TO COMPARE THE EFFECTIVENESS OF INTERMITTENT SUPPLEMENTATION OF ORAL LIPOSOMAL FERRIC PYROPHOSPHATE WITH FERROUS SULPHATE IN CHILDREN BETWEEN 6-59 MONTHS IN RURAL AREA OF BELAGAVI, KARNATAKA- A RANDOMISED CONTROL TRIAL

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ABSTRACT

Objective: To compare the effectiveness, compliance and safety of intermittent supplementation of oral liposomal ferric pyrophosphate(LFP) with ferrous sulphate(FS) in children between 6-59 months.

Method: Randomized controlled trial was conducted among children 6-59 months at a primary health centre in Belagavi, Karnataka. Baseline sociodemographic data, anthropometric measurements, and haematological parameters were collected. Participants were randomized into two groups: oral LFP and FS. Both received 20 mg of elemental iron twice a week. After 3 months, assessed for changes in haematological levels, side effects, and compliance. Intra-group comparisons were conducted using independent t-test and Mann-Whitney U test and intergroup comparisons using the dependent t-test and Wilcoxon matched pairs test.

Result: 40 in each group, were enrolled. Baseline parameters, including haematological levels, were similar between the groups. LFP group showed significant improvements in mean haemoglobin [10.35(1.28) to 11.10(1.21) gm/dL $p<0.0001$)], serum iron [58.28(33)to81.21(40.74) µg/dL,$p = 0.0444$],TSAT ($p=0.008$) , MCHC ($p=0.0491$), and RDW ($p=0.0225$) levels within the group. At follow-up, significant improvements in mean haemoglobin [LFP: 0.76 (0.67); FS: 0.16 (0.60) gm/dL] and serum iron [LFP: 22.93 (29.51); FS: 9.72 (27.37) µg/dL] levels were observed in the LFP group compared to the ferrous sulphate group. There were no significant changes in anthropometric measurements .LFP group exhibited fewer side effects and higher compliance .

Conclusion: Oral liposomal ferric pyrophosphate is effective ,well tolerated and safe compared to ferrous sulphate for intermittent prophylaxis in children between 6-59 months.

Keywords: Iron Prophylaxis , Liposomal iron ,ferrous sulphate

LIST OF ABBREVIATIONS

WHO	World Health Organization
IDA	Iron Deficiency Anemia
ID	Iron Deficiency
IFA	Iron Folic Acid
NHFS	National Health and Family Survey
AMB	Anemia Mukt Bharat
RBC	Red Blood Cell
Hb	Hemoglobin
FPN	Ferroportin
MCV	Mean Corpuscular Volume
MCHC	Mean Corpuscular Hemoglobin Concentration
MCH	Mean Corpuscular Hemoglobin
Hct	Hematocrit
RDW	Red cell Distribution Width
TIBC	Total Iron Binding Capacity
TSAT	Transferrin Saturation
AOCD	Anemia Of Chronic Disease
sTfrc	Serum soluble Transferrin receptor
IV	Intra Venous
SI	Sucrosomial Iron

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INTRODUCTION

Globally, anemia affects 39.8% of children aged 6-59 months, which translates to approximately 269 million children with anemia. (1). According to the National Health and Family Survey (NHFS-5) prevalence of anemia is on rise with an increase from 58.6% in NHFS-4 to 67.1% nationally, 53.5% in Karnataka(rural), and 66.3% in Belagavi district (2). According to the recent data from World Health Organization (WHO), iron deficiency anemia (IDA) is the primary cause of anemia in 50% of these children(1). Therefore, IDA is a major health concern which has implications on the growth and development in children.

The impact of IDA in children is detrimental, especially in the early infancy affecting brain development, including delay in neural and physiological development and significantly contributes to poor immunity leading to recurrent respiratory infections, poor physical growth and development. Iron deficiency (ID) without anemia can adversely effect on the long term neurodevelopment and behavior of infants and some of these effects may be reversible after correction. Suboptimal feeding practices leading to malnutrition is the most common cause for IDA in infants which manifests as excessive irritability and increased morbidity in this age group. The common manifestations of anemia in children and adolescents are extreme weakness, fatigue, shortness of breath, headache, dermatological signs including pale skin, atrophic glossitis, cracked corners of mouth and consumption of non-nutritive substance known as PICA (3,4).

Prevention therapies and strategies form the cornerstone to prevent the ever-increasing prevalence of ID in children leading to poor growth and neurodevelopmental outcome. Prevention of ID starts from appropriate diet, deworming and supplemental iron folic acid (IFA) therapy. The WHO recommends intermittent iron supplementation over daily iron supplementation for preventing anemia in children. Preschool-age children are given 25 mg of elemental iron in the form of drops or syrups, whereas school-age children receive 45 mg of elemental iron in tablet or capsule form, both administered once a week (5). In India, the National Nutritional Anemia Prophylaxis Programme (NNAPP) was launched in 1970 and later relaunched as Anemia Mukt Bharat (AMB) in 2018. The AMB program, under the National Health Mission by the Ministry of Family Health and Welfare, focuses on preventing iron deficiency anemia (IDA) through various preventive therapies. For children aged 6-59 months, the program provides bi-weekly prophylaxis of 1ml iron folic acid syrup containing 20mg elemental iron (ferrous sulphate formulation) and 100 mcg folic acid (6).

Oral iron formulations containing ferrous or ferric salts are the first-line preventive therapy for IDA in children. These formulations are preferred due to their availability, ease of administration, and relative low cost. However, the bioavailability of ferrous iron preparations (such as ferrous sulfate, gluconate, or fumarate) is only 10-15%, which is much lower than the bioavailability of ferric iron salts or complexes (such as those with amino acids, polysaccharides, or ovo-albumin) (7). Ferrous sulfate, a common iron supplement, dissociates into ferrous ions ($Fe2+$) and sulfate ions in the acidic stomach environment. However, these ferrous ions can interact with dietary components like phytates and tannins, reducing their absorption in the intestines. Despite being used commonly ferrous sulfate preparations have been associated with increased gastrointestinal side effects, leading to poor compliance.

A cross-sectional study by Parischa et. al. evaluated the factors influencing the receipt of iron supplementation of young children and their mothers in rural Karnataka and analyzed data obtained from across India in NHFS-3 survey. For Karnataka, the study reported 41.5% of children aged 12-23 months received iron supplements and 11.5% received them through the public system and nationally only 3.7% received iron supplements. The factors associated with children's receipt of iron at both locally and nationally included wealth, male sex, maternal iron intake, antenatal health visits, religion, attendance at anganwadi centers, and vaccination status influenced this outcome(8). Therapy failure can also be attributed to the peptide hepcidin, produced in the liver, which plays a crucial role in iron homeostasis. Hepcidin inhibits iron absorption, and elevated hepcidin levels render IDA resistant to oral iron therapy.

To address the persistent and growing issue of ID in children, it is crucial to identify and utilize newer, proven, and effective iron formulations that are safe for this age group. The primary objective is to develop improved prophylactic and therapeutic treatments that can help combat ID and ensure better growth, development, and health in children, ultimately leading to a higher quality of life in the future.

Liposomal iron is a cutting-edge formulation where iron is encapsulated within liposomes, which are spherical structures composed of phospholipids similar to those found in human cell membranes. This innovative approach allows the iron compounds to bypass the acidic environment of the stomach and reach the small intestine intact, thereby enhancing bioavailability and reducing side effects (7,9). This compound has been evaluated for treatment of IDA in adults and even pregnant women, showing significant improvement in hemoglobin levels and iron stores by increased bioavailability, reduced side effects and increased compliance. This compound has been used to treat IDA in heart failure and in chronic kidney disease patients with positive result. This iron preparation is not yet evaluated for the role in preventive therapy for ID specially in children.

We hypothesized that using oral liposomal ferric pyrophosphate as intermittent prophylactic therapy for ID in children aged 6 months to 59 months would demonstrate a significant improvement in hemoglobin levels and iron stores compared to ferrous sulfate, and which is used in the AMB program. Additionally, we compared the compliance and side effects between both compounds to identify a more efficacious, tolerable, and compliant method of preventing IDA in children in this age group.

OBJECTIVES

Primary Objective :

To study the effectiveness of liposomal ferric pyrophosphate with ferrous sulphate in intermittent oral iron prophylaxis in children between 6 months to 59 months.

Secondary Objective :

1)To compare growth in these children by anthropometrical measures.

2) To compare side effects and compliance of both compounds.

3) To find prevalence of mild to moderate anemia in the study population.

REVIEW OF LITERATURE

Prevalence of Anemia – Global, India and Regional

According to recent data from the WHO, approximately 39.8% of children globally, aged 6-59 months, are affected by anemia, which translates to around 269 million children, representing approximately 32.9% of the world's population. Notably, 50% of these anemia cases are attributed to iron deficiency anemia (IDA). The prevalence of anemia is particularly high in regions such as South Asia, Sub-Saharan Africa, and the Caribbean, affecting all age groups and both genders (10). Vulnerable groups such as children under five years old are particularly affected, with a prevalence rate of 42% among infants under two years of age (11). Globally, the prevalence of anemia in children aged 6-59 months is 39.8%, which equates to approximately 269 million affected children. The highest rate of 60.2% is observed in the African region (1). In India, the prevalence of anemia among children aged 6-59 months remains a significant public health concern. National data indicates a prevalence rate of 53.5% in Karnataka and 66.3% in the Belagavi region for this age group (12).

The fourth round of the National Family Health Survey (NFHS-4), conducted in 2015-16, reported the following data (13), the prevalence of anemia among children aged 6-59 months was 56%, indicating a relatively small reduction of 13.5 percentage points compared to the 2005-06 NFHS-3 study. The Comprehensive National Nutrition Survey reported a significantly lower prevalence of anemia, at 30.7%, based on venous blood sampling. This disparity suggests that the higher anemia prevalence figures reported by the NFHS might be overestimates, potentially due to differences in methodologies used for hemoglobin measurement

Kurpad and Sachdev (2022) (14) highlighted a significant burden of anemia in Indian children, with the NFHS estimating a prevalence of 67.1%. They noted that the actual prevalence of iron deficiency anemia might be around 10%, challenging the effectiveness of widespread iron supplementation policies.

In a recent study by Singh et al. (2022) (15) conducted in India, observed an increase in childhood anemia from 59% in NFHS-4 to 67% in NFHS-5, with mild anemia rising and moderate to severe anemia initially decreasing but then increasing in NFHS-5. This trend reversal was linked to factors such as maternal educational attainment, maternal anemia status, and socio-economic status. Shet et al. (2012) (16) found a high prevalence of anemia among HIV-infected children, with 52.5% of enrolled children being anemic. This prospective study, conducted in 2007-2008, in India, included 80 HIV-infected children aged 2-12 years. The prevalence of anemia was found to be associated with a multifactorial etiology, with iron deficiency being the primary cause in approximately 38.1% of cases. Anemia of inflammation was also observed in 38.1% of cases, while vitamin B12 (12) deficiency and combined deficiencies were present in smaller proportions. Puranik and N S (2022) (17) used data from the 2015–2016 National Family Health Survey (NFHS–4) in India to report a prevalence of 58% in children under five. Using NFHS-5 data from 335 districts and spatially weighted regression, the study found significant spatial variability and clustering of factors related to childhood anemia at the district level. A number of factors were shown to be strongly correlated, including birth order, prenatal care, the incidence of nutritional supplements in mothers and children, diarrhea in children, and stunting. Additionally, three notable local spatial clusters of anemia were found using the spatial scan statistics technique.

Onyeneho et al. (2019) (18) conducted a study analyzing a sample of 112,714 children from the 2015-2016 Indian National Fertility and Health Survey to investigate childhood anemia. It was discovered that 58.5% of the children who were surveyed had anemia, and that there were substantial correlations between parental anemia, dietary intake, and sociodemographic characteristics and childhood anemia. In order to determine relationships between parent anemia, household factors, and children's nutritional intake, multinomial logistic regression models were utilized. Additionally, a linear regression analysis was performed to investigate the relationship between childhood hemoglobin levels and nutritional consumption and household variables. The study found relationships between maternal age, type of housing, maternal education, and wealth index, as well as childhood anemia and these sociodemographic variables. For example, 63.2% of children in the poorest homes were anemic, compared to 52.9% of children in the richest households ($p < 0.001$). Furthermore, children with anemia had a higher likelihood of being iron and vitamin A deficient, as well as having reduced.

Chungkham et al. (2021) (19) investigated the risk factors of childhood anemia in India, utilizing geo-additive logistic regression models to analyze data. Strong evidence of residual spatial effects was discovered, with most states in the northeastern region of India exhibiting negative spatial effects and large positive spatial effects in Northern and Central India. There was shown to be a U-shaped non-linear association between childhood anemia and mother age, suggesting that children of younger and older mothers had a higher risk of anemia. Additionally, it was found that the length of nursing had non-linear impacts on childhood anemia. In addition to addressing unknown or unmeasured factors contributing to childhood anemia at the community level, the study emphasizes the significance of government-funded child health programs that focus on known measurable factors, such as mother's education, mother's anemia status, family wealth status, and child health indicators (fever, stunting, underweight, and wasting).

In a community-based field research project conducted in rural Karnataka, India, Pasricha et al. (2009) (20) examined the demographics and healthcare delivery. The purpose of the study was to look at anemia in the local youthful population. At first, it was thought that 470 kids living in particular areas could be interested in participating in the study. Following this, 415 kids (88.3%) showed up for screening; 10 were turned away because they had had fever and/or previous transfusions. In the end, after accounting for two sets of twins to avoid duplication, 405 kids were enlisted. 203 (50.3%) of the 403 youngsters who were included were male. The study offered a thorough profile of the mothers and kids in the studied community. It was found that 75.3% of the children and 63.1% of the moms were anemic.

The varying prevalence rates across studies can be attributed to differences in methodologies (e.g., capillary vs. venous blood sampling), population demographics, geographical areas studied, and the specific health and nutritional statuses of the subjects. These variations underscore the complexity of addressing anemia and the necessity for tailored, context-specific interventions to effectively combat this pervasive health issue.

Defining Anemia

Anemia is characterized by a deficiency in red blood cell (RBC) counts, leading to inadequate oxygen delivery to the body's tissues and organs. (21). Diagnosis typically relies on identifying low hemoglobin (Hb) levels. Severe anemia can cause the heart to work excessively to compensate for the lack of oxygen, leading to high-output heart failure, which is a clinically significant and potentially life-threatening condition (21,22). The Hb thresholds for diagnosing anemia take into account a range of factors, including age, gender, pregnancy status, genetic predispositions, and environmental factors such as smoking and high-altitude exposure (21).

In newborns, Hb levels are highest at 17-21 g/L, decreasing during early infancy before rising again in childhood (23–25). Despite these variations, the World Health Organization (WHO) recommends a universal cut-off value of 11 g/dL for children up to 59 months, regardless of gender and age groups (26).

Iron Deficiency Anemia (IDA) is a specific type of anemia characterized by a reduction in the oxygen-carrying capacity of RBCs and decreased production of these cells. This condition results in various symptoms due to inadequate oxygen supply to body tissues. (27) IDA is a global health concern, significantly impacting diverse populations. Its prevalence varies by demographic factors and geographic regions, notably affecting approximately 47.4% of children globally. Among women of reproductive age, particularly during pregnancy, the prevalence can reach up to 56% in certain areas. Low-income countries experience a heightened burden of IDA due to limited access to varied diets and adequate healthcare (10,28).

