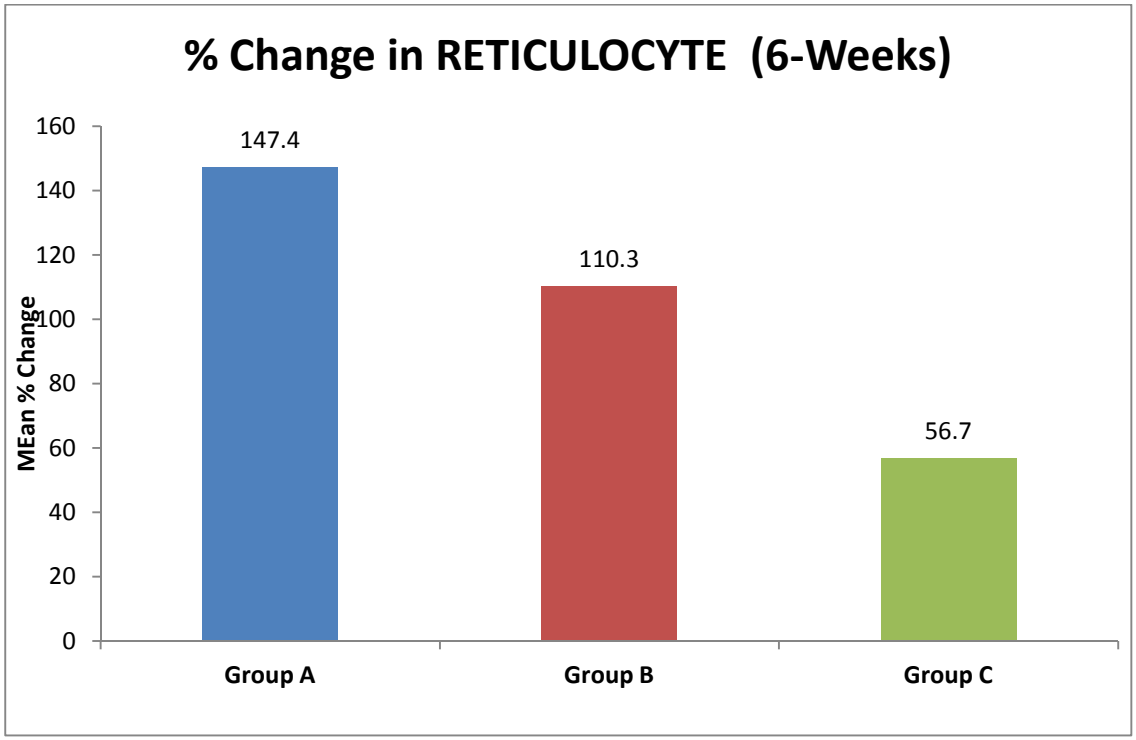

Figure 9b) The inter-group comparison of % change in RETICULOCYTE at 6-weeks across three study groups.

Table 11) The inter-group and intra-group comparison of Sr. Ferritin measurements across three study groups.

Sr. Ferritin	Group A (n=50)	Group B (n=50)	Group C (n=50)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	14.43 ± 0.82	13.06 ± 0.65	13.71 ± 0.71	0.564^{NS}	0.999^{NS}	0.999^{NS}
2-Weeks	40.02 ± 1.18	31.92 ± 0.87	27.56 ± 0.99	0.001***	0.001***	0.001***
6-Weeks	102.13 ± 2.07	78.28 ± 1.97	57.22 ± 1.81	0.001***	0.001***	0.001***
% change at 6-Weeks	691.8%	562.3%	350.4%	0.001***	0.001***	0.001***
Intra-Group Comparisons (P-value)						
Baseline v 2-Weeks	0.001***	0.001***	0.001***			
Baseline v 6-Weeks	0.001***	0.001***	0.001***			
2-Weeks v 6-Weeks	0.001***	0.001***	0.001***			

Values are Mean ± Standard error of mean (SEM). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using repeated measures analysis of variance (ANOVA) technique. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**

    a. The average baseline Sr. Ferritin did not differ significantly across three study groups (P-value>0.05 for all).

    b. The average 2-weeks post-treatment Sr. Ferritin is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 2-weeks post-treatment Sr. Ferritin is significantly higher in group B compared to group C (P-value<0.001).

    c. The average 6-weeks post-treatment Sr. Ferritin is significantly higher in group A compared to groups B and C (P-value<0.001 for all). The average 6-weeks post-treatment Sr. Ferritin is significantly higher in group B compared to group C (P-value<0.001).

    d. The average 6-weeks post-treatment % change in Sr. Ferritin is significantly higher in group A compared to groups B and C (P-value<0.05 for all). The average 6-weeks post-treatment % change in Sr. Ferritin is significantly higher in group B compared to group C (P-value<0.05).

2) **Intra-Group Comparison:**

    a. In Group A, the average 2-weeks and 6-weeks post-treatment Sr. Ferritin is significantly higher compared to baseline Sr. Ferritin (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment Sr. Ferritin is significantly higher compared to 2-weeks post-treatment Sr. Ferritin (P-value<0.001).

    b. In Group B, the average 2-weeks and 6-weeks post-treatment Sr. Ferritin is significantly higher compared to baseline Sr. Ferritin (P-

value<0.001 for both). Similarly, the average 6-weeks post-treatment Sr. Ferritin is significantly higher compared to 2-weeks post-treatment Sr. Ferritin (P-value<0.001).

c. In Group C, the average 2-weeks and 6-weeks post-treatment Sr. Ferritin is significantly higher compared to baseline Sr. Ferritin (P-value<0.001 for both). Similarly, the average 6-weeks post-treatment Sr. Ferritin is significantly higher compared to 2-weeks post-treatment Sr. Ferritin (P-value<0.001).

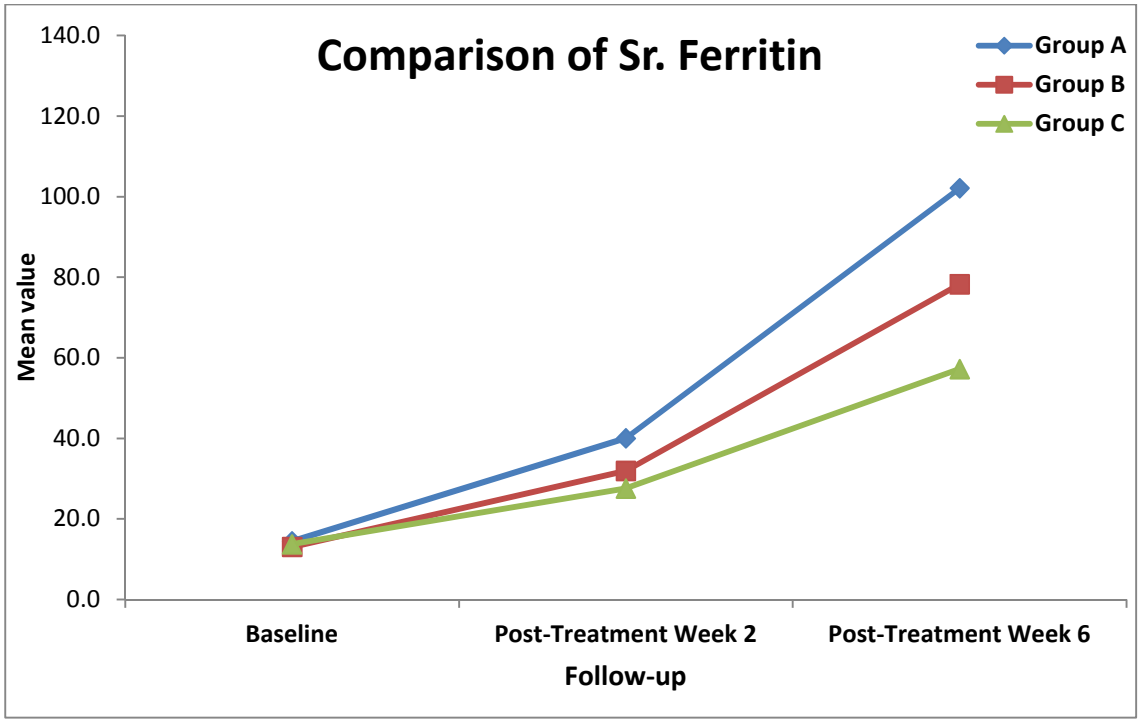

Figure 10a) The inter-group and intra-group comparison of Sr. Ferritin measurements across three study groups.