In India, IDA remains a significant public health concern. From 2005-2006 to 2015-2016, the prevalence of IDA decreased modestly by 3.5 percentage points, affecting 53.0% of women aged 15-49 in 2015-2016. Alarmingly, IDA increased in eight states, even in those with a higher Human Development Index. Despite guidelines for Iron and Folic Acid supplementation, their impact is limited due to irregular consumption (29).

The development of Iron Deficiency Anemia (IDA) is attributed to several interconnected mechanisms. A primary factor is inadequate dietary iron intake, which is particularly prevalent in regions with limited access to iron-rich foods. Additionally, impaired iron absorption can hinder the body's ability to utilize dietary iron effectively, often due to gastrointestinal conditions such as celiac disease or inflammatory bowel disease (30). Iron-deficiency anemia is a prevalent issue among young children, including infants and those aged 1 to 3 years, often associated with nutritional factors such as excessive consumption of cow's milk. Bottle-feeding with cow's milk, often combined with flour products, is a common practice, with infants consuming up to 2 liters per day, both during the day and at night, which can contribute to iron deficiency. However, this overconsumption of cow's milk can lead to difficulties in regulating milk intake, resulting in decreased iron levels. Introducing cow's milk at early ages can adversely affect iron stores, contributing to anemia and potentially causing ocular hemorrhages in healthy infants and young children. Furthermore, cow's milk, with its high calcium and casein content, can inhibit iron absorption and impose a significant renal load, exacerbating the issue (31).

Additionally, there is an increased need for iron during growth phases or pregnancy, and failing to meet these demands can lead to iron deficiency. Chronic blood loss, such as gastrointestinal bleeding or heavy menstruation, also contributes significantly to iron loss if not adequately compensated by dietary intake. These multifaceted mechanisms highlight the importance of addressing both dietary and physiological factors in the prevention and treatment of IDA (32).

Hepcidin, a liver-synthesized peptide, plays a vital role in regulating cellular iron transport. Transferrin, a plasma protein, transports iron from the bloodstream into cells, where iron levels are determined. The release of iron into circulation is facilitated by a number of cellular sources, including enterocytes in the duodenum, which take iron from meals, macrophages, which obtain iron from aged red blood cells, and liver reserves. The only known iron exporter, ferroportin (FPN), helps these cell components release iron into the bloodstream. Many tissues, including the placenta, liver, spleen, and duodenum, express FPN. By attaching itself to FPN, hepcidin causes internalization and destruction of the protein. Consequently, the inhibition of iron release from cells lowers iron absorption from the duodenum and restricts iron release from macrophages in the liver and spleen (33).

Anemia's etiology depends on whether the corrected reticulocyte count is less than 2% or more than 2%, it might be classified as hypoproliferative. By mean corpuscular volume (MCV), hypoproliferative anemias are further divided into three groups: macrocytic anemia (MCV >100 fL), normocytic anemia (MCV 80-100 fL), and microcytic anemia (MCV <80 fL). (34) Iron deficiency anemia, anemia of chronic disease (AOCD), sideroblastic anemia (which can potentially show up with a high MCV, leading to a dimorphic cell population), thalassemia, and lead poisoning are all potential causes of hypoproliferative microcytic anemia (MCV <80 fL). Hypoproliferative normocytic anemia (MCV 80-100 fL) includes conditions such as AOCD, renal failure, aplastic anemia, pure red cell aplasia, myelofibrosis or myelophthisic processes, and multiple myeloma Macrocytic anemia can result from either a hypoproliferative disorder, hemolysis, or both. Evaluating a patient with macrocytic anemia involves calculating the corrected reticulocyte count. In hypoproliferative macrocytic anemia, the corrected reticulocyte count is <2%, and the MCV is greater than 100 fL. If the reticulocyte count is >2%, hemolytic anemia should be considered. Myelodysplastic syndrome (MDS), refractory anemia (RA), refractory anemia with ringed sideroblasts (RA-RS), refractory anemia with excess blasts (RA-EB), refractory anemia with excess blasts in transformation, chronic myelomonocytic leukemia (CMML), drug-induced causes (including diuretics, chemotherapeutic agents, hypoglycemic agents, antiretroviral agents, antimicrobials, and anticonvulsants) can all lead to hypoproliferative macrocytic anemia (MCV >100 fL) (35). There are two categories of causes for hemolytic anemia (HA), extravascular and intravascular. The majority of cases of hemoglobinopathy (HA) are caused by extravascular hemolysis, which occurs when red blood cells are removed from circulation prematurely by the liver and spleen. Other potential causes of hemoglobinopathies include enzymopathies (like G6PD deficiency and pyruvate kinase deficiency), membrane defects (like hereditary spherocytosis and hereditary elliptocytosis), and drug-induced causes. Less frequently occurring conditions like paroxysmal nocturnal hemoglobinuria (PNH), autoimmune hemolytic anemia (AIHA), transfusion reactions, microangiopathic hemolytic anemia (MAHA), disseminated intravascular coagulation (DIC), infections, and snake bites/venom can cause intravascular hemolysis, which is the lysis of red blood cells within the circulation (11).

Emerging diagnostic techniques now integrate the serum soluble transferrin receptor (sTFRC) assay, which demonstrates an increase in cases of iron deficiency anemia (IDA). In instances of iron deficiency, the production of the transferrin membrane receptor is stimulated, leading to elevated levels of serum soluble transferrin receptor (sTFRC). Unlike traditional markers, sTFRC levels remain unaffected by inflammatory or infectious conditions, rendering it highly valuable for diagnostic purposes. Another significant indicator of iron metabolism is serum hepcidin, whose levels notably decline in cases of IDA as iron absorption should not be hindered in such circumstances. Conversely, hepcidin levels are raised in anemia associated with chronic diseases and obesity. In response to inflammatory signals, particularly those mediated by interleukin-6, hepatocytes release hepcidin. However, levels of hepcidin in genetically determined iron deficiency anemia (IRIDA) may be inappropriately normal or high (33)

In children, IDA is characterized by low hemoglobin levels resulting from insufficient iron levels in the body. Symptoms such as fatigue, pallor, and weakness are common, leading to reduced physical activity. The development of IDA in children is often due to a variety of factors, including inadequate iron consumption in food, limited access to diverse diets, and socioeconomic factors impacting nutrition. (28,36).

Iron deficiency during early childhood can have far-reaching consequences, such as impairments in growth and development. Stunted growth, delays in motor and cognitive development, and a weakened immune system increasing susceptibility to infections are some of the disorders associated with iron deficiency. IDA can also result in decreased school performance and cognitive deficits, which can have long-term implications for educational attainment and future productivity (37).

Clinical Significance of Anemia

The symptoms of anemia can vary depending on the rate of loss of blood. Classically, they consist of weakness, tiredness, lethargy, restless legs, and shortness of breath, particularly during exertion, along with near syncope. More severe anemia can lead to chest pain and reduced exercise tolerance. Additionally, individuals may experience pica, which is a desire to eat unusual and non-dietary substances. Mild anemia, however, may be asymptomatic (11).

Symptoms of anemia in children are primarily due to insufficient oxygen in the cells, with many symptoms not manifesting in cases of mild anemia. An elevated heart rate, dyspnea or difficulty breathing, fatigue or lack of energy, headaches, dizziness or vertigo, especially when standing, and irritability are common symptoms. Additional symptoms may A sore or swollen tongue, jaundice (yellowing of the skin, eyes, and mouth), an enlarged spleen or liver, irregular menstrual cycles, absent or delayed menstruation, slow or delayed growth and development, and poor wound and tissue healing. . These signs and symptoms frequently mimic those of other blood diseases or medical illnesses. Crucially, anemia frequently indicates the presence of an underlying illness (38).

The study conducted by Sen and Kanani (2009) (39) aimed to evaluate the effects of daily and intermittent iron-folate (IFA) supplementation on the physical work capacity of underprivileged schoolgirls in Vadodara. This randomized controlled trial involved 163 schoolgirls aged 9-13 years from municipal primary schools. For a year, IFA tablets were distributed to three schools—one every week, two every week, or every day—while the fourth school acted as the control. Hemoglobin levels and a modified version of the Harvard Step Test were used as outcome indicators for physical labor capability. The number of steps ascended and recuperation time among the three IFA supplemented groups were significantly better than the controls, according to the results. Additionally, compared to girls with lower hemoglobin gains, the effect was more noticeable in those with higher gains (>1 g/dL). Better results were also shown with increasing dose frequency; daily supplementation produced the greatest effects. On the other hand, it was discovered that twice-weekly IFA was equivalent to daily supplementation, especially in cases of high compliance.

Severe anemia from an early life can lead to poor neurological development, which can show up as developmental, mental, and cognitive disabilities. Neurological issues can cause symptoms like headaches, tinnitus, dizziness, poor attention, and irritability. These symptoms are frequently nonspecific. Undiagnosed or untreated anemia can lead to more serious disorders such as peripheral neuropathy, encephalopathy, myelopathy, cognitive impairment, and focal syndromes like transverse myelitis, convulsions, stroke, and chorea. (40–42)

Lozoff et al. (2006) (41) conducted a comprehensive review, emphasizing that iron deficiency in infancy can result in enduring developmental and behavioral disturbances. The study, conducted at the University of Michigan, United States, included a sample size involving numerous children. They found that children with iron deficiency anemia scored lower on cognitive, motor, social-emotional, and neurophysiological tests compared to non-anemic children. These deficits were noted to persist even after iron levels were restored.

Grantham-McGregor and Ani (2001) (43) conducted a review of studies on the effect of iron deficiency on cognitive development in children. The review analyzed a variety of correlational and longitudinal studies to examine proof of a causal relationship. Correlational investigations have regularly reported links between behavioral issues, poor cognitive and motor development, and iron deficiency anemia, the review highlighted the challenge of making causal inferences due to potential confounding effects of socioeconomic backgrounds. Longitudinal studies indicated that children anemic in infancy continued to experience cognitive and behavioral difficulties into middle childhood. However, short-term trials of iron treatment in children under two years old generally failed to show benefits, and longer trials lacked randomized placebo groups. Only one small randomized controlled trial demonstrated clear benefits, raising uncertainty about whether poor development in iron-deficient infants is reversible with iron treatment or due to irreversible damage. The review also noted design problems in preventive trials for older children and emphasized the need for further randomized controlled trials, particularly in younger children, to clarify the impact of iron deficiency on cognitive development.

A study by Armony-Sivan et al. (2004) (44) looked at the connection between premature infants' neurobehavioral development and iron status. Infants who were medically stable and born before 34 weeks postmenstrual age were included in the study. Hemoglobin levels ≤ 10 g/dL were considered anemia, while serum ferritin concentrations ≤ 75 µg/L were considered poor iron reserves. The infants were categorized into three groups: anemic with low ferritin (Group 1; n=18), anemic with normal ferritin (Group 2; n=14), and non-anemic with normal ferritin (Group 3; n=21). At 37 weeks postmenstrual age, reflex scores were measured; higher scores corresponded to a higher proportion of aberrant reflexes. As compared to infants in Group 3 (38.32% ± 17.75%), the results indicated that infants in Group 1 had a considerably higher reflex score (51.45% ±

18.32%). Group 2's score (45.40% ± 21.70%) was in the middle of the other two groups', although it was not substantially different. The study came to the conclusion that lower neurobehavioral state in premature newborns is linked to low iron status, as seen by both anemia and ferritin levels.

Beard and Connor (2006) (41) discussed the role of iron in brain development. Their research emphasized that iron is crucial for myelination, neurotransmitter function, and energy metabolism in the brain. Iron deficiency during critical periods of brain development can conclude in irreversible cognitive and behavioral impairments.

Pivina et al. (2019) (42) elucidated that iron deficiency anemia (IDA) significantly impacts cognitive functions and psychomotor development in children. They highlighted the role of iron in brain metabolism, emphasizing its involvement in neurotransmitter homeostasis, myelin production, synaptogenesis, and basal ganglia function. The review underscored the frequent comorbidity of iron deficiency with attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), exacerbating cognitive impairment. Furthermore, the authors discussed the potential for iron deficiency to induce or worsen deficiencies in other essential nutrients, thereby compromising overall brain and organ development in infants. Additionally, they emphasized the worldwide cost-effectiveness of iron fortification and supplementation programs in reducing cognitive impairment, based on World Health Organization (WHO-CHOICE) guidelines.

A study by Hannah et. al, (45) conducted in Germany in 2022 underscores the clinical significance of the link between iron deficiency anemia (IDA) and the unusual but potentially severe form of pediatric thrombosis due to its widespread prevalence. The study suggests that evidence from animal research also supports this connection, indicating that both IDA and secondary thrombocytosis serve as independent risk factors for the initiation and progression of blood clot formation. This correlation highlights the significance of addressing iron deficiency in children to mitigate the risk of thrombotic complications.

Preventive strategies:

By the age of 5 to 6 months, infants with a normal birth weight typically exhaust their iron stores. Traditional complementary foods that aren't fortified with iron don't have enough iron to meet the high needs of these developing babies. Those born with low birth weight, prematurely, or to mothers with anemia require additional iron beginning at one month of age, usually given at a dosage of 2 mg per kilogram per day.

Simple nonpharmacologic interventions can effectively prevent iron deficiency anemia (IDA) (46). Delayed cord clamping for more than one minute after birth is associated with reduced IDA in infancy. Cooking with iron pots is another beneficial practice (47). Avoiding bottle-feeding for infants and children, exclusively breastfeeding until six months of age, and refraining from feeding unmodified, non-formula cow's milk until one year of age are also recommended. For children aged one to five years, milk consumption should be restricted to no more than 500 ml per day. Preventing and treating iron deficiency in pregnant women is crucial to ensure that newborns have adequate iron stores. Encouraging the intake of iron-rich foods, such as chickpeas (chana sag), fenugreek leaves (methi), spinach (palak), amaranth (chaulai), mustard leaves (sarson ka sag), onion stalks (pyaaz ki kali), lentils (dal), Bengal gram (kala chana), other whole pulses, ground nuts, soybeans, jaggery (gur), eggs, meat, poultry, and fish, is essential. Additionally, including vitamin C-rich foods to improve iron absorption and avoiding consumption of absorption inhibitors like tea with or shortly after meals is beneficial. Since calcium inhibits iron absorption by almost 60%, it ought to be administered independently, with enough time elapsed between each.

Oral Iron Supplements:

Oral iron supplements are a commonly used as preventive and treatment modality for IDA in children. These supplements typically contain ferrous salts, such as ferrous sulfate or ferrous fumarate. When ingested, these salts release ferrous iron ions in the acidic surroundings of the stomach. The absorbed ferrous iron is then transported across the intestinal lining into the bloodstream, where the iron bound to transferrin is transported to different tissues including the bone marrow. There, it is utilized for haemoglobin synthesis and for replenishing iron stores (36,48).

Oral iron supplements have demonstrated efficacy in treating mild to moderate IDA in children. Clinical studies have shown significant improvements in haemoglobin levels and overall iron status with consistent and appropriate dosing. For instance, a study compared daily versus alternate day oral iron supplementation for treating iron deficiency anemia in 200 adults with hemoglobin ≤10 g/dL and/or serum ferritin <50 ng/mL. Participants received either two 60 mg ferrous sulfate tablets on alternate days or one 60 mg tablet daily for 8 weeks. The primary outcome was the mean change in hemoglobin at week 8. Results showed no significant difference in hemoglobin improvement between the alternate day (+1.05 ± 1.34 g/dL) and daily (+1.36 ± 1.51 g/dL) groups ($p = 0.47$). The study concluded that both dosing regimens are equally effective, suggesting further research is needed to determine the optimal supplementation strategy (49). Another study, investigated optimal oral iron supplementation for women with iron deficiency and mild iron deficiency anemia (IDA) revealed crucial insights. Findings suggest that administering oral iron doses of at least 60 mg on alternate days, preferably in the morning, enhances iron absorption and may reduce gastrointestinal side effects. This research advocates for a shift from traditional daily dosing to alternate-day regimens, potentially improving treatment efficacy and patient compliance in managing iron deficiency and IDA among young women (50). However, the efficacy may be hindered by factors such as non-compliance with regimens and gastrointestinal side effects, including nausea, constipation, or abdominal discomfort. Therefore, ensuring proper compliance and addressing side effects are crucial for the success of oral iron therapy (51,52).

Ferrous Sulfate:

Ferrous sulfate, a widely employed oral iron supplement, operates through a well-defined mechanism to address iron deficiency anemia (IDA). When ingested, ferrous sulfate tablets release ferrous iron (Fe2+) in the stomach. In their systematic review and meta-analysis, Tolkien et al. (2015) aimed to assess the tolerability of oral iron supplementation, specifically ferrous sulfate, for treating iron deficiency anemia in adults. They analyzed data from 43 randomized controlled trials involving 6,831 participants who were adults. Their findings revealed that ferrous sulfate supplementation notably increased the risk of gastrointestinal (GI) side effects compared to both placebo and intravenous (IV) iron. The odds ratio (OR) for GI side effects versus placebo was 2.32 [95% CI 1.74–3.08], and versus IV iron was 3.05 [95% CI 2.07-4.48]. Subgroup analyses in specific populations, such as patients with inflammatory bowel disease (IBD) and pregnant women, further supported these findings. The study found that ferrous sulfate supplementation is associated with a significant increase in GI-specific side effects in adults, even though meta-regression did not demonstrate a significant connection between iron dosage and side effects. (53)

In their study, Duque et al. (2014) compared the efficacy of ferrous sulfate and iron bis-glycinate chelate supplements in increasing ferritin concentration in iron-deficient schoolchildren. Over 12 weeks, 200 participants received either supplement. Both increased ferritin levels post-supplementation. Iron bis-glycinate chelate showed superior efficacy in maintaining elevated ferritin levels six months after supplementation. This highlights its potential long-term benefits.

The study underscores the importance of preventive interventions targeting iron deficiency in vulnerable populations. (54)

The double-blind randomized controlled trial conducted by Suryani et al (2022) enrolled 54 heart failure patients with IDA who were randomized to receive either oral Ferrous Sulphate (FS) 200 mg three times a day or placebo for 12 weeks. The primary outcome, measured by a six-minute walk test, showed a notable improvement in functional capacity in the FS group compared to the placebo group (46.23 ± 35 m vs -13.7 ± 46 m, $p < 0.001$, CI –86.8 to –33.2) after the intervention period. This study provides evidence that oral ferrous sulfate supplementation can enhance functioning ability in individuals with iron deficient anemia suffering from heart failure (55).

Intravenous (IV) Iron Therapy:

Intravenous (IV) iron therapy is an alternative for children with severe IDA or when oral supplements are not effective or tolerated. IV iron therapy involves the direct infusion of iron formulations, such as iron sucrose, ferric carboxymaltose, or ferric gluconate, into the patient's bloodstream. IV iron bypasses the gastrointestinal tract, delivering iron directly into the circulatory system. Iron is then readily available for uptake by RBC precursors in the bone marrow, which rapidly increases the haemoglobin and efficiently replenishes the iron stores (56,57).

IV iron therapy is highly effective, particularly in cases of severe IDA or when oral supplements are not well tolerated or effective. This approach causes a rapid increase in haemoglobin levels and efficiently replenishes iron stores, often within a matter of weeks. Clinical studies have consistently demonstrated the superiority of IV iron in terms of efficacy and speed of response compared to oral supplementation. However, IV iron should be administered by healthcare professionals, as it carries a risk of hypersensitivity reactions, although these are rare (58,59).

Hall et al. (2009) investigated the efficacy and safety of intravenous iron sucrose in pediatric patients with iron deficiency and/or gastrointestinal hemorrhage. Analyzing data from 157 children at Children's Medical Center Dallas, the study revealed significant improvements in hemoglobin levels across various indications, including refractory iron deficiency, primary iron malabsorption, and chronic gastrointestinal blood loss. Of the 38 patients analyzed, IV iron sucrose demonstrated a notable mean increase in hemoglobin levels: 3.5 g/dl in those refractories to oral iron, 1.8 g/dl in cases of primary malabsorption, and 2.9 g/dl in patients with chronic blood loss. Adverse reactions were infrequent, with only 6 out of 510 doses leading to mild reactions and one serious reaction reported (60).

In their retrospective review, Strachan et al. (2024) investigated the safety, efficacy, and adherence of intravenous (IV) iron infusions compared to oral iron therapy in pediatric patients with iron deficiency anemia (IDA) who had previously failed oral supplementation. Analyzing medical records of 107 pediatric patients aged 1-21 at Cooper University Hospital, they found significant improvements in hematologic indices including hemoglobin, ferritin, iron, and iron saturation post-IV iron infusion compared to pre-infusion levels. Subgroup analyses by race and etiology of IDA further supported these findings. Importantly, when compared to oral iron therapy, IV iron infusion adherence was substantially higher, and there were also fewer side effects associated with IV infusions than with oral supplements. This study suggests IV iron infusions as a promising alternative for children's patients with IDA who cannot tolerate oral supplements because of the safety, effectiveness, and better adherence associated with these treatments. (61). Although IV route is more effective than oral formulations, it will not be feasible to use it at community level for prevention of IDA. The higher expense of parenteral iron and its associated burden on the healthcare system prevent its widespread usage. (62,63). Despite its efficacy, many clinicians remain hesitant to prescribe IV iron due to concerns about potential hypersensitivity reactions (64).

WHO programs

The World Health Organization (WHO) has implemented several global programs aimed at addressing anemia in children. One notable initiative is the WHO Global Anemia Reduction Framework, which provides a comprehensive approach to combating anemia across all age groups, including children (65). This framework emphasizes the importance of multisectoral collaboration, evidence-based interventions, and monitoring and evaluation to achieve sustainable reductions in anemia prevalence. Additionally, the WHO recommends strategies such as universal iron supplementation for infants and young children, fortification of staple foods with iron and other micronutrients, promotion of optimal infant and young child feeding practices, and deworming interventions in areas with high prevalence of parasitic infections. These interventions are part of broader efforts to improve nutrition, enhance maternal and child health, and reduce the burden of preventable diseases worldwide (66).

Intermittent vs Daily therapy

The World Health Organization (WHO) suggests intermittent iron supplementation as a viable alternative to daily iron supplementation for preventing Anemia in children. This approach targets both preschool-age children (24–59 months) and school-age children (5–12 years). Preschool-age children are provided with 25 mg of elemental iron in the form of drops or syrups, while school-age children receive 45 mg of elemental iron in tablet or capsule form, all at a frequency of once a week (67). The supplementation spans a cycle of three months on supplements followed by three months without, after which supplementation resumes. Supplements may be given sporadically during the academic year or calendar year, if practical. This strategy is especially recommended in environments where anemia prevalence in these age groups is 20% or above. However, it's vital to acknowledge that the choice between intermittent and daily iron therapy should consider the specific context and anemia prevalence within the target population. Local health authorities and healthcare providers should be consulted to determine the most suitable iron supplementation strategy for a given region or population (48). This guideline was scheduled for review in 2015, emphasizing the importance of adapting strategies to evolving health needs.

In a study conducted by Siddiqui et al. (2004) (68) in Karachi, Pakistan, the efficacy of daily versus weekly oral iron supplementation was examined in schoolchildren. The study included a sample size of 60 children aged between 5 and 10 years, all diagnosed with iron deficiency anemia. These children were divided into two groups of equal size: one receiving daily supplementation and the other receiving weekly supplementation. Before the intervention, baseline measurements of hemoglobin (Hb), hematocrit (Hct), serum iron, total iron-binding capacity (TIBC), and serum ferritin were recorded for all participants. The daily supplementation group was administered 200 mg of ferrous sulfate daily, while the weekly supplementation group received the same dosage once a week, over a two-month period. Post-supplementation assessments indicated significant improvements across all parameters in both groups. The findings from Siddiqui et al. (2004) concluded that once-weekly iron supplementation was equally as effective as daily supplementation in treating iron deficiency anemia. This study highlighted the additional benefits of weekly supplementation, including cost-effectiveness and reduced side effects, suggesting a viable alternative to daily supplementation regimes in similar populations.

The study by Jian-Yun Li et al. (2022) (69) examined the effectiveness of intermittent iron supplementation compared to daily supplementation in children with mild IDA. This prospective trial, which took place in China, comprised 147 kids with mild IDA who were split into two groups: those receiving regular supplementation (n = 64) and those receiving intermittent supplementation (n = 83). Before and after treatment, as well as after one and three months, hemoglobin levels were tested to compare treatment response rates and adverse medication reactions. Both groups showed significant hemoglobin increases ($P<0.05$). Initially, the conventional group had a higher treatment response rate (61% vs 42%, $P<0.05$), but after 3 months, the response rates were similar (86% vs 78%, $P>0.05$). Notably, the intermittent group had significantly fewer adverse reactions (8% vs 25%, $P<0.05$). Thus, while intermittent supplementation may be less effective short-term, it matches long-term efficacy and offers advantages in reducing adverse reactions, financial burdens, and improving compliance, indicating its promise for managing pediatric mild IDA

Timothy Mott and Ethan Sellers (2021) (70) conducted a study to determine the comparative efficacy of intermittent versus daily oral iron supplementation in reducing anemia and its associated outcomes. The study focused on different demographics, including children younger than 12 years and menstruating or pregnant women. The results showed that while intermittent iron supplementation is just as effective as daily dosing in women who are menstruation or pregnant, daily iron supplementation is more effective in treating anemia in children under the age of twelve. Additionally, the study showed that women who are menstrual or pregnant had less negative side effects, mostly gastrointestinal ones, when they take iron supplements intermittently. However, children under the age of 12 did not show any discernible differences in side effects. Based on a meta-analysis of lower-quality randomized controlled trials with SORT B evidence quality ratings, the findings were drawn. This study emphasizes how different iron supplementation regimens are effective for different populations.

Luz Maria De-Regil et al (2011) (71). evaluated the efficacy of intermittent iron supplementation in children under 12 years old, aiming to address the widespread issue of iron deficiency anemia (IDA) affecting approximately 600 million children globally. The research evaluated daily supplementation, no intervention, and intermittent iron supplementation with 33 trials comprising 13,114 children from Latin America, Africa, and Asia. The outcomes showed that, in comparison to no intervention or a placebo, intermittent iron supplementation significantly reduced the likelihood of anemia and iron deficiency while raising hemoglobin and ferritin concentrations. However, intermittent iron supplementation was found to be less helpful in preventing anemia than regular administration. Despite this, the group receiving occasional supplements may have had superior adherence rates. Further research is necessary to fully understand the impact of intermittent iron supplementation on mortality, morbidity, developmental outcomes, and side effects. The findings suggest that iron supplementation on an intermittent basis could be a viable public health intervention in areas where daily supplementation has not proven effective.

The effectiveness of intermittent versus daily iron administration was examined in a clinical setting in research by Ahmad Faqih et al. in 2006 (72), involving Jordanian children aged 2 to 6 who had been diagnosed with iron-deficiency anemia (IDA). Out of 4,400 children who underwent screening, 134 were recruited and allocated at random to receive iron treatment twice a week, weekly, or daily for a duration of three months. Hemoglobin, serum ferritin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration all significantly increased in all groups, with no significant differences observed between them, according to the results. In the population under study, weekly and twice-weekly iron therapy combined with nutritional counseling was found to be just as successful in correcting iron deficiency anemia (IDA) as daily iron therapy. This finding suggests that intermittent iron supplementation may be useful in clinical settings.

Anemia Mukt Bharat:

The Anemia Mukt Bharat Programme, initiated by the Ministry of Health and Family Welfare (MoHFW), Government of India, aims to expedite the reduction of anemia across various age groups. It seeks to bolster existing mechanisms while introducing new initiatives to combat anemia effectively. Originally launched as the National Nutritional Anemia Prophylaxis Programme (NNAPP) in 1970, it was renamed Anemia Mukt Bharat in 2018. Under the POSHAN Abhiyan, the Anemia Mukt Bharat programme targets six beneficiary groups and employs six interventions and institutional mechanisms to fulfill its goal of reducing anemia (73).

The "Anemia Mukt Bharat" initiative is intended to deal with the complex and multifactorial causes of Anemia in India, emphasizing both preventive measures and targeted treatments to reduce the prevalence of this condition and enhance the overall health of the population. The core preventive therapies in this initiative include prophylactic iron and folic acid supplementation, deworming, and nutritional improvements. Prophylactic supplementation is provided across different age groups, from young children to pregnant women. Deworming is implemented biannually, and nutritional improvements aim to increase the intake of iron-rich foods. These therapies are essential components of the initiative to combat Anemia in India. It's important to note that the management protocol for Anemia involves treatment options based on the severity of Anemia, with a focus on screening, regular follow-ups, and referrals, when necessary, especially for severe cases. The initiative also highlights the need for early breastfeeding and cord clamping practices to enhance infants' iron reserves (12). Counseling to increase compliance can be given to beneficiaries or caregivers regarding the advantages and potential mild adverse effects of consuming IFA leading. (74).

In their study, William Joe et al. (2022) (75) investigated the progress of Iron and Folic Acid (IFA) supplementation coverage in India following the implementation of the Anemia Mukt Bharat (AMB) strategy. Utilizing Health Management Information System data from 2017–18 to 2019–20, the study revealed notable improvements in IFA coverage across beneficiary groups. Pregnant women's coverage increased from 78% to 90%, while lactating mothers' coverage rose from 34% to 49%. For school-going adolescent girls (boys), coverage improved from 23% to 40% (21% to 42%), and out-of-school adolescent girls witnessed an increase from 6% to 23%. Coverage for children aged 5–9 years increased from 3% to 8%, and for children aged 6–59 months, it rose from 7% to 15%.

The study also highlighted relatively lower coverage for groups served through multi-departmental convergence mechanisms compared to those served solely by the health department. However, no significant gender disparities were observed in IFA supplementation coverage among school-going girls and boys. State-specific differences accounted for most variations in coverage, emphasizing the importance of tailored interventions. In order to remove coverage inefficiencies, the authors advocated for synergy in program execution across line departments and stressed the importance of training and sensitization seminars for state and district authorities.

A study conducted by Usha Malagi et al. in 2006 (76) to assess the effectiveness of the National Nutritional Anaemia Control Programme in Dharwad, Karnataka, revealed that approximately 35% of beneficiaries received only a single dose of 30 tablets, suggesting irregular distribution. Of the participants, 58.34% consumed all the tablets, while 25% consumed half the prescribed dose.

Notably, 8.33% did not consume any tablets, and the same percentage did not receive any tablets at all. The study identified poor quality and irregular supply of iron and folic acid (IFA) tablets as major hindrances to the successful implementation of the program.

In the rural Karnataka study conducted by Shet et al. (2009) (20), findings indicated that fewer than half of the children, specifically 167 out of 402 (41.5% [36.7-46.4]), had ever received iron supplements. Furthermore, only 45 out of 393 people (11.5% [8.3-14.6]) had ever gotten iron from a government facility like an Anganwadi center, sub-center, or Primary Health Center (PHC). It's interesting to note that most youngsters who received iron—113 out of 158, or 71.5% [64.4-78.6]—got it from private companies as opposed to public ones.