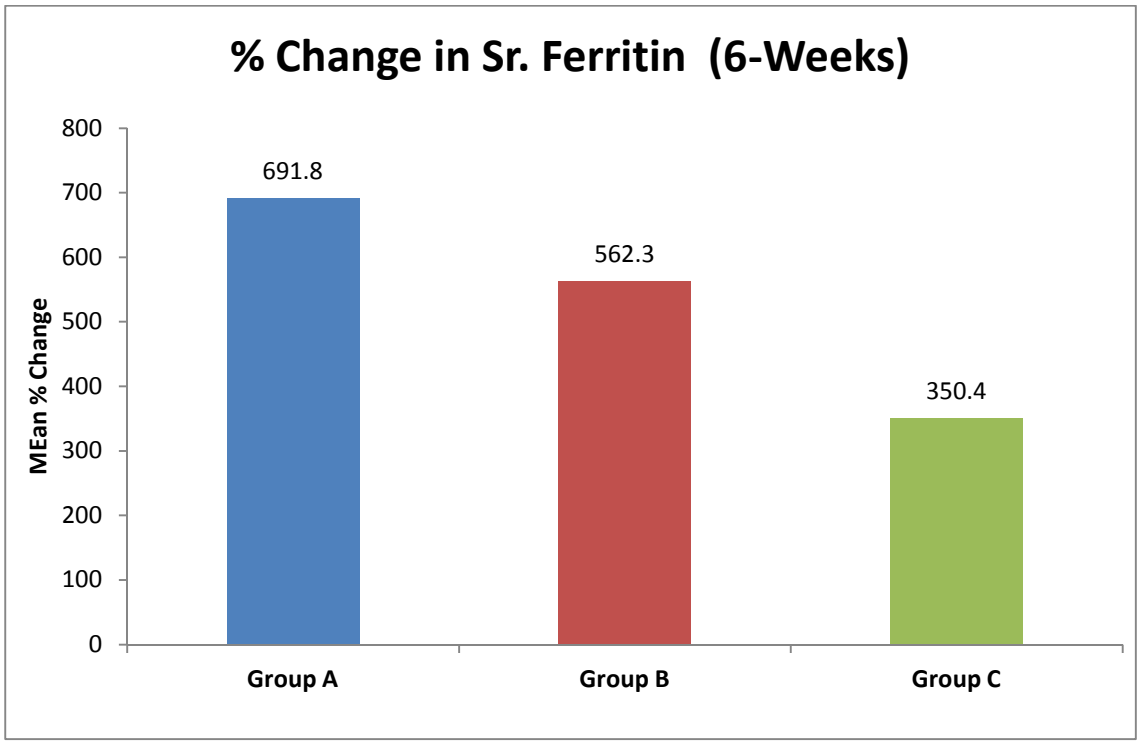

Figure 10b) The inter-group comparison of % change in Sr. ferritin at 6-weeks across three study groups.

DISCUSSION

Iron-deficiency anaemia is a major health problem worldwide, and responds well to iron supplementation. The constellation of factors producing iron deficiency anaemia generally precedes the pregnancy, including diet deficient in iron content coupled with menstrual losses and a rapid succession of pregnancies in which supplemental iron is not provided. Most women begin their pregnancy with partially or completely depleted iron reserves. Thus, the severity of the iron deficiency anaemia is inversely related to the amount of iron reserves.[8]

Compared to western women whose iron stores are sufficient and the requirement is 30-40 mg elemental iron per day for anaemia prophylaxis in pregnancy,[63,64] the stores in Indian women are deficient and they need 100 mg elemental iron per day for prophylaxis. Dose recommended for treatment of anaemia is 200 mg elemental iron per day.[64] During pregnancy, the total requirement of iron is approximately 1000 mg (500 mg for developing foetus and placenta and similar amount for red cell increment).[32]

Certain studies have shown that Hb levels <8 g% (moderate to severe anaemia) in pregnant women are associated with higher maternal morbidity. [6,32] Parentral iron therapy is superior to oral iron with respect to faster increase in Hb and faster replenishment of body iron stores[65] and it also reduces the need of blood transfusions.[66]

The rapid delivery option of a large single dose of ferric carboxymaltose offers a promising treatment modality for pregnant women with iron deficiency anaemia, over other IV iron formulations that have low dosage limits, such as iron sucrose (200 mg) and iron sorbitol citric acid. The properties of ferric carboxymaltose reduces the burden on the patient and the health care system. Two recent retrospective

observational studies comparing ferric carboxymaltose with other intravenous iron preparations highlights the safety and efficacy of ferric carboxymaltose.[15, 67]

In a study conducted by A. Wali et al[68] at Aga Khan Hospital for women and children Karachi on 60 pregnant women at 12-34 weeks gestation with iron deficiency anaemia, this study compared I/V iron sucrose to iron sorbitol. The mean increase of 2.6g/dl Hb was seen in IV iron sucrose group. In our study mean increase of 2.88 gm/dl was seen in IV iron sucrose group.

Guidelines from the American College of Obstetricians and Gynecologists on anemia of pregnancy (ACOG 2008) states that parenteral iron is useful in patients who cannot tolerate or will not take modest doses of oral iron. Patients having malabsorption syndrome and severe iron deficiency anemia may benefit from parenteral therapy.

Intravenous iron treated iron deficiency anaemia of pregnancy restores iron stores faster and more effectively than oral iron, having no serious adverse reaction.[69] Hookworm is one of the cause for anaemia in developing countries. Routine antihelminthic therapy in pregnancy is not recommended, but due to high prevalence in developing countries including India, it is advisable to give antihelminthic therapy to pregnant women who present with anaemia[70]. In our study, all women were given a single dose of Albendazole prior to the parentral iron therapy.

The study by Breymann C et al[71] showed a mean rise in the hemoglobin level was 1.7 g/dl, 25 days after the iron sucrose therapy. And in a study by Wali et al[68] showed the hemoglobin level rise of 2.6 g/dl after 3.6 weeks. In our study the earliest rise in Hb was seen at 15 days. Mean rise of Hb was 1.86 gm/dl, 1.24gm/dl and 0.84 gm/dl for FCM group, Iron sucrose group and Iron sorbitol group respectively. That means practically increase in Hb level is not as much as expected. At 6 weeks, mean

rise in Hb levels are 4.02 gm/dl, 2.88 gm/dl and 2.08 gm/dl for FCM group, iron sucrose group and iron sorbitol group respectively.

In our study too we obsevered that the rise in the hemoglobin concentration was not similar in the iron sorbitol citric acid group to that of the iron sucrose group and ferric carboxymaltose group after the 14 days of the parenteral therapy. The reason may be that nearly 33-35% of iron sorbitol citric acid is excreted just after the injection and also its release from the reticuloendothelial system is much slower compared to iron sucrose release from liver parenchymal cells.[72, 73]

Two conclusions that we have drawn from this observation is :

a) A dose of 1000mg of sorbitol is not equivalent to the 1000mg of Ferric Carboxymaltose and iron sucrose.
b) Probably a higher dose of sorbitol is needed to achieve the same change in blood parameters. The side effects would increase proportionately.

The main problem with the iron sorbitol citric acid was its side effects. As iron sorbitol has much low molecular weight and has high transferrin saturation capacity, it cannot be given as high intravenous bolus or infusion.[74,75] Therefore, it is used only intramuscularly. But, the most common complaint in this study was pain at the site of injection (24%) with intramuscular injection of iron sorbitol citric acid, which was found to be similar to the study by Wali et al.[68] Other side effects such as swelling and blackening of skin (20%) were major complaints in the iron sorbitol citric acid therapy group. There is no patient dropout in our study but the patient dropout is higher in the iron sorbitol citric acid therapy group, as seen in the study conducted by Wali et al.[68] Therefore, all these side effects of the iron sorbitol citric acid contributes for decrease in the compliance of the pregnant women and increase in drop rates.

Table 12: Side effects of three drugs

	GROUP A	GROUP B	GROUP C
Local Pain	0	0	12
Skin staining	0	0	10
Shivering	2	3	0
Local Phlebitis	4	7	0
Headache	1	4	6
Local Induration	0	0	4

There are minor adverse effects seen in Group A and Group B. Shivering is seen in 4% of group A and 6% of group B while local phlebitis in 8% and 14% respectively. Headache and weakness (12%) and local induration (8%) is observed in group C where as headache and weakness is seen 2% in group A and 8% in group B. The adverse events seen in iron sorbitol citric acid group are not seen with the iron sucrose complex and ferric carboxymaltose therapies. Till date, one death has been reported with intravenous iron sucrose injection[76] and the explanation given for this was because of very slow infusion (1-2 h) and the cause of death may be free radicals released from the iron sucrose. The injection should be given within 15-20 min upto 200 mg. This case is available on clinical trial registry site[76] and has not been mentioned in the literature. In the present study, there has been no major side effect reported. In vitro study using a dual-placenta perfusion model shows that ferric carboxymaltose does not cross the placental barrier to the fetal side.[23]

The main problem with iron sucrose and ferric carboxymaltose therapies is its cost compared to iron sorbitol citric acid group. A total dose of therapy with the iron sucrose complex (inclusive of storage) costs between Rs. 2500 to 3000 compared to

Ferric carboxymaltose which costs between Rs. 5000 to Rs. 6000 and iron sorbitol which costs between Rs. 400 to Rs. 500. In country like India the majority of the pregnant women suffering from iron deficiency anemia belong to middle to lower socioeconomic class and to purchase a complete dose of parenteral iron therapy is an economic burden.