Liposomal Iron:

Innovative approaches to iron supplementation, particularly liposomal iron, and Sucrosomial Iron (SI), have garnered significant attention. A study demonstrated the efficacy of liposomal iron supplementation, revealing its potential as a novel approach to addressing iron deficiency(77). Encapsulating iron salts within liposomes offers unique advantages, including improved absorption and bioavailability compared to conventional forms. The liposomal structure facilitates intact passage through the gastric acid barrier and direct uptake by intestinal M cells, bypassing the need for specific transporters. This mechanism ensures maximal delivery to hepatocytes, enhancing iron utilization while minimizing gastrointestinal side effects. Comparative studies have shown that liposomal iron exhibits superior absorption rates, with plasma concentration peaking within two hours post-administration. Furthermore, liposomal formulations may mitigate inhibitory effects of compounds like phytic acid and zinc on iron absorption (77)

A study by de Alvarenga Antunes et al. (2020), (78) investigated the efficacy and safety of oral liposomal iron supplementation in treating iron deficiency anemia (IDA) in patients with inflammatory bowel disease (IBD). This interventional pilot trial, which ran from November 2016 to March 2018, evaluated 200 patients with inactive or mildly active IBD for anemia; 40 patients (20%) were found to be anemic. Thirteen patients (62%) out of the twenty-one who received oral liposomal iron for eight weeks showed signs of responding to the treatment, with a mean increase in hemoglobin levels from 11.4 to 12.6 g/dL. Furthermore, there was an average increase in the transferrin saturation index of 10.2 ($p = 0.006$), an improvement in quality-of-life scores of 26.3 ($p < 0.0001$), and an average decrease in the impression of fatigue of 9.2 ($p < 0.0001$). According to these results, oral liposomal iron supplementation can help patients with inactive or mildly active IBD feel less fatigued and improve their quality of life and mild IDA. This study highlights the potential of liposomal iron therapy as a beneficial treatment approach for IDA in IBD patients, warranting further investigation and consideration in clinical practice.

Research by Visciano and colleagues has explored the unique attributes of liposomal iron, highlighted its elevated bioavailability and reduced gastrointestinal side effects (79,80). As Gómez-Ramírez and collaborators have extensively investigated, SI represents a new generation of iron supplementation with remarkable clinical potential (8,9,81).

Liposomal iron, enveloped by liposomes as elucidated by Visciano, exhibits exceptional characteristics. Liposomes are spherical structures composed of phospholipids similar to those found in human cell membranes. This innovative setting up enables these iron compounds to traverse through the challenging gastric acid barrier and eventually reach the small intestine unharmed. According to Gómez-Ramírez, specialized M cells within the intestine, characterized by low lysozyme content, are responsible for the efficient absorption of liposomal iron without requiring any specific transporters. Subsequently, as noted by Fabiano and Zambito, liposomal iron is taken up through endocytosis by macrophages and transported intact through the lymphatic system to reach hepatocytes in the liver. The protective shield provided by the liposome, as discussed by Fabiano et al., allows the iron to bypass the harsh gastric environment, preventing early degradation or inactivation. This unique mechanism, according to Visciano, grants liposomal iron greater bioavailability, reduces the occurrence of gastrointestinal side effects, and safeguards against iron instability in the gastrointestinal tract, ensuring its direct absorption into the intestine and eventual liberation into the liver.

Furthermore, the research of Fabiano and colleagues indicates that liposomal pyrophosphate iron's absorption or bioavailability surpasses that of free pyrophosphate iron by a factor of 3.5, exceeds iron sulfate by a factor of 2.7, and outperforms iron gluconate by a factor of 4.1. Moreover, the peak plasma concentration of liposomal iron occurs approximately 2 hours after ingestion, ensuring greater bioavailability of this essential element for various metabolic processes (79).

Nevertheless, it's worth noting that circulation of iron can be influenced by the size of liposomes, as discussed by Baomiao et al. larger liposomes tend to exhibit reduced iron transport efficiency. Moreover, depending on liposome size, various uptake pathways may be employed, as indicated by Baomiao and Xiangzhou. These pathways can include alterations in signaling processes critical for fundamental cellular functions, receptor-mediated endocytosis, and phagocytosis, rather than traditional absorption routes (82).

On the other hand, Sucrosomial Iron (SI), developed by Alesco srl in Pisa, Italy, as reported by Gómez-Ramírez, is an innovative oral iron-containing carrier that represents a significant advancement in iron supplementation. SI is designed to protect ferric pyrophosphate, an iron compound, using a sophisticated encapsulation method (8). The core of SI consists of ferric pyrophosphate, an essential source of iron, which is enveloped and safeguarded by a phospholipid bilayer membrane primarily derived from sunflower lecithin. The addition of a sucrester matrix, derived from the esterification of fatty acids with sucrose, further enhances SI's absorption-enhancing properties, as detailed by Fabiano and colleagues. To ensure stability and effective delivery, SI also includes additional ingredients like tricalcium phosphate and starch. These components collectively form what is referred to as the "sucrosome" (83).

SI boasts a distinctive set of structural, physicochemical, and pharmacokinetic attributes, setting it apart from conventional oral iron salts, as described by Gómez-Ramírez. Its exceptional iron absorption rate and remarkable gastrointestinal tolerability, as studied by Fabiano et al., make it an ideal formulation for the oral treatment of iron deficiency, even in clinical scenarios (9). SI's behavior in the gastrointestinal tract, as outlined by Visciano and Nazzaro, ensures not only its excellent tolerability but also its high bioavailability when compared to traditional iron salts. Remarkably, SI can serve as a suitable therapeutic option in clinical contexts where intravenous (IV) iron is typically considered the standard treatment, as emphasized by Gómez-Ramírez. These clinical scenarios include individuals undergoing bariatric surgery, patients with iron deficiency (ID) or iron deficiency anemia (IDA), and patients with chronic renal disease, inflammatory bowel disease, celiac disease, and cancer, among other illnesses. This versatility positions SI as a promising and well-tolerated alternative for diverse patient populations seeking effective iron supplementation (81).

Liposomal treatments hold profound significance, especially in pediatric populations, as acknowledged by Aksan et al., addressing the unique nutritional needs and challenges faced by children. Their enhanced bioavailability and absorption mechanisms, as explored by Visciano and Fabiano, are especially crucial during childhood, a period characterized by rapid growth and development. These formulations ensure that children receive an adequate supply of iron to support hemoglobin and myoglobin synthesis, vital for oxygen transport and overall physiological function (84). Furthermore, the reduced risk of gastrointestinal discomfort associated with liposomal and SI, as reported by Gómez-Ramírez and Fabiano, enhances treatment compliance, a critical factor in achieving successful iron supplementation in children (8,83). The prevention of ID and its progression to IDA is a pivotal objective, safeguarding the long-term health and cognitive development of pediatric populations.

Gaps in literature:

Our study is motivated by the substantial concern surrounding iron deficiency Anemia, particularly its widespread prevalence in rural regions of India. It underscores the need to explore more effective preventive modalities. Our primary objective is to evaluate the effectiveness of liposomal ferric pyrophosphate in children aged 6-59 months afflicted by this condition. We hypothesize that liposomal iron offers a superior approach to prevent IDA in children when compared to conventional methods. This research aims to provide evidence-based insights to address this pressing public health challenge and improve the well-being of affected pediatric populations.

In conclusion, liposomal iron treatments, as reviewed by Gómez-Ramírez and Fabiano, could represent indispensable tools in pediatric healthcare, as iron supplementation is crucial for optimal growth and development, ensuring effective treatment with reduced side effects. They can also offer pediatric-specific products tailored to the unique requirements of children, ensuring appropriate dosing and ease of administration. These advances in iron supplementation would not only improve the overall health and well-being of children but also address the practical challenges of treating young patients. Despite this, studies on the effectiveness of liposomal iron in the pediatric age group is lacking.

To address this, the current study was undertaken to evaluate the efficacy and safety of liposomal iron in the age group of 6 months to 59 months. We plan to compare the effects of this compound with the conventional ferrous sulfate treatment and to evaluate compliance and side effects of both the compounds.

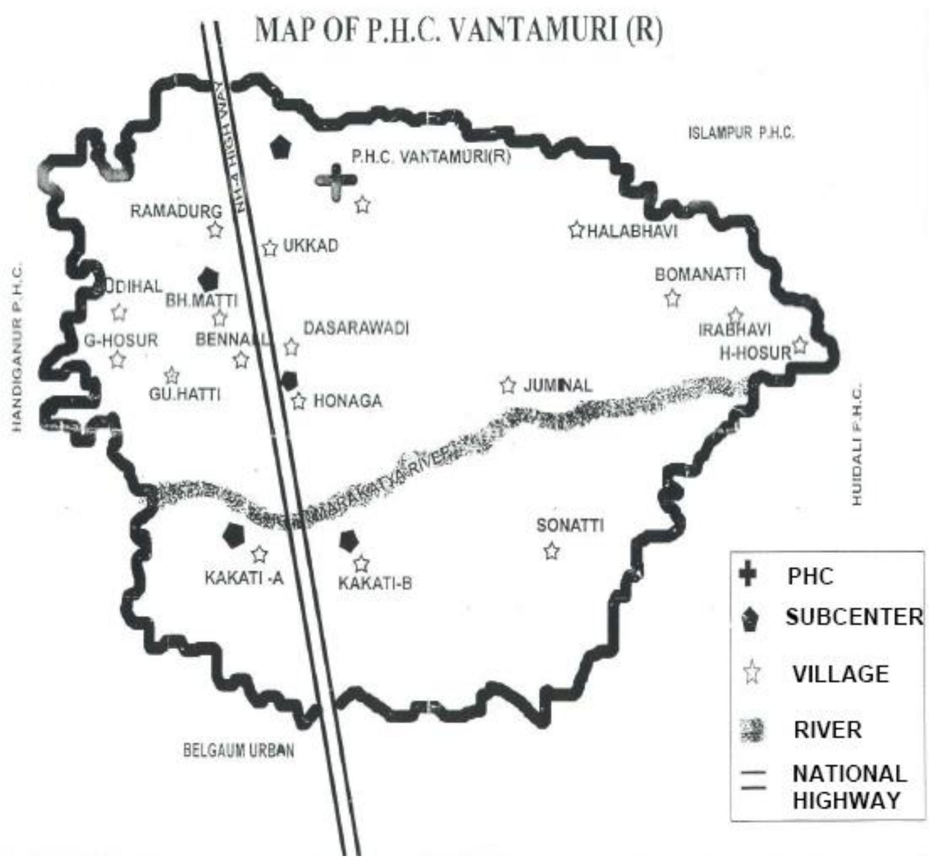
MATERIALS AND METHODS

Study Design: Randomized Control Trial

Study Duration: One year (April 2022 – March 2023)

Study Population: Children in age group of 6 months to 59 months.

Study Setting: Anganwadis under Primary Health Center, Vantamuri which is a field practice area of Jawahar Lal Nehru Medical College, Belagavi, Karnataka



Sample Size:

Two Means - Hypothesis testing for two means (equal variances)

Standard deviation in the Ist group S1 = 1.58

Standard deviation in the IInd group S2 = 2.547

Mean difference between Ist and IInd sample = 2.25

Effect size = 1.09038042161376

Alpha Error(%) = 1

Power(%)= 85

sided = 2

Number needed (n) =24 should be taken in each group

Sample size formula

Where, Z1-a= Z-value for a level (2.58 at 5% alpha error or 95% confidence)

Z1-b = Z-value for b level (1.037 at 15% b error or 85% power)

d=Margin of error=2.25

S=Pooled SD= (S1+S2)/2

Estimated Sample size – 48 (24 in each group)

With a possibility of withdraw of consent for allowing to draw blood sample for follow-up upto 50% which is expected in this population, we have taken extra samples to keep the data statistically appropriate.

Actual sample size – 80(40 in each group)

Sample selection:

- **Inclusion Criteria:**

1. Children in age group of 6 months to 59 months.
2. Children started on complementary feeds with breast feeding.
3. Parents who gave consent for the study.

- **Exclusion Criteria**:

1. Diagnosed case of Iron deficiency anemia on treatment.
2. Severe anemia (Hb <7 g/dL)
3. History of blood transfusion.
4. Children diagnosed with chronic illnesses or any medical condition.

Institutional ethical Clearance: The ethical clearance was obtained prior to the conduct of the study, from Institutional Ethics and Research Committee, KAHER's Jawaharlal Nehru Medical College, Belagavi.

C.T.R.I. registration: The study was registered with Clinical Trial Registry of India prior to sample collection and clearance was granted with registration number **CTRI/2023/03/050585**

Method of collection of data: Participants accompanied by their parents or caregivers were selected during their visits to anganwadis, subcenters, or primary health centers for health checkups, vaccinations, or routine visits. Parents and caregivers received counseling about IDA, its impact on the growth and development of the child, and its implications. They were educated about the importance of preventive measures and the necessity of iron supplementation therapy.

Informed consent: A written informed consent was obtained from the parents of the children who fulfilled the selection criteria after explaining the nature of the study. (Annexure I).

Baseline parameters at enrolment:

Participants fulfilling the inclusion criteria were enrolled for the study and information regarding the baseline parameters were collected and documented in a pretested, structured questionnaire (refer to Annexure II) after obtaining informed consent from parents/caregivers. The baseline parameters collected at enrolment were socio-demographic data, date of birth, birth history, and past clinical history. Physical examination including anthropometric measurements, including weight, height, head circumference, and mid-upper arm circumference, were measured and recorded, followed by a general physical examination and systemic assessment.

Collection of blood sample:

2ml of blood was collected in plain vial and EDTA vial, each by a trained health professional under all aseptic precautions and processed for complete hemogram comprising hemoglobin, MCV, MCHC,MCH,RDW, hematocrit, RBC counts, WBC count and platelet count along with iron studies comprising serum iron, total iron binding capacity, transferrin saturation and serum ferritin. Hemogram was processed by Sysmex XN 350 machine (Sysmex Corporation, Kobe, Japan), a fully automated blood cell counter, and Iron studies by cobas® c 503 machine (Roche Diagnostics, USA) at High Tech Lab, K.L.E. Hospital, Belgaum.

Randomization: Participants were then randomized into 2 groups, namely Group A and Group B using computer generated sequencing and by using opaque sealed envelope method.

Intervention:

Group A:

Participants were administered oral syrup containing liposomal ferric pyrophosphate (CoeHB-Max, manufactured by Koyé Pharmaceuticals), with a dosage of 5ml twice daily, providing 20 mg of elemental iron. This supplementation occurred twice a week, specifically on tuesday and thursday, and was to be administered by the mother or caretaker.

Group B:

Participants received oral syrup containing ferrous sulphate (provided by the Karnataka Government Health Service, under AMB programme), with a dosage of 1ml once daily, also providing 20 mg of elemental iron and 100 mcg of folic acid. Similar to Group A, this supplementation was given twice a week on tuesday and thursday, to be administered by the mother or caretaker.

Follow up visits:

The participants were followed up after a 3 months duration. At follow up visits, repeat blood tests were drawn for complete hemogram and iron studies comprising serum iron, serum ferritin, total iron binding capacity and transferrin saturation. Anthropometric measurements at follow up consisted of weight, height, mid upper arm circumference and head circumference.

The compliance was monitored by history of intake of total number of doses taken weekly over the three month duration in both groups via telephonic conversation.

Participants were enquired about any side effects experienced during the course of study such as vomiting,diarrhea, flatulence, passing of black colored stool or a combination.

The prevalence of anemia was determined using a cutoff of Hemoglobin levels between greater than 7 and less than 11 grams per deciliter, as defined by the Indian Academy of Pediatrics as indicative of mild to moderate anemia.

Primary outcome variables:

Hemoglobin:

We assessed hemoglobin levels at the enrolment and follow-up in both groups and analyzed the change in values to determine if there was a significant difference in hemoglobin change within the group and between both groups. Normal hemoglobin level was >11gm/dL in this age group.

Iron Stores:

Iron stores were evaluated using markers such as serum iron with normal levels in 6-24 months >35µg/dL and in 2-6 years >22 µg/dL., serum ferritin with normal levels in 6-24 months >6ng/dL and in 2-6 years >6µg/dL, transferrin saturation levels in 6-24 months >10% and in 2-6 years >7%, and total iron-binding capacity in 6-24 months <434 µg/dL and 2-6 years <441 µg/dL These measurements were recorded at the enrolment and at follow-up, and the discrepancies in values were evaluated to assess whether any significant changes occurred within each group and between the two groups.

Red Blood Cells parameters:

Red blood cell (RBC) parameters including mean corpuscular volume (MCV) with normal levels of 72-84fl, mean corpuscular hemoglobin concentration (MCHC) with normal levels of 32-36g/dL , mean corpuscular hemoglobin (MCH) with normal levels of 25-29pg , red cell distribution width (RDW) of 12-15% , and hematocrit levels with normal levels of 30-38% in this age group were also recorded at enrolment beginning and follow-up. Differences in these values were analyzed to determine if any significant changes occurred within each group and between the two groups.

W.B.C count and Platelet count:

White blood cell (WBC) count with normal level of 6 to 16 x 10^3 and platelet count 200-550 x 10^3 with normal level in this age group of were measured at the beginning and end of the study period. The differences in these values were analyzed to determine if there were any statistically significant changes over time.

Secondary outcome variables:

Growth parameters:

Measurements of weight (in kilograms), height (in centimeters), head circumference (in centimeters), and mid-upper arm circumference (in centimeters) were taken at the beginning and end of the study period. These values are expected to increase at follow-up , values were analyzed to assess if there were any significant changes between the two groups.

Number of doses taken:

Participants were asked about the number of doses they took over a three-month period. This data was collected via weekly phone calls, where either the mother or a family member, assisted by ASHA workers assigned to the area, provided the information. The total number of doses expected to be taken was 24 (administered twice weekly over the three-month duration).

Side effects:

Caregivers were inquired about the most common side effects associated with iron supplementation, including flatulence, diarrhea, and black-colored stool during follow-up assessments. The data collected from both groups were compared to evaluate incidence of side effects.

Statistical analysis:

The continuous variables were expressed as Mean ± SD or Median [IQ] and categorical variables were expressed as N (%). To determine the normality of the clinical parameters on enrolment and follow-up, Shapiro-Wilk's test was performed (ANNEXURE III). Statistical significance was estimated using chi-square test or test for proportions as appropriate. For intra-group comparisons, independent t-test was performed when the data was normally distributed, and Mann-Whitney U test was performed when the data distribution was skewed. For intergroup comparison, dependent t-test was performed when the data was normally distributed, and Wilcoxon matched pairs test was performed when the data distribution was skewed.

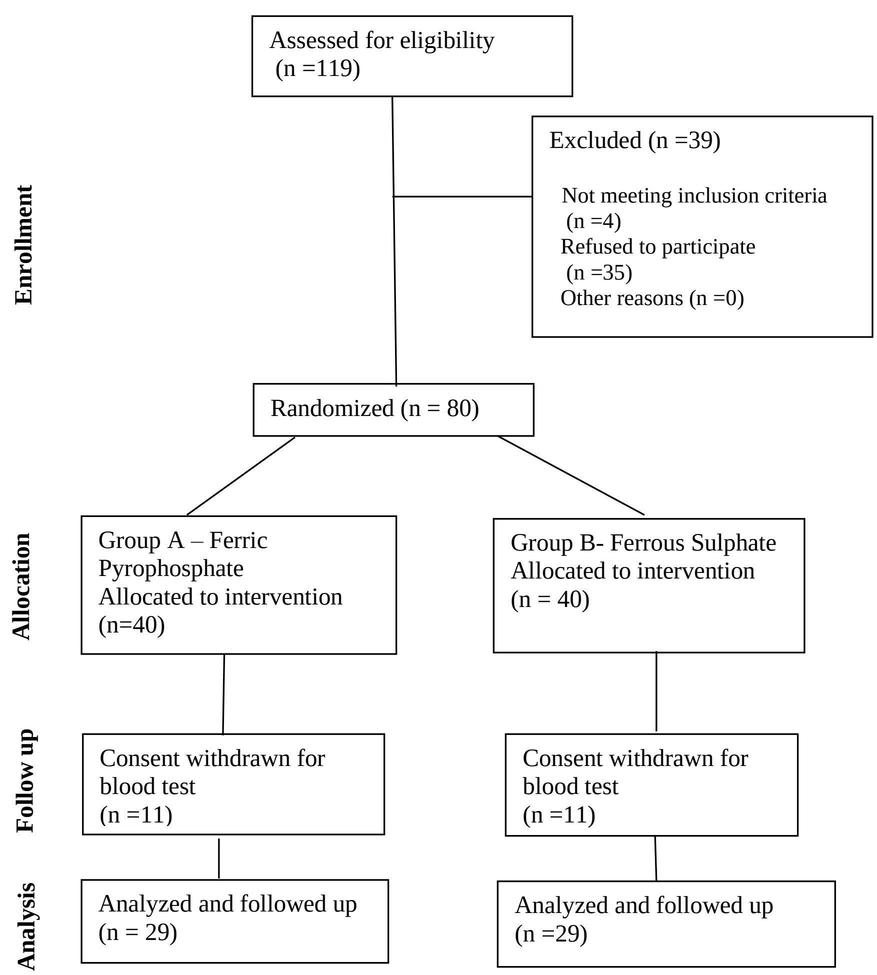
Correlation analysis was performed to understand the association between compliance to medication and changes in Hb. A p-value of <0.05 was considered to be statistically significant.

RESULTS

Out of the total 119 children screened in the community, 80 were enrolled for the study and 39 were excluded as per the selection criteria i.e. severe anemia (Hb <7gm/dl) (n=4) and not consenting for the study (n=35). 80 enrolled participants were randomized in Group A and Group B with 40 in each group. A total of 11 in each group withdrew consent for repeat blood tests, and data from 29 participants in each group were analyzed in the study as per the consort diagram.(Figure 1)

Figure 1 : Flow of Participants during the study.

CONSORT



1. **Socio-demographic details**:

Table 1: Baseline characteristics of study population in Group A and Group B.

Parameters	*Group A(n=40)*	*Group B(n=40)*	p value
Age (in months)	32.82±16.91	33±13.97	0.957
Males	17(42.5%)	28(70%)	0.0131*
Females	23(57.5%)	12(30%)	
Birth weight (in Kg)	2.78±0.45	2.77±0.40	0.916
Vegetarian diet	9(22.5%)	6(15%)	0.389
Non- Vegetarian diet	31(77.5%)	34(85%)	
Father's occupation			0.9071
Driver	7(17.5%)	5(12.5%)	
Engineer	3(7.5%)	0	
Factory Worker	6(15%)	6(15%)	
Farmer	10(25%)	11(27.5%)	
Daily wage laborer	4(10%)	7(17.5%)	
Police	2(5%)	2(5%)	
Security	1(2.5%)	2(5%)	
Teacher	0	2(5%)	
others	7(7.5%)	5(12.5%)	
Father's education			0.3088
Secondary school	29(72.5%)	30(75%)	
Higher secondary	3(7.5%)	6(15%)	
Graduate	6(15%)	4(10%)	
Postgraduate	2(5%)	0	
Mother's Occupation			0.5562
Homemaker	39(97.5%)	38(95%)	
Teacher	1(2.5%)	0	
Farmer	0	2(5%)	
Mother's Education			0.1667
Secondary school	31(77.5%)	34(85%)	
Higher secondary	2(5%)	4(10%)	
Graduate	6(15%)	2(5%)	
Postgraduate	1(2.5%)	0	
Modified Kuppuswamy Scale	11.6 ± 2.1	10.9 ± 1.2	0.0710

The baseline characteristics in both the groups were similar except gender distribution(Table 1).

The mean age(in months) of the participants in Group A was 32.82 ± 16.91 and Group B was 33 ± 13.97, and the difference was not statistically significant (p value=0.957).

The gender distribution in the groups showed that Group A had 42.5% (n=17) male and 57.5% (n=23) female participants, Group B had 70% (n=28) male and 30%(n=12) female participants, the difference was statistically significant ($p<0.05$).

When the birth weight (in kg) was compared, Group A had mean weight of 2.78±0.45 and Group B 2.77±0.40 and the difference between the data was not statistically significant (p value=0.916).

On comparing the diet preferences, Group A had 77.5% (n=31) with non-vegetarian diet and 22.5% (n=9) with vegetarian diet. In Group B, 85% (n=34) were non vegetarian diet and 15% (n=6) vegetarian diet, difference was not statistically significant (p value=0.389).

In Group A, the prevailing occupation among fathers was farming, comprising 25% of respondents (n=10), followed by driving at 17.5% (n=7) and in Group B, farming was also the primary occupation, representing 27.5% (n=11), trailed by daily wage laborers at 17.5% (n=7). The disparity between the two groups was not statistically significant (p-value = 0.9071).

In both the groups, secondary school education was predominant (Group A 72.5% ,n=29) (Group B 75%, n=30) among fathers and difference was not statistically significant (p value = 0.3088).

The predominant occupation for mothers in both Group A and B was being a homemaker, with percentages of 97.5% (n=39) and 95% (n=30) respectively. The observed difference between the two groups was not statistically significant (p value = 0.5562).

When comparing mothers' education levels, 77.5% (n=31) of mothers in Group A had education up to the secondary school level, whereas in Group B, it was 85% (n=34). The difference between the two groups in terms of education level was also not statistically significant (p value = 0.1667)

Socio-economic status assessed using the Modified Kuppuswamy Scale showed that in Group A, the mean socio-economic status was 11.6 ± 2.1, while in Group B, it was 10.9 ± 1.2 suggesting that participants were from lower middle class. However, the difference in socio-economic status between the two groups was not statistically significant (p= 0.071).

2. **Baseline anthropometric measurements:**

The baseline anthropometric measurements at enrolment were similar between Group A and Group B (Table 2).

Table 2: Baseline anthropometrical measurements at enrollment.

Parameters	*Group A(n=40)*	*Group B(n=40)*	p- value
Weight (in Kg)	10.74 ± 2.63	11.25 ± 2.79	0.4655
Height (in cm)	86.72 ± 11.91	87.5 ± 10	0.9775
Head Circumference (in cm)	46.38 ± 1.84	46.76 ± 1.91	0.5839
Mid upper arm circumference (in cm)	12.59 ± 0.65	12.56 ± 0.60	>0.9999

Data indicates that the mean weight of participants at enrolment in Group A was 10.74± 2.63kg and in Group B was 11.25 ± 2.79 with no significant statistical difference (p=0.4655). Mean height in Group A was 86.72± 11.91cm and Group B was 87.5 ± 10cm with no significant statistical difference (p-value= 0.9775) . On comparing head circumference, Group A had a mean of 46.38 ± 1.84cm and Group B had 46.76 ± 1.91cm with no significant statistical difference(p value=0.5839). Mid upper arm circumference when compared showed a mean value of 12.59 ± 0.65cm in Group A and 12.56 ± 0.60cm in Group B, with no significant statistical difference(p-value>0.999)

3. Baseline values of investigations

Baseline values of investigations between both the groups(Table 3).

Table 3: Comparison between baseline values of investigations in both groups at enrolment.

Parameters	*Group A (n=40)*	*Group B (n=40)*	p- value
Hb(gm/dL)	10.64±1.32	10.98±1.21	0.4107
S. iron(µg/dL)	61.13±33.39	56.03±26.86	0.5412
TSAT(%)	19.63±16.66	17.80±13.49	0.9080
TIBC(µg/dL)	366±86.92	368.33±88.91	0.7558
S. Ferritin(ng/mL)	58.44±56.78	41.09±29.97	0.6755
Hematocrit (%)	37.53±3.80	38.38±3.50	0.3141
MCV(fl)	82.90±11.78	85.45±7.90	0.2586
MCH(pg)	23.68±4.01	24.67±3.08	0.2181
MCHC(g/dl)	28.46±1.28	28.39±1.61	0.9962
RDW(%)	15.44±1.52	15.83±1.41	0.1826
RBC count	457125±42798.4	452775.0±40859.7	0.9463
WBC count(x10^3)	10.12±2.63	10.57±2.49	0.3683
Platelet count	390725.0±98934.6	382900.0±82330.7	0.9195

The mean Hb level at enrolment in Group A and Group B was 10.64 ± 1.32gm/dL and 10.98 ± 1.21 gm/dl respectively, difference was not statistically significant(p=0.4107). Mean serum iron levels in Group A was 61.13±33.39 µg/dL and Group B was 56.03±26.86 µg/dL, difference was not statistically significant(p=0.5412). Mean TSAT level at enrolment in Group A was 19.63±16.66% and in Group B was 17.80±13.49%, difference was not statistically significant(p=0.9080). Mean TIBC in Group A was 366±86.92 µg/dL and in Group B was 368.33±88.91 µg/dL at enrolment, difference was not statistically significant(p=0.7558). Mean serum ferritin levels at enrolment in Group A was 58.44±56.78ng/dl and in Group B was 41.09±29.97 ng/dl, difference was not statistically significant(p=0.6755). Mean hematocrit levels in Group A was 37.53±3.80% and in Group B was 38.38±3.50% at enrolment and the difference was not statistically significant(p=0.3141).Mean MCV levels at enrolment in Group A was 82.90±11.78fl and in group B was 85.45±7.90fl, the difference was not statistically significant(p=0.2586).Mean MCH level at enrolment in Group A was 23.68±4.01pg and in Group B was 24.67±3.08pg, the difference was not statistically significant(p=0.2181). Mean MCHC level at enrolment in Group A was28.46±1.28 g/dl and in Group B was 28.39±1.61g/dl, the difference was not statistically significant(p=0.9962). Mean RDW level in Group A at enrolment was 15.44±1.52% and in Group B was 15.83±1.41%, no statistical difference was noted(p=0.1826). Mean RBC counts in Group A at enrolment was 457125±42798.4 and inn Group B was 452775.0±40859.7, difference was not statistically significant(p=0.9463). Mean WBC counts in Group A at enrolment was 10.12±2.63 x 10^3 and in Group B was 10.57±2.49 x 10^3 difference was not statistically significant(p=0.3683). Mean Platelet count in Group A at enrolment was 390725.0±98934.6 and in group B was 382900.0±82330.7, difference was not statistically significant(p=0.9195).