SUMMARY

Anemia in pregnancy is a potentially fatal condition in itself. Besides, it compounds a number of other problems like APH, PPH, possibly infections in mother and FGR in the fetus.

Parentral iron is a sound option in patients when i) tolerance, ii) oral not effective, iii) less time to delivery. In our study ferric carboxymaltose has found to be the most effective and the fastest drug in correction of anemia compared to iron sucrose and iron sorbitol. Iron sucrose has also found to be an extremely effective parentral preparation but effectivity less than ferric carboxymaltose. Iron sorbitol has found to be least effective and the slowest, but in our study, it still stood its ground and came out as a viable option for patients who cannot afford. The a) high costs of the other two drugs, b) had 4 weeks - 6 weeks to delivery and c) were ready to take multiple intramuscular injections.

CONCLUSION

In our study, a 150 anemic pregnant women were randomised to one of the three treatment options- ferric carboxymaltose 1000mg infusions, iron sucrose 1000mg infusion and iron sorbitol 1000mg intramuscular injections.

All patients were also dewormed at the beginning of the study. Vitamin B12 500 mcg and folic acid 15 mg were added to the FCM and sucrose group patients. These vitamins were already present in the iron sorbitol citric acid complex (650 mcg Vitamin B12 and 6.5 mg Folic acid in 13 injections).

Ferric carboxymaltose was the parentral iron preparation which induced the maximum increase in all the blood parameters significant are Hb and Serum Ferritin. FCM was the most convenient single dose therapy compared to the other iron preparations, it caused the minimum side effect. The only negative point for FCM was the prohibitive cost for a single dose, that is, Rs. 5000 to Rs. 6000. Hence, in cases where there time is the limiting factor FCM would be the drug of choice for getting the fastest rise in Hb levels but at the cost of increased expenses. The effects for iron sucrose were in between FCM and iron sorbitol groups. The increase in Hb at 2 weeks has significantly less than FCM but significantly more than iron sorbitol. Hence in cases where at least 6 weeks are anticipated to be available for getting an increase in Hb level, iron sucrose could be a cheaper alternative to FCM, but at the cost of a slightly less rise in Hb and Serum Ferritin.

Iron Sorbitol- The “Poor Mans Iron” cuases an average increase in Hb of 2.08 gm/dl and Serum Ferritin of 43.51ng/ml at 6 weeks. Even though these values are statistically very low compared to the other groups, the rise in the above parameters is clinically satisfactory. Hence, if we have sufficient time (6 weeks) on hand but the patient is unable to spend on the other two drugs, iron sorbitol is still a viable option

to improve the anemia status of the woman. The Poor Mans Iron is significantly poor in improvement in blood parameters when compared to the other two drugs, but standing alone, where there is no other option, either due to non availability or due to prohibitive costs, it gives a satisfactory improvement in patient profile than with no therapy alone.

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ANNEXURE-I

ETHICAL CLEARANCE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. SD/13
Date 14-11-13
BLDE U's Shri B.M. Patil

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2013 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Intravenous ferric carboxymaltose intraven-ous iron Sucrose & intramuscular iron Sorbitol in pregnancy: A Randomised Controlled trail"

Name of P.G. student Dr. Patil Keval Ashok.

Department of Obstetrics and Gynecology.

Name of Guide/Co-investigator Dr Manpreet J. Tekalia, Professor.

Department of Obstetrics and Gynecology.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-I I

CONSENTS FORM

<u>TITLE OF THE TOPIC</u>: COMPARISON OF INTRAVENOUS FERRIC CARBOXYMALTOSE, INTRAVENOUS IRON SUCROSE AND INTRAMUSCULAR IRON SORBITOL IN ANEMIA IN PREGNANCY: A RANDOMISED CONTROLLED TRIAL

DURATION OF STUDY **:** October 2013 - June 2015

PRINCIPAL INVESTIGATOR **:** **Dr. PATIL KEVAL ASHOK**

PG GUIDE NAME **:** **Dr. MANPREET KAUR J. TEHALIA**

PURPOSE OF RESEARCH:

To find out the relative efficacy and cost effectiveness of three therapeutic agents in patients with iron deficiency anemia in pregnancy.

PROCEDURE

I understand that I will be a part of this study. My history and physical findings will be recorded and evaluated in a systematic way, but will be kept confidential. I may be asked for follow-up.

RISK AND DISCOMFORTS

I understand that this procedure is not expected to aggravate any side effect or cause detrimental effect to me.

BENEFITS:

As I am suffering from Iron deficiency anemia, I will be treated for the same, as this condition can give rise to serious complications for both me and my child, if left untreated.

CONFIDENTIALITY

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality and privacy regulation of BLDE University's Shri B. M .Patil Medical College. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting names to numbers will be kept in a secured location**.**

If the data are used for publication in the medical literature or for teaching purpose no names will be used**.**

I understand that the relevant designated authority and permitted to have an access to my medical record and to the data produced by the study for audit purpose. However, they are required to maintain confidentiality**.**

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. PATIL KEVAL ASHOK has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(witness to signature) Date

ANNEXURE-III

PROFORMA

Name	:	**IP No:**
Age	**:**	**Case. No:**
Address	**:**	**Occupation:**
DOA	**:**	
DOD	**:**	**Time of admission:**

Chief complaints **:**

History of present pregnancy **:**

Obstetrics history

Married Life :

Obstetric Score : G P L A

Menstrual History

PaMC :

LMP :

EDD :

POG :

Past History **:**

Family History **:**

Personal History :

General Physical Examination

Build and Nourishment :

Height :

Weight :

Temp :

RR :

PR :

BP :

Breast :

Thyroid :

Spine :

Pallor / icterus / cyanosis / clubbing / edema / lymphadenopathy:

Systemic Examination

CVS :

RS :

Per Abdomen :

Obstetric Examination:

INVESTIGATIONS

Peripheral Blood Film	Serum Ferritin Level	CBC and Reticulocyte count

After 2 Weeks

Serum Ferritin Level	CBC and Reticulocyte Count

After 6 weeks

Serum Ferritin Level	CBC and Reticulocyte Count

RESULT:

REMAKS:

ANNEXURE- IV

A Randomization Plan

from

http://www.randomization.com

1. gr 1
2. gr3
3. gr 2
4. gr 2
5. gr 1
6. gr3
7. gr 2
8. gr3
9. gr 1
10. gr3
11. gr 2
12. gr 1
13. gr 2
14. gr 1
15. gr3
16. gr3
17. gr 2
18. gr 1
19. gr3
20. gr 2
21. gr 1
22. gr 1
23. gr 2
24. gr3
25. gr 1
26. gr 2
27. gr3
28. gr3
29. gr 2
30. gr 1
31. gr3
32. gr 2
33. gr 1
34. gr 2
35. gr 1
36. gr3
37. gr3
38. gr 1
39. gr 2
40. gr3
41. gr 2
42. gr 1
43. gr 2
44. gr 1
45. gr3
46. gr 2
47. gr3
48. gr 1
49. gr3

50. gr 2
51. gr 1
52. gr3
53. gr 2
54. gr 1
55. gr 2
56. gr 1
57. gr3
58. gr 2
59. gr 1
60. gr3
61. gr 2
62. gr3
63. gr 1
64. gr 1
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66. gr 2
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69. gr3
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72. gr3
73. gr 2
74. gr3
75. gr 1
76. gr 2
77. gr3
78. gr 1
79. gr 2
80. gr3
81. gr 1
82. gr 1
83. gr 2
84. gr3
85. gr 1
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88. gr 1
89. gr 2
90. gr3
91. gr 1
92. gr3
93. gr 2
94. gr 1
95. gr 2
96. gr3
97. gr 1
98. gr 2
99. gr3
100. gr3
101. gr 1
102. gr 2
103. gr3
104. gr 1
105. gr 2
106. gr 1

107.	gr 2
108.	gr3
109.	gr 1
110.	gr3
111.	gr 2
112.	gr3
113.	gr 2
114.	gr 1
115.	gr 1
116.	gr3
117.	gr 2
118.	gr3
119.	gr 2
120.	gr 1
121.	gr3
122.	gr 1
123.	gr 2
124.	gr 1
125.	gr 2
126.	gr3
127.	gr 2
128.	gr3
129.	gr 1
130.	gr 2
131.	gr 1
132.	gr3
133.	gr 1
134.	gr 2
135.	gr3
136.	gr3
137.	gr 2
138.	gr 1
139.	gr 1
140.	gr 2
141.	gr3
142.	gr 2
143.	gr 1
144.	gr3
145.	gr3
146.	gr 2
147.	gr 1
148.	gr 2
149.	gr 1
150.	gr3