4. Primary outcomes:

Hemoglobin levels:

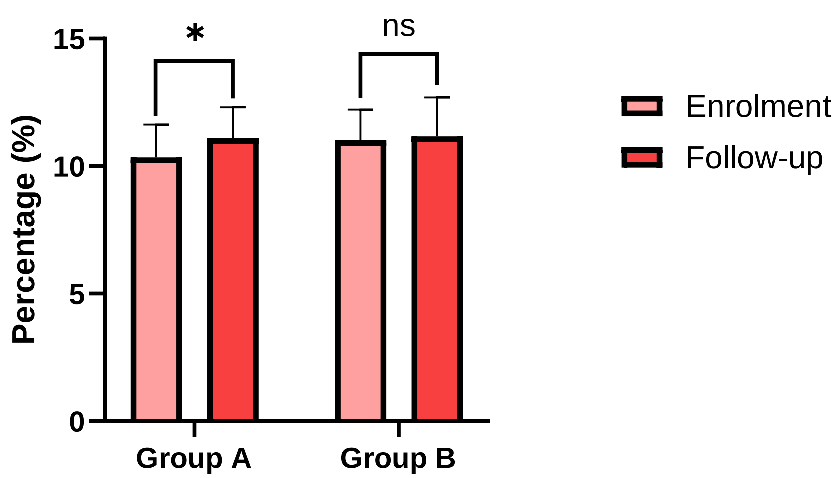
The mean Hb level at enrolment in Group A and Group B was 10.35 ± 1.28gm/dL and 11.02 ± 1.20 gm/dL respectively. The follow-up Hb values of Group A and Group B were 11.10 ± 1.21% and 11.17 ± 1.52gm/dl respectively. When compared within the group by Wilcoxon matched pairs, Group A showed a significant improvement in Hb levels(p value=0.0001), Group B also showed improved levels but the difference was not statistically significant(p value=0.1766)(Table 4).

Table 4: Comparison of enrolment and follow-up Hb levels within Group A and Group B by Wilcoxon matched pairs

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	10.35	1.28	0.0001*
	Follow-up	11.10	1.21	
Group B (n = 29)	Enrolment	11.02	1.20	0.1766
	Follow-up	11.17	1.52	

*p<0.05

Figure 2: Comparison of enrolment and follow-up Hb levels within Group A and Group B



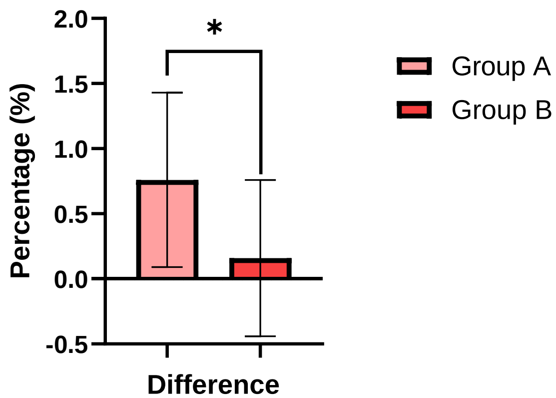
On comparison by Mann- Whitney U test the Hb levels between both groups, at enrolment Group A mean levels were 10.35±1.28 gm/dl and group B mean levels 11.02±1.20 gm/dl difference was statistically significant(p value=0.0444), both groups showed a mean increase of 0.76±0.67 and Group B showed 0.16±0.60, this difference in increment was statistically significant (p=0.0001) (Table5).

Table 5: Comparison between Group A and Group B with enrolment and follow-up Hb levels by Mann-Whitney U test

Times	**Group A**		**Group B**		**P-value**
	Mean	SD	Mean	SD	
Enrolment(n = 29)	10.35	1.28	11.02	1.20	0.0444*
Follow-up(n = 29)	11.10	1.21	11.17	1.52	0.9752
Difference (n = 29)	0.76	0.67	0.16	0.60	0.0001*

*p<0.05

Figure 3: Comparison of change in Hb levels between both groups.



Serum Iron:

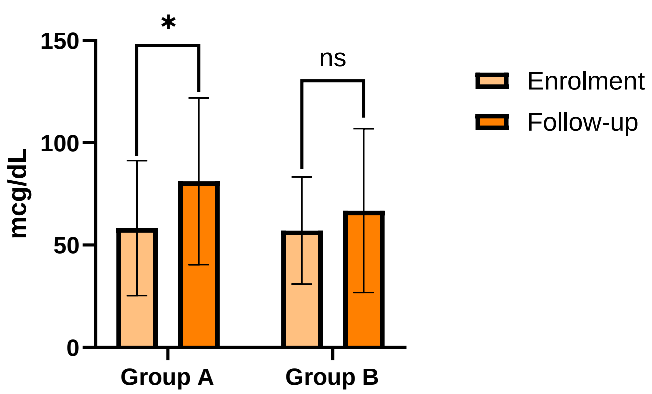
The improvement in mean serum iron levels within both groups at follow-up were estimated by Wilcoxon matched pairs test. Comparison showed improved values in both groups but Group A observed statistically significant difference (58.28 vs 81.21µg/dL;P<0.0001*), no significant differences were observed between enrolment and follow-up mean serum iron in Group B (57.10 vs 66.83µg/dL ; P=0.1766) (Table 6).

Table 6: Comparison of enrolment and follow-up S. iron levels within Group A and Group B by Wilcoxon matched pairs

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	58.28	33.00	0.0001*
	Follow-up	81.21	40.74	
Group B (n = 29)	Enrolment	57.10	26.18	0.1766
	Follow-up	66.83	40.08	

*p<0.05

Figure 4: Comparison of change in serum iron levels within both groups



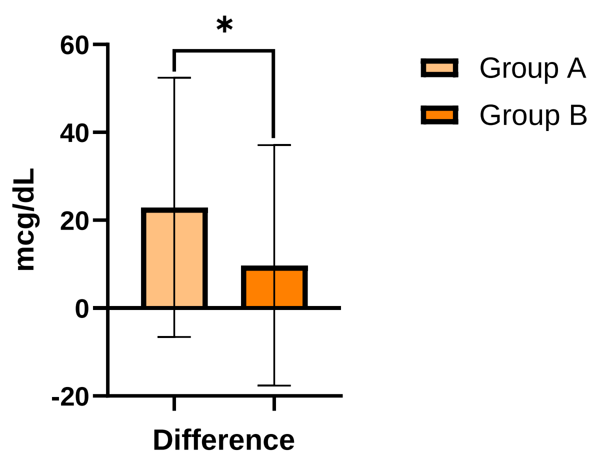
The change in mean serum iron levels between the groups were compared by Mann- Whitney U test which showed improved levels in both groups, but the increment at follow-up in Group A(22.93±29.51) as compared to Group B (9.72±27.37) was statistically significant(p-value=0.0177)(Table 7).

Table 7: Comparison between Group A and Group B with enrolment and follow-up S. iron levels by Mann-Whitney U test

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment(n = 29)	58.28	33.0	57.10	26.18	0.8806
Follow-up(n = 29)	81.21	40.74	66.83	40.08	0.1375
Difference (n = 29)	22.93	29.51	9.72	27.37	0.0177*

*p<0.05

Figure 5: Comparison of change in Serum iron levels between both groups.



TSAT levels:

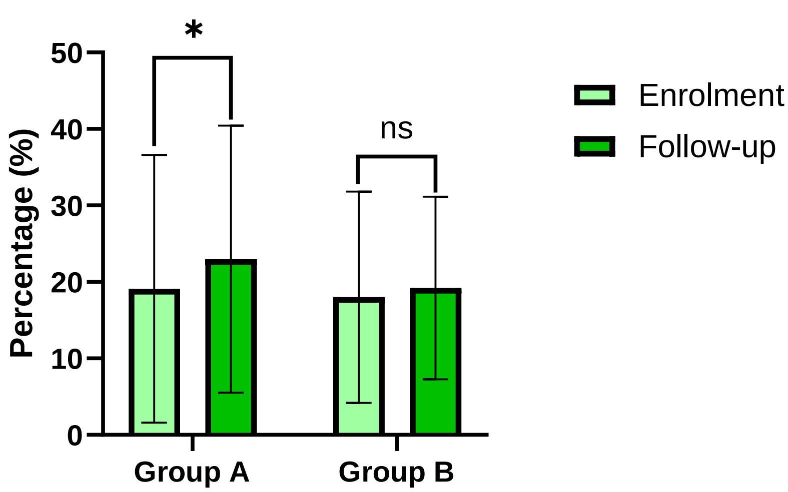
The enrolment and follow-up mean TSAT levels were compared within Group A and B using Wilcoxon matched pair test. In group A, follow up mean TSAT levels were significantly higher than enrolment mean TSAT levels (22.97% vs 19.10%; P=0.0080*). In group B, no significant differences in the enrolment and follow-up mean TSAT levels were observed (19.21% vs 18.0%; P=0.2845) (Table 8).

Table 8: Comparison of enrolment and follow-up TSAT levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	19.10	17.51	0.0080*
	Follow-up	22.97	17.47	
Group B (n = 29)	Enrolment	18.00	13.81	0.2845
	Follow-up	19.21	11.94	

*p<0.05

Figure 6: Comparison of TSAT% score within both groups.



The difference between enrolment and follow-up values between Group A and B were 3.86 ± 10.15% and 1.21 ± 7.69% respectively. Comparison using Mann-Whitney U test observed no significant differences (p-value = 0.1687) (Table 9).

Table 9: Comparison between Group A and Group B with enrolment and follow-up TSAT levels

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n= 29)	19.1	17.51	18.0	13.8	0.7915
Follow-up (n = 29)	22.97	17.47	19.21	11.94	0.2760
Difference (n = 29)	3.86	10.15	1.21	7.69	0.4956

TIBC level:

The mean TIBC levels were compared between Group A and B. Dependent t-test conducted observed no significant increase in the mean TIBC level at follow-up in both Group A (P=0.7317) and Group B (P=0.2272)(Table 10).

Table 10: Comparison of enrolment and follow-up TIBC levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	369.45	91.27	0.7317
	Follow-up	374.76	81.38	
Group B (n = 29)	Enrolment	377.10	95.08	0.2272
	Follow-up	398.14	80.47	

On comparing the change in mean TIBC levels between both groups it was noted that in Group A mean change was 5.31±82.59 µg/dL and in Group B was 21.03±91.74 µg/dL, with no statistical significance(p- value = 0.495)(Table 11).

Table 11: Comparison between Group A and Group B with enrolment and follow-up TIBC scores

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	369.45	91.27	377.10	95.08	0.7558
Follow-up (n = 29)	374.76	81.38	398.14	80.47	0.2760
Difference (n = 29)	5.31	82.59	21.03	91.74	0.4956

Serum Ferritin:

The mean serum ferritin values when compared within the groups showed no significant difference in values were observed at follow-up in both groups , Group A(p=0.5705) and Group B (p value=0.5909)(Table12).

Table 12:Comparison of enrolment and follow-up S. ferritin levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n= 29)	Enrolment	54.29	57.82	0.5705
	Follow-up	46.84	39.99	
Group B (n= 29)	Enrolment	35.37	23.37	0.5909
	Follow-up	39.13	29.26	

Similarly, no significant differences was observed in mean serum ferritin at enrolment and follow-up between the groups A and B (7.45 ± 39.86 ng/mL vs -3.76 ± 28.65 ng/mL; P=0.4744)(Table13).

Table 13: Comparison between Group A and Group B with enrolment and follow-up S. ferritin levels

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Follow-up (n = 29)	54.29	57.83	35.37	23.37	0.1080
Enrolment (n= 29)	46.84	39.99	39.13	29.26	0.9318
Difference (n= 29)	7.45	39.86	-3.76	28.65	0.4744

Haematocrit :

The comparison between mean haematocrit at enrolment and follow-up within Group A by dependent t test observed no statistically significant difference (36.72 vs 36.67; P=0.8957). Similarly, no significant differences was observed between enrolment and follow-up mean haematocrit levels within group B (38.35% vs 38.54%; P=0.6734) (Table14).

Table 14: Comparison of enrolment and follow-up Haematocrit levels within both groups

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	36.72	3.80	0.8957
	Follow-up	36.67	3.55	
Group B (n = 29)	Enrolment	38.35	3.55	0.6734
	Follow-up	38.54	3.61	

The difference in mean hematocrit value at enrolment and follow-up between group A and group B were 0.06 ± 2.25% and -0.19 ± 2.35% respectively. However, comparison between the groups using independent t-test observed no significant differences in mean heamtocrit value (P=0.6910)(Table15).

Table15:Comparison between Group A and Group B with enrolment and follow up Hematocrit levels.

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	36.72	3.80	38.35	3.55	0.5168
Follow-up (n = 29)	36.67	3.55	38.54	3.61	0.0512
Difference (n =29)	0.06	2.25	-0.19	2.35	0.6910

MCV:

Comparison of the mean MCV levels within the groups showed no significant differences in both groups, [Group A 81.25 vs 80.94fl; P=0.8362 and Group B 86.02 vs 85.82fl; P=0.0776](Table16)

Table16: Comparison of enrolment and follow-up MCV levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (N = 29)	Enrolment	81.25	12.72	0.8362
	Follow-up	80.94	8.91	
Group B (N = 29)	Enrolment	86.04	7.16	0.0776
	Follow-up	85.82	6.96	

The difference in mean MCV level at enrolment and follow-up MCV scores in group A and group B were 0.31 ± 7.92fl and 3.22 ± 6.05 fl. No significant differences were observed between the groups (P = 0.1205)(Table17).

Table17: Comparison between Group A and Group B with enrolment and follow-up MCV scores

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	81.25	12.72	86.04	7.16	0.0826
Follow-up (n = 29)	80.94	8.91	82.82	6.96	0.3744
Difference (N = 29)	0.31	7.92	3.22	6.05	0.1205

MCH:

Comparison of the mean MCH level at enrolment and follow-up within group A (23.14 vs 23.78pg; P=0.1444) and group B (24.99 vs 24.98pg; P=0.9744) observed were not statistically significant (Table18).

Table18: Comparison of enrolment and follow-up MCH levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	23.14	4.34	0.1444
	Follow-up	23.78	3.41	
Group B (n = 29)	Enrolment	24.99	2.94	0.9744
	Follow-up	24.98	3.02	

Comparison of difference between mean MCH levels at enrolment and follow-up between group A and group B observed no significant differences (0.64 vs 0.01 pg , P=0.2834)(Table19).

Table19: Comparison between Group A and Group B with enrolment and follow-up MCH levels

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n= 29)	23.14	4.34	24.99	2.94	0.0625
Follow-up (n = 29)	23.78	3.41	24.98	3.02	0.1638
Difference (n = 29)	-0.64	2.29	0.01	2.29	0.2834

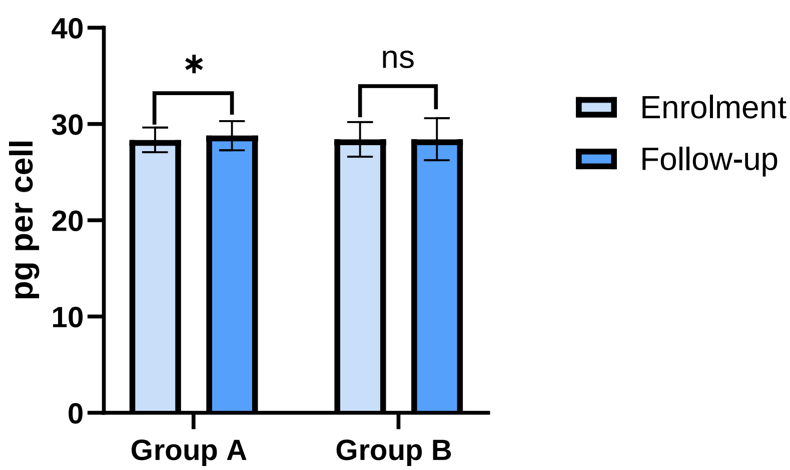
MCHC:

The mean MCHC levels within Group A showed a significant improvement at follow-up (28.80 vs 28.36g/dl; Diff: 0.45; P=0.0491*). However, the difference was not statistically significant in Group B(28.42 vs 28.43 g/dl; p value=0.811) (Table20).