150 subjects randomized into 50 blocks
To reproduce this plan, use the seed 21185
along with the number of subjects per block/number of blocks
and (case-sensitive) treatment labels as entered originally.
Randomization plan created on Friday, October 25, 2013 2:17:21 PM

ANNEXURE- V

KEY TO MASTERCHART

- Hb - Hemoglobin
- PCV- Packed Cell Volume
- MCV- Mean Corpuscular Volume
- MCHC- Mean Corpuscular Haemoglobin Concentration
- MCH- Mean Corpuscular Haemoglobin
- Srm Ferritin- Serum Ferritin
- RBC- Red Blood Cell

MASTER CHART

Sr_ no	age	Baseline									2-Weeks (Post-treatment)									6-Weeks (Post-treatment)									Group
		hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	
1	22	8.3	2.78	3.51	24.7	24.7	23.9	60.8	1.5	17.3	9.9	3.11	3.87	26.8	26.5	26.4	74.3	2.3	39.6	11.7	4.23	5.04	30.6	31.2	32.8	86.4	3.5	89.8	**Group A**
2	24	8.8	3.45	4.04	25.1	25.1	27.3	75	1.7	18.2	11.1	2.97	4.43	30.3	27.2	34.3	87.2	2.5	43.7	12.3	2.45	4.87	34.5	34.6	33.7	91.4	3.4	101.1	**Group A**
3	26	7.9	3.54	3.08	21.6	20.7	26.1	67.2	1.4	14.3	11	2.67	4.11	29.4	23.4	30.3	84.1	2.3	38.6	11.4	1.56	4.47	35.6	32.9	34.9	92.1	3.6	97.8	**Group A**
4	29	7.3	2.12	3.78	22.3	17.2	24.9	72.1	1.3	12.1	9.1	3.13	4.18	27.5	21.1	28.7	86.6	2.1	28.9	11.7	2.43	4.44	33.2	33.2	34.1	88.2	3.3	90.7	**Group A**
5	19	7.1	3.98	4.2	21.8	19.3	26.2	67.8	1.2	8.1	9.4	2.89	4.57	25.6	22.6	29.1	80.1	2.1	27.4	12.5	2.78	4.12	33.6	30.5	32.1	88.6	3.4	93.5	**Group A**
6	21	8.1	2.97	3.01	22.9	23.8	24.6	75.9	1.4	7.2	10.3	2.12	3.78	28.4	26.1	30.7	83.9	2.2	38.9	11.8	2.67	4.87	34.7	35.2	33.8	90.1	3.4	79.4	**Group A**
7	32	6.9	3.85	2.87	20.7	18.2	24.1	66.3	1.1	8.1	8.5	3.45	3.18	25.1	19.5	26.3	77.1	1.9	29.2	11.7	1.87	4.05	36.1	29.4	31.3	88.4	3.1	74.8	**Group A**
8	27	7.3	2.93	3.1	21.1	20.5	26.5	59.8	1.2	17	8.9	3.11	3.66	24.4	22.7	29.1	72.4	2	41.9	12.6	4.12	4.6	32.1	29.8	35.1	84.2	3.2	92.5	**Group A**
9	23	7.8	3.41	2.88	22	19.7	28.4	61.2	1.4	13.1	9.7	2.76	3.97	27.1	22.3	28.1	77.8	2.2	37.8	12.5	2.78	4.52	35.7	33.2	33.2	89.3	3.4	110.4	**Group A**
10	23	8.1	4.23	3.06	24.6	23.8	31.3	72.4	1.4	21.3	10.3	1.58	4.05	29.8	25.6	34.2	83.2	2.3	45.1	12.8	3.76	4.25	36.5	34.5	34	88.5	3.5	101.6	**Group A**
11	27	8.3	2.13	3.52	25.3	20.4	29.4	71.4	1.5	20.2	10.1	2.61	3.98	27.1	22.8	30.1	84.8	2.3	44.3	13.1	3.87	4.81	32.1	36.1	34.7	90.4	3.5	124.3	**Group A**
12	29	6.6	1.56	2.69	19	17.3	21.2	63.6	1	8.3	9	2.89	3.57	25.3	20	29.4	76.1	1.9	38.5	10.3	2.39	4.03	31.1	29.3	33.8	88.2	3.1	96.2	**Group A**
13	31	8.9	2.11	3.87	24.1	19.6	27.6	67.5	1.7	21.1	10.8	3.42	4.12	29.3	23.3	31.4	78	2.5	37.7	12.7	2.34	4.88	35.1	31.9	34.7	87.4	3.7	95.4	**Group A**
14	33	7.4	3.56	3.71	22.6	21.5	25.4	74.2	1.3	14.7	9.5	3.41	4.04	28.7	24.2	29.8	82.1	2.1	42.6	11.1	1.77	4.79	30.5	30.1	33.1	88.7	3.3	100.8	**Group A**
15	26	7.7	3.13	3.18	26.7	22.9	24.7	69.4	1.4	12.1	9.5	3.76	3.78	28.1	25.1	31.9	77.2	2.2	46.2	11.9	2.35	4.09	31.1	29.6	30.8	89.8	3.4	105.6	**Group A**
16	23	6.9	2.54	3.67	21.7	18.7	23.4	67.2	1.2	9.3	8.4	2.65	4.2	24.5	21.2	29.1	78.6	2	31.5	10.8	2.46	3.67	29.9	29.4	32.9	86.8	3.2	87.4	**Group A**
17	21	7.5	1.98	4.1	25	20.5	28.5	76.2	1.3	11.4	9.1	3.09	4.25	27.3	22.7	32.4	83.4	2.1	26.9	11.6	3.55	4.42	32.1	31.8	31.7	88.1	3.3	78.5	**Group A**
18	25	8.3	2.45	3.67	26.5	23.2	24.9	70.4	1.5	17.3	10.1	2.79	4.07	29.1	25.6	30.1	79.3	2.3	39.6	11.4	3.12	4.89	33.3	32.1	33.8	87.4	3.5	69.3	**Group A**
19	28	9	2.97	4.03	27.2	25.6	28.3	83.8	0.9	28	10.9	2.86	4.41	29.7	27.8	33.4	90.2	1.7	57.5	13.8	4.13	4.78	34.7	35.9	34.6	93.5	2.8	121.5	**Group A**
20	27	8.6	1.88	3.34	23.4	21.8	25.8	77.4	1.6	17.2	10.5	2.34	4.57	28.1	24.2	30.5	85.4	2.5	44.2	11.1	2.67	4.76	32.2	36.7	31.1	91.2	2.7	102.6	**Group A**
21	25	8.2	2.98	4.22	22.8	20.1	27.3	79.3	1.4	11.2	10.4	3.52	4.89	27.4	22.5	30.3	84.9	2.2	32.4	11.9	2.11	3.96	31.6	32.5	32.4	90.2	3.4	89.3	**Group A**
22	29	7.1	2.55	3.31	21.2	19.8	24.7	71.6	1.2	9.7	8.8	2.97	3.87	24.5	21.9	29.7	80.2	2	42.8	11	3.89	4.21	30.8	33.8	31.9	88.8	3.3	94.6	**Group A**
23	22	7.8	3.67	4.2	22.9	20.7	29.2	68.4	1.3	8.8	10.1	3.88	4.65	29.3	23.1	32.2	77.1	2.1	47.1	11.9	2.75	4.32	33.4	34.1	33.5	89.2	3.3	96.5	**Group A**
24	18	7.7	3.85	3.19	21.3	22.1	24.4	69.8	1.3	12.3	9.2	3.12	3.78	25.6	24.1	30.2	78.3	2.1	37.9	12.7	1.78	4.73	34.6	35.8	34.1	88.9	3.3	110.3	**Group A**
25	26	8.2	3.88	3.81	23.4	20.3	25.4	76.3	1.4	10.2	10	3.46	4.31	28.5	22.8	31.7	85.1	2.2	35.2	11.7	2.32	4.93	35	33.1	32.3	88.1	3.5	108.6	**Group A**
26	28	8.4	2.13	3.9	23.5	22.4	26.3	70	1.5	9.4	9.7	2.97	4.19	30.1	24.2	30.5	81.9	2.3	23.1	12.6	3.22	5.03	35.7	34	34.6	87.3	3.5	120.5	**Group A**
27	29	8.1	1.87	4.31	26.7	22.5	27.3	72.4	1.4	14.3	9.5	2.15	4.66	29.3	24.7	31.8	80	2.2	27.4	12.4	3.15	4.97	38.1	32.1	33.2	90.6	3.4	130	**Group A**
28	33	8	2.19	3.85	28.2	17.5	24.5	66.7	1.3	28.2	9.4	2.88	4.23	28.4	19.8	29.3	75.6	2.1	52.7	11.7	2.76	4.55	36.3	30.5	30.8	86.8	3.4	110.8	**Group A**
29	31	7.1	1.67	3.59	27.1	19.3	24	74.3	1.2	13.5	8.9	3.17	3.97	26.3	23.7	28.4	80.7	2	39.7	11.6	3.66	4.45	35.4	31.4	31.3	88.1	3.2	98.6	**Group A**
30	24	7.6	3.98	4.11	24.6	21.7	28.1	67.2	1.3	12.6	8.8	1.89	4.64	25.7	22.6	27.4	78.2	2.1	42.1	11.1	2.05	5.11	33.2	30.9	32.7	88.5	3.3	87.5	**Group A**
31	26	8.3	2.87	3.98	22.3	25.3	28.3	73.4	1.5	14.4	10.1	3.21	4.22	29.8	26.8	30	82.6	2.3	49.2	12.8	2.43	4.95	35.7	33.1	32.6	86.2	3.5	88.6	**Group A**
32	27	7.3	1.75	3.42	20.1	22.9	26.7	68.2	1.1	11.3	9.8	2.78	4.1	26.4	24.1	29.4	79.5	2.9	31.8	10.2	3.11	3.92	31.1	29.6	30.8	85.9	2.5	92.3	**Group A**
33	29	6.8	3.45	2.78	22.7	19.1	24.1	63.1	1	8.2	8.5	3.01	3.56	26.1	21.3	29.8	72.8	2.8	47.1	10.9	2.98	3.97	30.6	28.4	31.3	83.4	2.2	97.6	**Group A**
34	30	7	3.75	3.23	24.2	20.1	23.7	71.5	1.1	9.3	8.6	2.76	3.45	24.7	23.6	27.4	79.8	2	43.4	11.4	1.78	4.43	32.7	32.9	31.9	87.1	3.2	104.5	**Group A**
35	21	8.4	2.54	3.38	26.5	21.7	25.5	76.8	1.5	10.2	10.1	1.98	4.55	28.4	24.1	28.5	87.3	2.3	39.5	11.9	2.19	4.76	34.1	31.1	30.8	91.3	3.5	109.6	**Group A**
36	25	7.6	1.98	3.23	22.1	19.9	25.1	71.3	1.3	11.3	9.7	2.45	4.11	28.5	20.7	26.5	81.8	2.1	41.8	12.6	2.25	4.67	32.5	30.8	33.9	90.8	3.3	117.1	**Group A**
37	24	8.5	2.13	4.01	23.1	22.5	30.4	66.4	1.5	16.1	10.1	2.96	4.53	29.1	24.2	30.1	77.1	2.3	36.8	12.5	2.89	4.95	36.4	33.7	34.6	88.5	3.5	110.9	**Group A**

38	24	8.8	3.12	4.78	24.2	22.1	26.3	70.7	1.7	18.2	10	3.04	4.68	27.8	25.4	32.3	83.9	2.5	38.4	12.3	1.98	4.87	34.2	32.6	33.4	89.1	3.7	127.4	**Group A**
39	27	8.1	1.43	3.45	22.8	19.7	25.2	62.4	1.4	29.3	9.9	4.01	3.97	27.4	22.1	30.8	75.3	2.2	48.2	11.6	3.89	4.55	33.1	29.8	31.9	86.1	3.4	97.9	**Group A**
40	22	7.4	2.98	3.67	24.8	20.6	23.6	70.1	1.2	16.3	9.1	3.67	4.01	29.1	22.8	28.7	79.4	2.1	42.7	11.2	2.81	4.78	31.7	31.1	34.7	86.4	3.3	123.8	**Group A**
41	28	7.7	3.21	4.03	23.6	21.3	24.5	60.3	1.3	11.3	9	2.78	4.15	27.5	23.7	27.3	72.8	2.1	47.6	12	3.15	4.87	33.4	33.7	30.5	84.2	3.4	101	**Group A**
42	25	7.4	2.86	3.34	23.5	22.1	27.1	70.1	1.2	10.2	9.2	2.55	3.78	27.1	23.3	29.8	82.6	2	29.4	12.9	1.76	4.89	35.1	34.9	31.1	86.2	3.2	115.3	**Group A**
43	27	7.9	1.89	3.76	22.8	20.3	28.3	76.3	1.4	9.3	9.6	3.62	4.14	30	22.5	30.5	81.2	2.2	49.2	12.3	2.24	4.65	36.5	32.1	33.1	85.3	3.4	104	**Group A**
44	26	8.2	2.81	4.08	24.1	22.9	22.4	79.1	1.5	13.2	10.4	3.88	4.48	28.7	24.4	29.3	87.3	2.3	31.5	11.8	3.41	4.76	31.3	33.6	35	90.1	3.6	87.9	**Group A**
45	27	7.9	3.87	4.11	25.3	19.4	23.7	70.9	1.4	10.1	10.3	3.56	4.52	30.2	23.1	28.8	80.7	2.2	37.1	11.5	2.13	4.48	33.2	33.8	33.5	88.9	3.3	96.7	**Group A**
46	23	8.9	4.22	3.38	26.2	20.1	28.6	77.1	1.8	32	11	2.75	3.67	31.9	25.5	33.2	86.3	2.6	67.2	13.1	1.96	5.1	35.2	31.6	35.4	90.5	3.8	135.6	**Group A**
47	29	8.2	2.43	3.12	26.1	23.7	29.1	74.7	1.4	19.4	10.2	2.17	3.79	29.1	24.9	30.6	81.6	2.2	48.7	12.6	2.67	4.89	34.7	34.7	31.9	88.6	3.4	123.8	**Group A**
48	21	7.6	2.77	3.78	23.7	21.6	25.3	67.3	1.3	16.3	9.5	1.78	4.89	28.4	22.4	29.3	75.2	2.1	43.3	11.1	2.79	4.53	32.3	34.8	32.1	86.1	3.3	117.6	**Group A**
49	18	7.1	1.98	3.2	22.7	19.9	23.7	70.1	1.2	18.3	9.4	2.03	4.1	28.1	21.6	30.5	79.9	2	36.2	10.2	3.04	4.27	30.6	27.3	31.6	86.1	3	103.4	**Group A**
50	29	7.9	1.66	3.47	23.8	18.8	24.8	68.4	1.4	10.2	9.8	2.97	4.42	29.5	24.7	27.7	79.1	2.2	31.4	10.6	2.5	4.33	30.9	33.5	30.5	84.7	2.8	91.8	**Group A**