Table20: Comparison of enrolment and follow-up MCHC levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	28.36	1.29	0.0491*
	Follow-up	28.80	1.51	
Group B (n = 29)	Enrolment	28.42	1.79	0.8110
	Follow-up	28.43	2.17	

Figure 7: Comparison of MCHC levels at enrolment and follow-up within both groups



Comparison of the difference in mean MCHC levels at enrolment and follow-up levels between group A and group B was not statistically significant (0.45 vs 0.01; P=0.1417)(Table21).

Table21: Comparison between Group A and Group B with enrolment and follow-up MCHC levels by Mann-Whitney U test

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	28.36	1.29	28.42	1.79	0.8841
Follow-up (n= 29)	28.80	1.51	28.43	2.17	0.9690
Difference (n = 29)	-0.45	1.23	-0.01	1.90	0.1417

RDW:

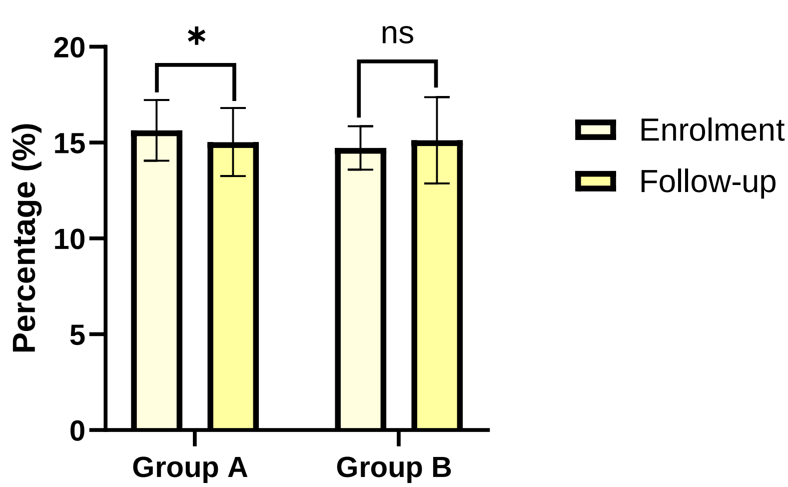
Comparison of the mean RDW value at enrolment and follow-up within Group A was statistically significant (15.64 vs 15.83%; Diff: 0.61, P=0.0225*). However no significant difference between was observed at enrolment and follow-up within Group B (14.72 vs 15.12%; Diff = 0.39, P=0.5888)(Table22).

Table22: Comparison of enrolment and follow-up RDW levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	15.64	1.58	0.0225*
	Follow-up	15.83	1.78	
Group B (n = 29)	Enrolment	14.72	1.13	0.5888
	Follow-up	15.12	2.25	

*p<0.05

Figure 8: Comparison between RDW scores at enrolment and follow-up within both groups.



On comparison of difference in mean RDW levels between both groups at follow-up it was noted that the difference in Group A (0.61±1.43) and Group B (-0.39±1.84) was not statistically significant(p value=0.0763) (Table23).

Table23: Comparison between enrolment and follow-up RDW levels in Group A and Group B

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	15.64	1.58	14.72	1.13	0.1630
Follow-up (n = 29)	15.03	1.78	15.12	2.25	0.8398
Difference (n = 29)	0.61	1.43	-0.39	1.84	0.0763

RBC:

When the mean RBC count at enrolment and follow-up were compared within group A, no statistically significant difference was noted (457448.28 vs 464172.41; P=0.1120) and in group B also no statistical significance was observed (450034.48 vs 450241.38; P=0.6654) (Table24).

Table24: Comparison of enrolment and follow-up RBC count within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	457448.28	44303.81	0.1120
	Follow-up	464172.41	49684.77	
Group B (n = 29)	Enrolment	450034.48	42620.82	0.6654
	Follow-up	450241.38	60830.36	

The difference in enrolment and follow-up mean RBC count between both groups observed no statistically significant difference were observed (6724.1 vs 206.9; P=0.8095)(Table25).

Table25: Comparison between Group A and Group B with enrolment and follow-up RBC levels

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment(n = 29)	457448.28	44303.81	450034.48	42620.82	0.5187
Follow-up (n = 29)	464172.4	49684.8	450241.4	60830.4	0.6408
Difference (n = 29)	6724.1	33993.6	206.9	55172.7	0.8095

WBC:

Comparison of mean WBC count(x10^3) enrolment and follow-up within Group A (10.32 vs 10.26; P=0.4300) and Group B (10.55 vs 10.48; P=0.9569) observed no statistically significant differences (Table26).

Table26: Comparison of enrolment and follow-up WBC levels within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	10.32	2.78	0.4300
	Follow-up	10.26	3.44	
Group B (n = 29)	Enrolment	10.55	2.58	0.9569
	Follow-up	10.48	2.52	

Comparison of difference in mean WBC count between group A and B observed no statistically significant difference (p value=0.5862) (Table27).

Table27: Comparison between Group A and Group B with difference in WBC levels

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	10.32	2.78	10.55	2.58	0.7452
Follow-up (n = 29)	10.26	3.44	10.48	2.52	0.4554
Difference (n = 29)	-0.07	2.82	-0.07	2.15	0.5862

Platelet count:

No statistical difference was observed upon comparison of enrolment and follow-up mean platelet count within Group A (400724.1 vs 388379.3, p=0.9483) and Group B(379965.5 vs 362931.0 p=0.2748) (Table28).

Table28:Comparison of enrolment and follow-up platelet count within Group A and Group B

Group	Time	Mean	SD	p-value
Group A (n = 29)	Enrolment	400724.1	106818.9	0.9483
	Follow-up	388379.3	103217.3	
Group B (n = 29)	Enrolment	379965.5	77852.65	0.2748
	Follow-up	362931.0	79914.21	

When difference in mean platelet count between group A and group B were compared, no statistically significant difference was observed(p value=0.6576)(Table29).

Table29: Comparison between Group A and Group B with enrolment and follow-up Platelet count

Times	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Enrolment (n = 29)	400724.1	106818.9	379965.5	77852.65	0.4013
Follow-up (n = 29)	388379.3	103217.3	362931.0	79914.2	0.3967
Difference (n = 29)	-12344.8	119588.7	-17034.5	73597.1	0.6576

5. **Secondary Outcomes**

a) **Growth parameters at enrollment and follow up**

At enrolment, the baseline anthropometric measurements were comparable with no statistically significant difference(Table2). An increase in weight, height, HC and MUAC was noted during follow-up in group A and group B following treatment. However, no statistically significant differences are observed between the groups(Table30)

Table30: Comparison of baseline and follow-up anthropometric parameters between the groups

Parameters	Group A (n = 29)		Group B (n = 29)		t-value	p-value
	Mean	SD	Mean	SD		
Enrollment Weight (kg)	10.74	2.63	11.25	2.79	-0.8314	0.4083
Follow up Weight (kg)	11.56	2.71	12.53	2.73	-1.5832	0.1174
Weight gain (kg)	0.77	0.79	1.24	1.15	1.814	0.0750
Enrollment Height (cm)	86.73	11.91	87.50	10.00	-0.3105	0.7570
Follow up Height (cm)	86.93	12.06	87.63	10.16	-0.2807	0.7797
	Median [IQR]		Median [IQR]			
Change in height (cm)	0 [0,0]		0 [0,0]		-	-
HC (cm)	46.39	1.84	46.76	1.91	-0.8801	0.3815
Follow up HC (cm)	46.58	1.96	46.76	1.94	-0.4302	0.6682
	Median [IQR]		Median [IQR]			
Change in HC (cm)	0 [0,0]		0 [0,0]		-	-
MUAC (cm)	12.59	0.65	12.56	0.60	0.2450	0.8071
Follow up MUAC (cm)	12.90	0.58	12.76	0.69	1.0038	0.3186
Change in MUAC (cm)	0.32	0.31	0.17	0.24	2.060	0.4410

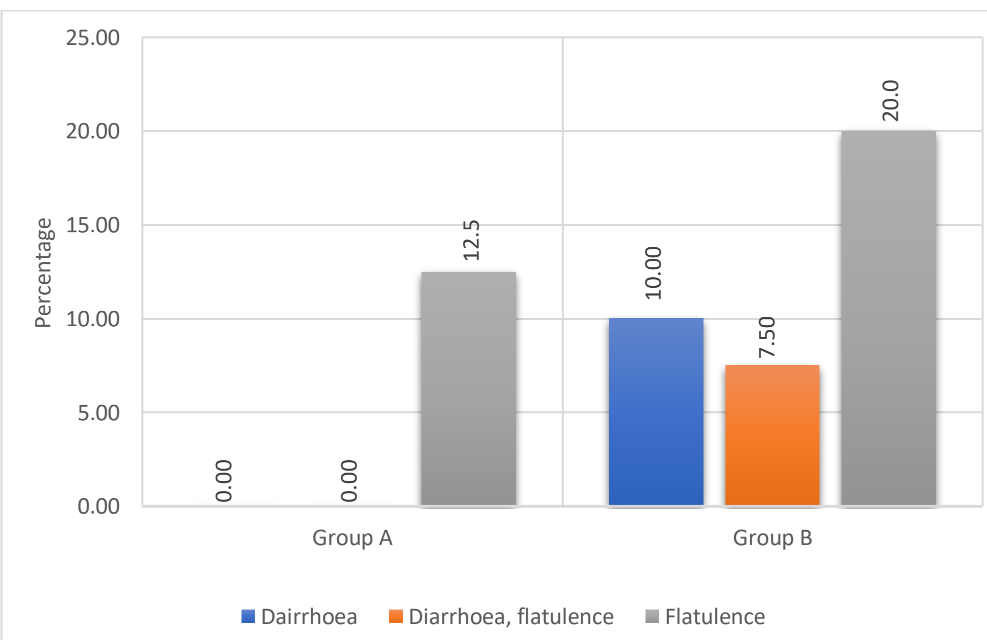
b) Side effects

Table30 shows lesser number of side effects in Group A as compared to Group B. Most common side effect observed in Group A was flatulence in 12.5% (n=5) participants in the group .In Group B the side effects were flatulence in 20%(n=8), diarrhea 10%(n=4) and diarrhea and flatulence in 7.5% (n=3). Most common side effect in both groups was flatulence with incidence of 16.25%(n=13) combined in both groups(Table31)(Figure9).

Table31 : Comparison of Group A and Group B with side effects

Side effects	Group A	%	Group B	%	Total	%
Diarrhea	0	0.00	4	10.00	4	5.00
Diarrhea, Flatulence	0	0.00	3	7.50	3	3.75
Flatulence	5	12.50	8	20.00	13	16.25
Total	5	12.50	15	37.5%		

Figure9 : Comparison between Group A and Group B with incidence of side effects.



c) Compliance

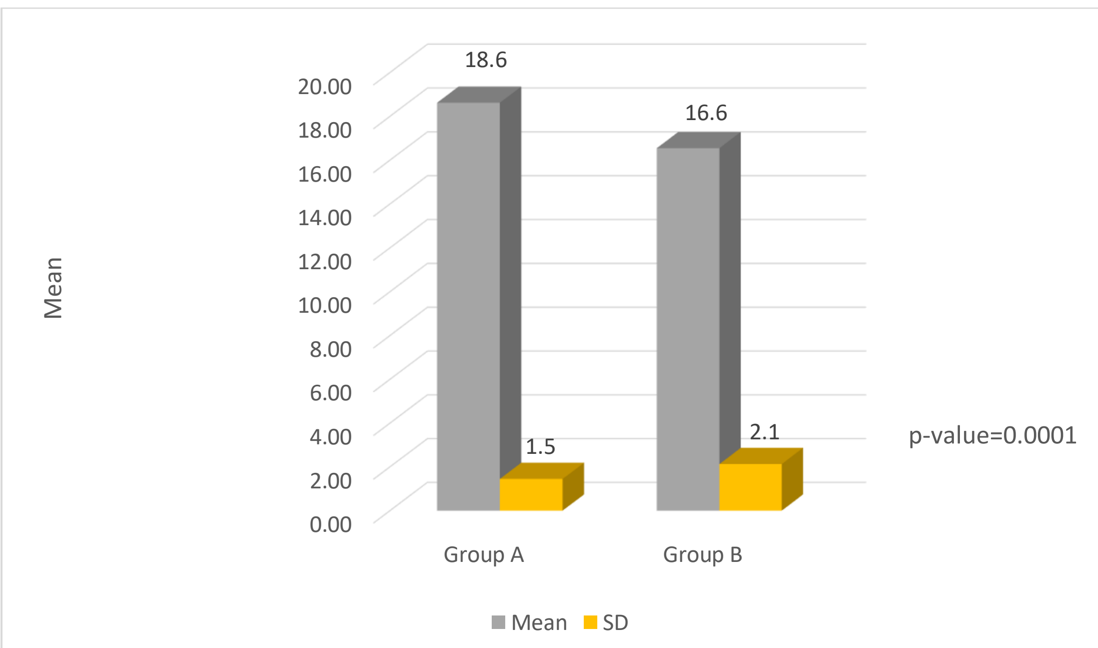
Compliance of medication was checked by the number of doses taken. The mean number of doses taken was higher in Group A(18.62±1.45) as compared to Group B(16.55±2.13) which was statistically significant ($p<0.05$). (Table 32, Figure 10).

Table32: Comparison of Group A and Group B with mean dose taken by independent t test

Groups	n	Mean	SD	SE	t-value	P-value
Group A	29	18.62	1.45	0.27	4.3229	0.0001*
Group B	29	16.55	2.13	0.40		

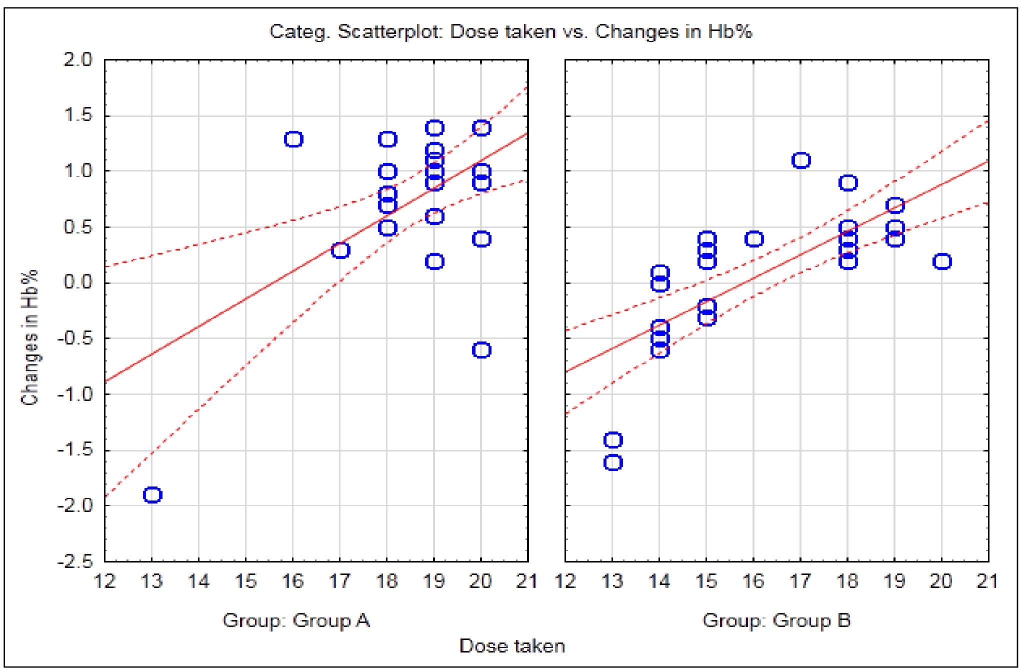
*p<0.05

Figure10 : Comparison of Group A and Group B with mean dose taken



The scatter plot demonstrates that in Group A, where more number of doses were taken, there was a higher correlation with significant improvement in Hb values. Whereas, in Group B, where fewer number of doses were taken, there was less improvement in Hb values. This implies a potential relationship between the number of doses administered and the resulting change in Hb values, with Group A showing a stronger correlation(Figure11).