Sr_ no	age	Baseline									2-Weeks (Post-treatment)									6-Weeks (Post-treatment)									Group
		hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	
1	28	7.7	3.76	3.31	23.3	21.7	26.8	65.4	1.4	11.4	8.6	2.75	3.84	25.2	22.6	28.3	74.3	1.9	31.2	9.9	2.54	4.05	27.6	25.2	31.3	87.2	2.9	66.5	**Group B**
2	25	8.8	3.85	4.2	24.5	19.6	27.5	69.3	1.8	17.1	9.7	3.2	4.31	27.7	20.7	32.1	79.5	2.3	35.6	11.5	3.21	5.03	30.1	29.1	31.1	88.4	3.3	71.7	**Group B**
3	33	7.2	3.34	3.19	22.7	20	24.5	63.4	1.2	13.5	8.3	2.87	3.47	25.8	21.1	27.3	74.2	1.6	41.3	10.4	2.78	4.56	29.7	29.3	30.1	86.8	2.5	65.7	**Group B**
4	26	7.7	1.45	3.81	23.1	20.3	26.9	74.3	1.4	9.9	8.9	2.19	4.11	26.5	21.2	27.1	83.5	1.9	27.1	10.5	2.96	4.23	29.8	28.5	29.5	90.2	3	56.3	**Group B**
5	24	8.3	2.54	3.9	25.2	23.7	26.4	67.2	1.5	10.1	9.2	1.98	4.23	28.7	24.9	28	78.8	2.1	28.6	10.7	4.01	4.45	30.5	30.1	31.1	88	3.1	60.1	**Group B**
6	26	8.9	4.11	4.31	24.8	21.8	29.3	73.8	1.8	16.7	10.1	2.08	4.78	29.8	23	31.2	86.2	2.3	31.6	12.1	1.78	5.11	35.3	28.7	34.5	92.5	3.2	89.4	**Group B**
7	27	7.8	3.87	3.78	22.4	19.6	30.1	68.2	1.4	8.8	9	3.19	4.11	27.8	21.1	34.1	81.1	1.9	39.2	10.7	2.65	4.25	29.6	28.3	33.4	93.9	2.8	65.4	**Group B**
8	25	7.4	2.41	3.23	21.1	24.1	27.4	63.5	1.2	14	8.6	2.84	3.61	24.4	25.5	27.3	75.3	1.7	38.6	10.9	2.11	3.87	28.8	31.1	31.5	84.8	2.6	79.2	**Group B**
9	30	7.7	3.12	3.55	23.5	19.7	24.6	69.8	1.4	12.6	8.6	2.97	3.84	24.9	21.2	26.6	80.1	1.9	28.4	11.3	3.16	3.97	31.5	28.4	30.9	91.2	2.8	86.9	**Group B**
10	21	8.6	2.99	2.89	23.9	22.4	25.2	58.4	1.6	19.4	9.4	1.79	3.92	28.2	23.8	29.3	70.3	2.1	31.3	11.3	2.78	4.43	33.5	29.3	33.8	82.7	4	92	**Group B**
11	25	8.9	2.1	3.85	23.6	24.8	24.3	78.2	1.8	16.7	9.8	2.31	4.13	28.4	26.2	29.1	88.3	2.3	38.3	11.4	1.58	4.76	33.7	32.3	31.4	95.6	3.8	76.8	**Group B**
12	25	6.6	4.23	3.34	20.1	19.2	22.2	55.1	1	11.4	7.9	3.21	3.76	22.4	20.9	24.5	67.3	1.5	31.7	10	2.75	4.1	29.2	26.5	30.1	81.2	2.5	68.2	**Group B**
13	24	7.9	2.45	3.45	22.3	20.1	24.5	58.4	1.4	8	9.2	1.87	4.12	27.6	22.3	28.4	78.5	1.9	27.1	10.8	3.07	4.24	30.6	27.1	30.6	87.5	2.9	85.1	**Group B**
14	27	8.2	1.56	2.54	26.3	22.9	25.4	62.4	1.5	19.8	10	2.27	4.45	29.2	24.5	30.4	79.2	2.1	39.2	11.3	2.67	4.87	31.4	28.4	33.7	88.1	3.1	73.9	**Group B**
15	22	8.5	2.43	4.11	25.7	21.7	26.8	70.1	1.6	21.4	9.8	3.12	4.49	28.1	23.2	29.9	80.7	2.1	40.5	11.1	2.51	4.92	32.7	29.5	32	89.2	3.2	94.6	**Group B**
16	28	6.9	4.12	3.87	21.4	20.3	23.3	59.4	1	8.5	8.5	2.89	4.11	24.3	22.1	26.4	71.3	1.5	29.4	10.1	2.66	4.23	29.8	30.3	29.8	83.7	2.5	64.9	**Group B**
17	23	7.6	2.67	3.41	22.5	18.8	27.5	68.6	1.2	9.4	9.1	1.78	4.56	27.5	20.3	31.8	76.5	1.7	21.4	10.4	3.88	4.44	30.3	31.4	30.5	86	2.6	56.3	**Group B**
18	29	8.8	1.56	3.12	25	21.2	25.2	74.4	1	17.3	10.4	2.41	4.78	28.8	23.4	32.1	84.3	1.4	35.8	11.5	2.76	4.89	30.1	29.8	34.8	92.2	2.4	67.4	**Group B**
19	23	7.4	4.12	3.21	24.7	23.7	22.4	71.2	1.2	15.9	9.1	2.87	4.51	29.2	25.2	28.4	81.4	1.7	32.7	10.3	1.89	4.65	28.4	28.4	31.4	90.5	2.7	80.2	**Group B**
20	21	7.9	2.78	3.97	23.3	21.8	26.5	70.5	1.4	13.3	9	3.31	4.1	27.9	23.6	30.5	79.9	1.9	27.4	9.4	2.63	3.78	28.9	26.8	31	88.3	2.9	52.2	**Group B**
21	24	8.3	3.45	2.68	25.8	23.5	24.2	74.7	1.5	11.7	10	1.9	3.45	30	25.1	30.1	85.3	2.1	30.2	10.7	2.95	3.96	30.8	28.9	31.8	92.4	3.1	63.7	**Group B**
22	26	8.9	3.87	3.43	26.1	23.1	27.5	79.1	1.8	21.4	10.3	2.05	4.71	29.7	24.7	31.5	84.7	2.4	41.4	11.8	3.17	4.49	31.2	29.7	33.7	88.1	3.4	96.5	**Group B**
23	31	8.2	2.12	3.98	24.7	20.9	28.6	74.2	1.4	20	9.9	3.1	4.12	27.8	22.2	29.8	81.3	1.9	38.9	10.1	2.56	4.39	30.7	28.5	31.5	84.2	2.9	79.7	**Group B**
24	19	7.7	3.98	3.76	22.4	19.6	24.1	70.1	1.3	8.3	9	2.81	4.21	27.9	21.3	29.4	79.9	1.8	28.4	10.5	2.98	4.53	31.3	28.2	34.1	88.5	2.8	76.8	**Group B**
25	21	7.9	2.97	3.85	23.8	19	23.7	68.4	1.4	12.4	9.1	2.45	4.23	29.6	20.5	29.4	79.1	1.9	28.6	10.1	2.76	4.45	30.5	28.6	32.8	88.7	2.8	83.7	**Group B**
26	26	8.6	3.85	3.1	26.1	20.3	24.1	64.4	1.6	9.3	9.8	1.98	3.76	28.7	21.4	26.2	75	2.1	23.1	11.5	2.59	4.67	29.9	29.8	31.4	85.2	3.1	93.5	**Group B**
27	27	7.4	3.1	3.39	24.7	21.2	23.6	69.3	1.2	10	8.8	3.78	3.88	25.2	21.7	25.1	77.1	1.6	29.3	10.1	1.89	4.46	28.7	28.1	30.3	85.3	2.6	70.4	**Group B**
28	23	8.9	3.41	4.23	25.8	21.8	28.8	69.8	1.7	14	10.3	1.99	4.09	28.5	22.3	31.4	80.2	2.2	31.4	11.7	3.34	3.99	30.3	30.3	33.8	90.1	3.2	84.5	**Group B**
29	23	7.7	4.23	3.51	22.1	19.6	29.1	65.7	1.3	11.3	9.1	2.09	4.1	26.7	22.4	33.4	76.8	1.9	27.5	11	2.45	4.45	29.6	31.1	30.5	86.2	2	77.8	**Group B**
30	27	6.8	2.32	3.66	21.2	20.1	20.8	70.9	1	10.2	8.1	3.77	3.98	23.4	22.5	24.3	79.1	1.5	27.4	9.7	2.89	3.86	27.6	26.8	30.1	81.4	2.5	73.9	**Group B**
31	29	8.1	1.56	4.43	24.6	19.7	24.7	56.7	1.4	27.4	9	4.01	4.24	26.7	20.2	27.6	70.5	1.9	45.3	11.3	2.16	4.11	30.7	28.4	33.7	83.6	2.9	99.6	**Group B**
32	33	7.8	2.67	3.78	23.1	22.4	25.8	75.1	1.3	10.3	8.9	3.12	4.08	25.7	23.7	27.9	83.3	1.8	30.4	10.9	3.78	4.33	29.7	27.3	31.3	85.1	2.8	65.9	**Group B**
33	27	8	2.78	3.67	24.7	24.8	26	76.3	1.4	18	8.8	2.87	4.11	24.8	25.5	27.1	84.2	1.9	41.2	10.5	4.07	4.45	28.6	29.3	31.1	88.8	3	89.4	**Group B**
34	26	7.5	1.56	3.87	24.8	19.2	25.9	67.2	1.3	10.9	8.6	2.17	4.25	25.4	21.1	24.8	79.1	1.8	27.7	10.8	2.67	4.07	31.1	26.6	28.9	85.2	2.7	73.8	**Group B**
35	23	7.3	4.12	4.12	26.9	20.1	24.8	76.4	1.2	9.5	8.4	1.67	4.34	25.7	20.9	26.1	83.5	1.7	19.8	9.9	2.5	3.79	28.7	26.5	31.4	88.2	2.5	51.8	**Group B**
36	27	7.9	3.33	4.08	24.1	22.9	23.6	70.1	1.4	15.3	8.8	2.83	4.14	25.4	23.9	27.3	78.9	1.9	34.5	10.3	3.78	3.98	29	28.9	29.1	84.8	2.9	72.9	**Group B**
37	25	8.2	3.45	3.31	25.8	21.7	25.8	62.5	1.5	10.2	9.5	3.09	3.91	27.8	22.3	28.9	73.7	2	24.5	10.7	2.65	4.99	29.8	29.1	30.4	84.1	3.1	55.9	**Group B**
38	28	8.9	3.64	3.76	23.9	23.5	30.2	68.6	1.8	6.5	10.2	2.1	4.51	30.1	24.8	32.1	81.2	2.2	25.8	11.4	3.05	4.76	31.2	30.1	34.8	88.7	3.2	85.7	**Group B**
39	27	8.4	2.15	3.41	24.7	22.8	28.9	78.2	1.6	14.3	10	2.87	3.84	29.9	24.1	30.3	85.2	2.1	34.7	11.8	3.98	4.11	30.1	31.7	33.1	86.1	3.1	102.4	**Group B**

40	23	8.2	3.98	3.98	26.2	19.8	26.5	73.5	1.5	8.8	9.5	2.63	4.39	29.3	23.1	30.4	84.8	2	31.2	12.1	3.53	4.67	34.2	30.5	32.6	88.8	3.5	94.6	**Group B**
41	21	8.5	2.97	4.1	25.7	21.4	28.4	77.3	1.6	17.4	9.6	3.31	4.43	27.8	22.1	29.9	86.4	2.1	40	11.6	2.76	4.76	33.1	28.4	33	88.2	3.1	97.5	**Group B**
42	29	6.7	4.23	3.38	22.1	18.7	24.8	57.8	1	9.1	7.8	3.89	3.98	24.7	19.5	25.3	70.1	1.5	35.4	10.3	3.89	4.25	30.4	26.8	29.6	82.5	2.5	75.8	**Group B**
43	18	7.3	3.15	3.57	22.7	19.5	23.6	74.2	1.2	15.4	8.4	2.98	3.66	25.2	20.7	28.3	79.1	1.7	36.5	11.1	3.54	4.02	30.5	27.1	31.3	86.9	2.7	88.5	**Group B**
44	29	7.8	3.41	3.98	23.5	22.6	22.7	65.8	1.4	8.3	8.9	1.97	4.23	24.6	22.8	27.9	74.2	1.9	28.1	10.3	2.54	3.67	29.7	28.4	30.1	81.4	2.9	94.8	**Group B**
45	28	6.7	4.23	3.19	20.1	20.1	23.4	54.2	1	10.2	8.3	2.55	3.79	24.1	21.4	25.1	66.1	1.5	28.4	9.8	2.98	3.89	28.9	29.1	28.9	78.4	2.5	62.6	**Group B**
46	20	7.7	2.96	4.21	19.2	19.7	25.3	70.2	1.3	11	8.6	2.34	4.17	23.6	21.3	27.2	80.4	1.8	29.7	10.1	2.53	4.08	30.3	29.5	29.1	82.1	2.8	77.5	**Group B**
47	33	8.3	1.56	3.91	24.7	23.4	28.7	81.1	1.5	21.2	9.7	3.31	4.37	27.5	24.7	30.1	86.2	2.1	43.4	11	2.47	4.68	32.6	30.1	33.8	88.5	3.2	82.1	**Group B**
48	28	7.9	2.67	4.45	26.2	17.3	29.5	70.9	1.4	8.5	9.2	2.89	4.77	28.9	19	31.2	81.1	1.9	27.5	10.7	2.55	4.23	30.1	29.3	30.6	85.3	2.8	90	**Group B**
49	25	8.8	1.56	3.98	25.6	19.7	28.1	79.3	1.7	7.4	10.1	1.78	4.23	29.4	24.1	29.1	85.3	2.2	20.4	11.9	1.99	4.05	31.2	31.1	32.7	90.2	3.2	96.5	**Group B**
50	25	8.5	4.11	2.87	25.8	22.1	27.4	63.2	1.6	9.3	9.7	3.71	3.42	28.5	22.3	28.3	73.9	2.1	28.9	12.1	3.39	4.98	33.4	30.6	31.9	84.1	3.2	103.4	**Group B**

Sr_no	age	Baseline									2-Weeks (Post-treatment)									6-Weeks (Post-treatment)									Group
		hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	hb	platelet	rbc	pcv	mch	mchc	mcv	reticulocyte	Sr. Ferritin	
1	22	8.9	1.95	3.56	27.6	21.2	28.3	64.4	1.7	17.4	9.5	2.25	3.87	28.1	21.9	30.1	72.1	1.9	28.3	11.1	3.31	4.45	30.3	27.1	33.4	81.3	3.3	54.1	**Group C**
2	29	9.2	2.32	4.2	28.9	24	30.2	80	2.5	15.6	10	1.88	4.27	29.1	25.1	31.8	84.8	2.8	23.1	11.3	3.85	4.67	34.2	28.3	34.5	86.3	3	64.4	**Group C**
3	30	8.3	3.45	4.23	25.5	19.5	25.4	69.8	1.6	13.7	8.7	3.21	4.01	26.3	20.6	27.1	81.5	1.6	19.2	9.9	3.77	4.22	30.1	24.4	30.1	88.8	2.1	44.2	**Group C**
4	26	7.1	3.56	3.77	23.6	18.7	23.7	60.2	0.9	10.1	7.9	3.89	3.86	23.8	19.5	24.2	66.5	1.1	18.2	9.4	2.27	3.99	29.4	25.1	28.3	78.2	1.8	44.8	**Group C**
5	25	8.5	2.54	3.23	25.5	21.3	25.5	70.9	1.6	16.7	9.2	2.81	3.67	27.7	22.8	26.4	75.3	1.8	24.7	10.7	3.98	4.45	31.7	27.5	30.1	84.2	2.4	59.9	**Group C**
6	24	7.3	1.98	4.12	22.1	20.4	25.1	56.7	1	9.4	8.3	3.78	4.03	24.3	21.3	28.1	61.3	1.1	21.2	9.4	3.11	4.14	28.9	25.9	31.3	78.5	1.7	41.3	**Group C**
7	29	9	2.21	4.78	28.3	24.2	30.4	78.2	1.7	23.2	10.2	1.76	4.86	30.5	25.6	30.5	83.1	1.9	37.3	11.3	2.78	3.95	33.6	28.7	33.5	88.3	2.8	71.4	**Group C**
8	25	8.8	2.97	3.45	26.4	23.4	26.3	74.4	1.6	21	9.4	2.24	3.98	28.1	24.5	28.1	79.3	1.6	34.5	10.2	3.23	3.89	29.8	27.8	30.2	86.7	2.2	65.2	**Group C**
9	22	8	1.68	3.67	25	17.6	24.7	68	1.3	14.2	8.9	3.68	3.79	26.2	18.4	27.1	76.3	1.5	27.9	10.1	2.99	4.45	29.5	26.5	29.5	85.9	2	51.1	**Group C**
10	27	8.3	2.43	4.03	26.2	18.5	23.6	79.2	1.4	16.7	8.9	4.1	3.96	25.7	19.7	25.8	80.1	1.6	24.3	10.5	3.23	4.07	30.1	25.1	30.6	88.2	2.1	48.4	**Group C**
11	25	8.8	2.98	3.34	27.8	19.9	24.5	73.5	1.6	19.4	9.5	3.87	4.1	26.4	21	27.6	79.7	1.8	29.4	10.2	2.78	4.22	31.3	25.7	30.1	84.1	2.4	57.2	**Group C**
12	30	7.7	3.76	3.54	22.4	23.1	27.1	61.9	1.2	9.4	8.5	2.78	3.86	24.5	23.9	28.3	72.2	1.5	19.8	9.4	2.81	4.06	28.7	25.3	30.7	80.7	2.1	39.5	**Group C**
13	26	9.1	3.85	4.44	27	25.1	31	68.6	1.7	18.9	10.1	2.19	4.51	29.1	25.8	32.1	71.3	1.9	27.6	11	3.45	4.99	31.4	29.2	34.5	81.6	2.5	66.3	**Group C**
14	21	9.4	3.1	4.45	25.7	21.3	26.5	78.2	1.8	20.3	10.2	1.67	4.35	28.3	22.3	27.3	84.5	2	38.1	11.3	1.99	4.76	33.5	27.1	32.1	91.1	2.6	71.6	**Group C**
15	23	6.9	3.39	3.38	20.2	17.2	22.4	57.1	0.8	7	7.8	2.99	3.49	22.1	18.1	23.1	66.1	1.1	17.2	9.2	3.89	3.87	27.6	23.5	28.9	78.3	1.7	43.7	**Group C**
16	25	7.6	4.23	3.12	21.8	19.3	24.9	60.3	1.2	9.4	8.7	3.97	3.21	23.6	20.2	26.7	69.8	1.4	17.9	9.4	2.97	4.01	28.6	23.7	29.8	80.4	2	49.5	**Group C**
17	21	8.7	2.45	3.78	23.4	20.1	23.7	80.1	1.6	11.4	9.4	2.78	3.94	26.5	21.3	27.1	82.7	1.8	21.3	10.1	2.09	4.45	30.1	27.9	29.7	90.5	1	59.4	**Group C**
18	19	8.9	1.56	4.2	27.3	21.6	27.3	74.2	1.8	25.6	9.6	1.89	4.14	28.1	22.4	29.4	79.7	2	34.7	10.7	2.11	4.25	31.4	26.8	31.9	85.6	2.6	53.8	**Group C**
19	29	8.1	2.43	3.19	24.5	20.5	25.6	65.8	1.5	13.3	9.3	2.03	3.32	27.2	21.4	28.5	72.4	1.7	23.4	9.9	3.78	3.75	29.8	25.1	29	83.9	2.3	47.9	**Group C**
20	23	7.3	2.78	3.81	23.4	18.4	24.8	54.9	1.1	11.2	8.1	2.32	3.91	24.7	19.5	24.9	62.8	1.3	20.1	9.6	3.38	3.67	27.5	24.2	27.3	80.2	1.9	51.1	**Group C**
21	25	7.9	2.67	3.9	22.9	23.8	23.9	58.5	1.3	9.7	8.8	3.88	4.02	24.1	24.7	24.3	61.4	1.5	31	9.3	3.12	3.89	26.5	26.8	26.8	77.3	2.1	52.6	**Group C**
22	31	8.6	1.87	4.31	24.1	21.6	24.3	78.1	1.7	9.3	9.3	3.97	4.52	27.3	22.7	26.7	80.4	2	21.2	10.9	3.55	4.74	30.1	28.1	30.1	87.2	2.6	53.7	**Group C**
23	27	7.4	4.12	3.78	23.7	20.2	27.8	57.1	1.2	8.5	8.5	2.81	3.99	24.2	21.1	28.6	68.3	1.4	19.1	10.3	3.2	4.68	29.6	24.9	30.4	76.3	2.1	66.8	**Group C**
24	22	8.9	2.78	3.23	24.2	22.4	28.1	78.5	1.7	11.6	9.6	2.19	3.57	27.5	23.5	30.5	82.1	1.7	20.5	10.5	3.47	3.98	31.3	26.1	34.5	93.1	2.3	78.9	**Group C**
25	23	7.5	3.76	2.89	23.6	19.6	27.2	63.2	1.2	7.9	8.3	3.91	3.08	24.9	20.8	28.1	70.5	1.4	21.9	9.7	3.76	3.57	29.5	23.2	33.1	81.4	1.9	45.4	**Group C**
26	27	6.8	3.87	3.33	20.6	17.5	23.4	53.8	1.1	6.4	7.5	3.53	3.86	22.1	19.1	25.6	65.4	1.3	22.3	8.9	3.85	4.03	26.4	23.7	27.8	74.2	1.9	33.1	**Group C**
27	25	7.1	2.39	3.16	21.4	19.3	25.1	60.8	1.3	10.4	7.9	2.95	3.76	23.4	20.8	24.5	68.3	1.5	27.8	8.3	3.1	3.88	24.5	24.6	28.1	73.4	2.1	40.5	**Group C**
28	30	7.8	2.34	4.09	22.7	21.7	24.3	70.2	1.5	11.7	8.5	2.21	4.12	24.1	22	26.2	74.6	1.8	32.5	10.4	3.39	4.05	28.7	26.4	29.3	81.3	2.4	53.8	**Group C**
29	26	9	1.77	4.35	26.1	25.3	29.8	78.5	1.8	19.3	10.1	1.87	4.55	29.5	26.2	31.7	81.7	2	38.2	11	4.23	4.47	34.1	29.7	33.6	89.6	2.6	71.4	**Group C**
30	25	8.6	2.35	2.98	25.8	23.8	27.6	80.3	1.6	18.4	9.4	1.94	3.41	28.7	24.7	29.8	83.4	1.8	40.4	10.3	2.45	3.78	30.2	29.8	31.9	89.2	2.4	82.1	**Group C**
31	21	8.9	2.46	3.65	26.3	22.1	26.9	75.9	1.7	10.3	9.6	2.21	4.03	29.6	23.1	30.1	80.8	1.9	24.8	11.1	1.56	4.12	31.1	31.6	34.9	90.1	2.5	69.5	**Group C**
32	28	8.8	3.55	3.76	26.1	20.6	25.4	71.2	1.7	13	9.9	2.81	4.44	28.8	21.9	29.3	79.3	2	29.4	10.7	3.1	4.87	30	25.2	31.1	87.2	2.6	74.8	**Group C**
33	21	7.2	3.12	4.23	22.7	20.1	23.6	68.2	1.2	12.5	8.1	3.22	3.58	23.4	21.2	25.2	73.7	1.4	30.1	9.9	2.59	3.78	27.6	24.7	28.4	84.8	2.1	61.4	**Group C**
34	27	7.9	4.13	4.03	21.6	22.5	24.7	59.5	1.4	10.9	8.8	3.89	4.22	24.3	23.3	22.7	64.3	1.6	22.3	10.4	3.55	4.6	29.6	27.5	28.1	75.1	2.2	69.3	**Group C**
35	23	8.3	2.67	3.89	25.8	23.9	26.8	72.4	1.5	13.1	9.3	1.78	4.05	27.6	24.6	28.9	77	1.7	25.6	10.7	2.24	4.52	30.1	27.8	30	83.2	2.3	57	**Group C**
36	21	8.9	2.11	3.68	26.3	22.1	28.5	71.4	1.8	15.2	9	1.99	3.79	28	23.4	30.1	78.9	2.1	34.2	10.4	3.75	3.99	29.9	28.2	33.2	87.3	2.7	48.6	**Group C**
37	20	6.7	3.89	3.58	21.1	17.2	24.9	63.6	1.3	7.7	7.6	2.9	3.43	23.3	18.1	24.7	69.1	1.6	19.2	8.9	2.54	3.75	25.3	24	26.8	76.7	2.2	30.1	**Group C**
38	24	7.2	3.12	3.71	21.7	19.5	25.4	68.5	1.2	9.6	8.1	3.43	4.1	24.5	20.6	26.7	73.2	1.4	24.3	9.1	1.98	4.03	28.7	25.3	29.3	79.1	2.1	42.4	**Group C**
39	27	7.9	2.11	3.26	20.6	20.8	25.8	74.2	1.4	9.3	8.8	3.91	3.67	26.5	21.7	27.3	79.5	1.6	27.1	10.7	2.13	4.08	29.6	26.8	30.1	88.3	2.2	54.3	**Group C**
40	28	8.6	1.95	4.2	20.8	21.3	24.7	69.4	1.7	17.4	9.3	2.89	4.23	25.6	22.2	29.1	76.2	1.9	37.4	11.3	2.97	4.79	32.2	27.4	33.2	87.2	2.5	74.4	**Group C**

41	21	8.3	2.45	4.23	21.5	22.9	27.8	67.2	1.4	11.1	9.2	2.91	4.28	26.3	24.1	30.2	79.1	1.7	35.4	10.6	1.68	4.09	30.5	28.7	32.5	88.8	2.3	56.7	**Group C**
42	29	7	3.56	3.77	24.7	21.6	29.2	76.2	1.2	15.4	7.9	3.76	3.89	22.5	22.3	26.7	77.5	1.2	34.3	9.7	2.98	3.67	28.8	25.1	28.8	83.1	1.7	57.3	**Group C**
43	28	7.4	3.75	3.23	21.4	19.8	24.4	70.4	1.4	9.8	8.2	4.12	3.49	24.3	20.6	26.2	73.9	1.6	28.9	9.3	2.55	3.98	27.7	24.6	27.3	84.3	2.3	60.6	**Group C**
44	31	8.7	2.54	4.01	22.6	24.2	25.4	58.3	1.7	20.2	9.4	1.76	4.42	28.4	25.6	29.5	69.1	1.9	40	10.9	3.76	4.89	31.3	28.4	30.9	80.6	2.5	68.1	**Group C**
45	25	7.5	1.98	3.67	25.2	21.9	27.5	68.9	1.4	9.2	8.4	2.11	3.83	25.1	22.5	26.3	75.1	1.6	26.5	9.7	3.85	3.97	28.6	26.2	29.7	86.4	2.2	52.1	**Group C**
46	19	6.9	2.13	4.1	18.2	19.1	24.8	54.4	1.1	7.1	7.6	1.19	4.15	23.6	20.2	25.8	62.8	1.4	19.4	9.1	3.34	4.03	26.4	24.3	26.4	75.2	2	45.7	**Group C**
47	23	7.1	2.97	3.67	26.9	20.7	22.9	59.6	1.2	12.4	8.1	3.91	3.82	24.4	21.4	24.9	63.9	1.4	25.8	9.5	1.45	3.96	29.1	26.1	29.8	70	2.1	49.6	**Group C**
48	20	8.4	1.68	4.03	25.1	21.8	24.6	72.7	1.6	22.1	9.3	2.63	4.13	29.2	22.8	27	80.3	1.9	39.5	10	2.54	4.21	29.6	27.9	30.4	86.5	2.5	64.8	**Group C**
49	26	8	2.98	3.34	26.4	23.5	22.8	69.8	1.4	16.3	9.1	2.81	3.77	27.8	24.2	27.9	77.2	1.4	27.9	10.3	4.11	4.32	30.7	28.6	31.8	81.8	2	73.5	**Group C**
50	23	8.9	2.55	3.54	27.2	23.1	29.2	77.2	1.8	26	10	2.61	4.76	29.9	24.2	30.2	81.2	2.1	42.6	11.4	3.87	4.73	33.2	29.1	33.4	89.9	2.7	87.6	**Group C**