Figure11: Scatter plot comparing number of doses taken and change in Hb in both groups.



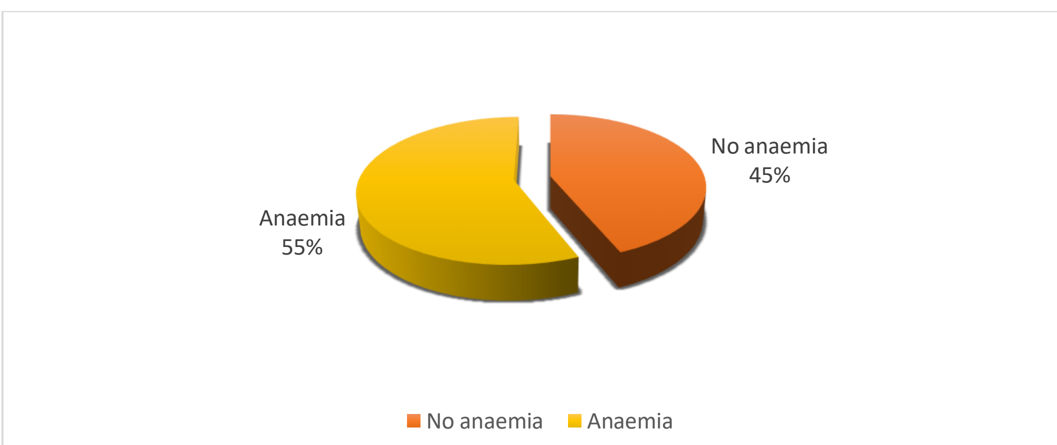
d) Prevalence of mild to moderate anemia in the study population

Anemia, defined by WHO criteria with a cutoff value of 11gm/dL, was assessed in the study population. Participants with Hb levels below 7gm/dL were excluded during screening, focusing on the prevalence of mild to moderate anemia, with Hb levels ranging from 7 to 11gm/dL. The study revealed that 55% (n=44) of the participants exhibited mild to moderate anemia, with a mean ± SD hemoglobin level of 10.56±1.68 gm/dL. At follow-up after excluding dropouts, prevalence was 58.6%(n=34, Group A:19 Group B:15) (Table33; Figure12).

Table 33: Prevalence of mild to moderate anemia in children.

Status of anemia	No of children	% of children
No anemia	36	45
Mild to moderate anemia	44	55
Total	80	100.00
Mean	10.56	
SD	1.68	

Figure12 : Prevalence of mild to moderate iron deficiency anemia in study population

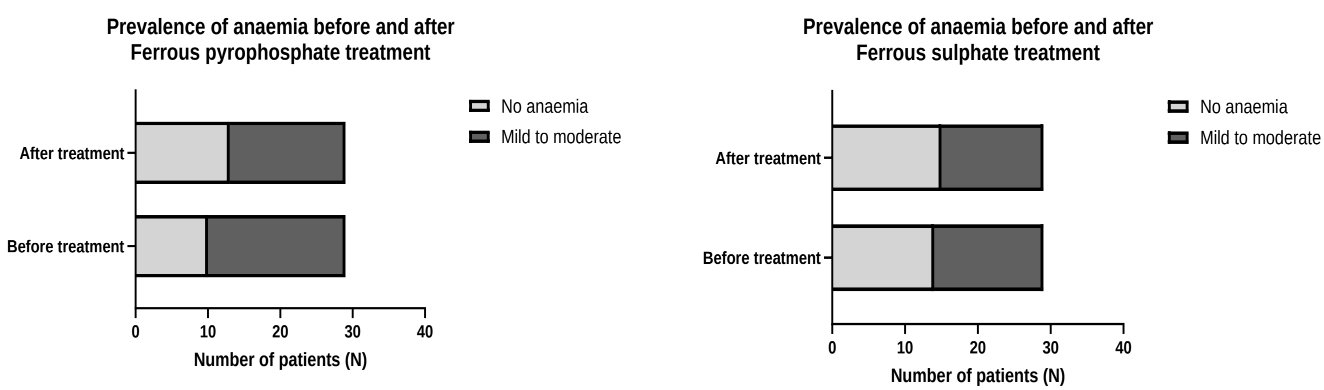


It was noted that in Group A, 3 participants improved from being mild to moderate anemic status to non anemic status i.e Hb>11gm/dL and in Group B only 1 participant showed this improvement. However, no statistically significant differences in the prevalence were noted at enrolment and follow-up in both the groups. (Table34;Figure13)

Table34: Comparison of anemia prevalence in group A and B at enrolment and follow-up

Status of anemia	**Group A (n = 29)**		**P-value**	**Group B (n = 29)**		**P-value**
	Enrolment	**Follow-up**		**Enrolment**	**Follow-up**	
No anemia	10 (34.5%)	13 (44.8%)	0.4179	14 (48.3%)	15 (51.7%)	0.7948
Mild to moderate anemia	19 (65.5%)	16 (55.2%)		15 (51.7%)	14 (48.3%)	
Total	29	29		29	29	

Figure13: Graph showing improvement in anemia status in both groups at follow-up



DISCUSSION

The increase in prevalence of anemia among children aged 6-59 months is a global health concern. IDA is the most common type of anemia especially in infants and children, accounting for more than 50% of global prevalence of anemia. Impact of iron deficiency(ID) on long term neurodevelopmental outcomes is irreversible. Therefore preventive strategies are the need of the hour to combat the effects of ID. Anemia Mukt Bharat programme by Government of India focuses on preventing iron deficiency by improving quality of nutrition, deworming and iron and folic acid supplementation. Despite these strategies increasing prevalence of iron deficiency continues to be a major health issue. Poor compliance and higher incidence of gastro intestinal side effects of ferrous sulphate are among the major factors affecting the poor outcome of this programme in children. Need of the hour is to find a more effective, tolerable and acceptable iron salt. Liposomal ferric pyrophosphate which is a newer iron preparation with good absorption and lesser gastrointestinal side effects is used to treat IDA in adults and children. There is no evidence for its role in prophylaxis for prevention of IDA in pediatric population. The present study was conducted to test the effectiveness of liposomal ferric pyrophosphate with ferrous sulphate in intermittent oral iron prophylaxis in children between 6 months to 59 months.

Socio-demographic factors:

In the present study, at enrolment all the baseline characteristics namely mean age, diet preferences, mean birth weight, father's occupation, father's education, mother's education and mother's occupation revealed no statistically significant differences within the group. However a statistically significant difference was noted in gender distribution amongst the groups.

The mean age of the participants in the study was 32.91±15.44 months with no significant difference between the groups (Group A:32.82 ± 16.91; Group B : 33 ± 13.97, p value=0.957). In a study to know the impact of daily iron supplementation and deworming among 140 Beninese children by Dossa et al. have reported mean age of 46 ± 6 months. However study which had a similar objective, to study the effectiveness of ferrous, ferric and liposomal salts among infants between 6-12 months of age had a mean age of 9.1±1.3 months(85)

In this study we observed a male preponderance (56%) among the participants. Similar observations of male preponderance (60%) was reported in a study to find effectiveness of sucrosomial iron (liposomal iron) for treatment of IDA in adult population with heart failure(86). However in our study we observed female preponderance in liposomal ferric pyrophosphate group and male preponderance in ferrous sulphate group. In a prospective observational multicentric study of monitoring oral iron therapy in children with IDA from Italy also reported a similar female preponderance in liposomal iron group(87). Contrary to our observations in a similar study of comparison of efficacy of ferrous, ferric and liposomal iron preparation in infants have reported equal gender distribution amongst participants(88).

When the mean birth weight was compared, no significant difference between liposomal ferric pyrophosphate iron group and ferrous sulphate group was observed (Group:2.78±0.45kg ;Group B:2.77±0.40kg) (p value=0.916). In a study by Ana Vareaa et al. (2023) on comparison of daily vs weekly iron supplementation for prevention of IDA reported a mean birth weight of 3.33±3.70kg in daily intervention group and 3.30±3.33kg in weekly intervention group however this study was conducted in infants at 3 months of age(89).

On comparing the diet preferences in the study, both groups had a preponderance to non vegetarian diet [Group A had 77.5% (n=31) and Group B, 85% (n=34)], difference was not statistically significant (p value=0.389). Socio-economic status revealed lower middle class using the Modified Kuppuswamy scale in both the groups . (Group A, 11.6 ± 2.1 and Group B,10.9 ± 1.2). However, the difference in socio-economic status between the two groups was not statistically significant (p= 0.071).

Baseline anthropometric measurements:

In the study we observed no statistically significant difference in growth parameters which included mean weight(Group A: 10.74± 2.63kg; Group B:11.25 ± 2.79kg, p-value=0.4655), mean height(Group A: 86.72± 11.91cm; Group B: 87.5 ± 10cm, p-value= 0.9775), mean head circumference(Group A: 46.38 ± 1.84cm; Group B: 46.76 ± 1.91cm p value=0.5839) and mid upper arm circumference (Group A: 12.59 ± 0.65cm; Group B: 12.56 ± 0.60cm, p-value>0.999) at enrolment between the participants in both the groups. Similar observations were reported in a study on impact of iron supplementation on performance of growth in preschool Beninese children with mean weight of 13.2±1.6kg, mean height of 92.8±4.5cm and mean MUAC of 15.1±1.2cm(85).

Baseline blood investigations:

Baseline blood investigations which comprised of complete hemogram consisting of hemoglobin(Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH), mean corpuscular hemoglobin concentration (MCHC), hematocrit, red cell distribution width(RDW), red blood cell count(RBC), white blood cell count(WBC) and platelet count along with iron studies which included serum iron, total iron binding capacity(TIBC), transferrin saturation(TSAT) and serum ferritin did not have any statistically significant difference at enrolment and similar between the groups.

Primary outcomes:

The primary outcomes of the study demonstrates the effectiveness of intermittent oral liposomal ferric pyrophosphate(Group A) when compared to oral ferrous sulphate (Group B) for prevention of iron deficiency in children aged between 6-59 months. Statistically significant improvement in hemoglobin levels and serum iron levels was observed in oral liposomal ferric pyrophosphate iron group as compared to ferrous sulphate group. The hemoglobin levels, serum iron levels, transferrin saturation, RDW and MCHC levels also showed statistically significant improvement within the group receiving liposomal ferric pyrophosphate iron.

There was increase in mean hemoglobin (Hb) levels in both groups from Group A:10.35 ± 1.28gm/dL to 11.10 ± 1.21gm/dl and Group B 11.02 ± 1.20 gm/dl to 11.17 ± 1.52gm , however it was significantly higher with liposomal ferric pyrophosphate iron group as compared to ferrous sulphate group (0.76 ± 0.67 vs 0.16 ± 0.60; P<0.0001). Mean serum iron levels in liposomal ferric pyrophosphate iron group increased from 58.28±33 to 81.21±40.74 and in ferrous sulphate group from 57.10±26.18 to 66.83±40.08, liposomal ferric pyrophosphate group showed a significant increment (Group A:22.93±29.51; Group B:9.72±27.37 p=0.0017). Transferrin saturation levels also demonstrated increase in liposomal ferric pyrophosphate group with statistical significance (19.10% vs 22.97% P=0.0080). MCHC showed significant improvement in liposomal ferric pyrophosphate group (28.36 vs 28.80; Diff: 0.45; P=0.0491). RDW on evaluation showed improvement in liposomal ferric pyrophosphate group on follow-up in which was significant (15.64 vs 16.25; Diff: 0.61, P=0.0225).

Majority of the studies available in the literature have tested the effectiveness of liposomal iron in the treatment of IDA especially in adults in special situations like chronic renal disease ,cancer, gastrointestinal disease etc. and not for prevention of ID. The very few of these reported in children also have proven its effectiveness in the treatment of IDA. These studies have proven the effectiveness of liposomal iron in the treatment of IDA. De Alvarenga Antunes et al. (2020) in their study to know the efficacy and safety of using liposomal iron in adult patients with IDA with inflammatory bowel disease reported that among the 21 patients, 62% (13 patients) reported a mean increase in hemoglobin levels from 11.4 to 12.6 g/dL after completing an 8-week treatment with oral liposomal iron(78). Similarly Bertani et al., (2021) observed that sucrosomial(a form of liposomal) iron as a treatment for IDA over a period of 4 weeks increased serum iron levels by 37 μg/dl and also observed an improvement of 1.1 g/dl (+11%) after 4 weeks of therapy in both groups compared to 0.76 g/dL in the current study(90). In a study by Karavidas in 2021 among adult heart failure patients, they observed significant increase in serum iron levels with sucrosomial treatment compared to control group (17.58 vs −1.36; P<0.0010)(86). Liposomal iron treatment has been observed to increase TSAT levels in adult populations by study conducted by Pisano et al., in 2014 among adult CKD patients observed an increase in TSAT levels (16.5% vs 18.3%) after 3 months of sucrosomial iron treatment(91).

A recent study on the effects of different regimens of daily iron prophylaxis on maternal iron status and pregnancy outcomes in non anemic pregnant women from Italy in which they observed increase in Hb level from 11.9±0.6 on 11-13 weeks of gestation to 12.6±0.7 at 6 weeks post partum, they have also reported improvement in serum iron, ferritin levels, transferrin saturation, confirming that liposomal iron supplementation during pregnancy significantly reduces maternal ID and IDA incidence compared to no intervention in non-anemic healthy women. Thus it was established that liposomal iron can be used to prevent anaemia during pregnancy(92).

There are no such studies in children to demonstrate efficacy and safety of intermittent oral liposomal ferric pyrophosphate iron for prevention of ID. The only available evidence is a recent study from Turkey, which was conducted to compare the efficacy of daily prophylactic supplementation of ferrous, ferric and liposomal preparations of iron for preventing IDA among 317 children enrolled and assessed at 6-12 months of age who were on prophylaxis from 4 months of age. In this study a significant difference in the mean Hb ,mean serum ferritin levels were observed in the infants with ferrous group ,but not in the liposomal iron supplementation . They reported infants receiving ferrous iron demonstrated higher hemoglobin values compared to other groups and that infants on liposomal iron had a higher risk of iron deficiency than the ferrous iron group in this study(88).

There was no statistically significant difference observed in TIBC, serum ferritin, MCV, MCH and hematocrit levels within and between the two groups in present study.

Serum ferritin values in both the groups were higher compared to other studies at enrolment and did not show any statistical difference between the groups at follow-up. Similar observation was noted by Kılıç et al.,(2024) mentioned above also reported mean serum ferritin levels (µg/L) were higher in ferrous group (30.1±10.8) compared to infants receiving ferric (17.6 ±14.50) and liposomal iron (15.4 ±12.1) ($P < 0.001$) (88).

Serum ferritin being an acute phase reactant is elevated in chronic inflammation, infection , malignancy and liver disorder therefore simultaneous analysis of C reactive protein (CRP) is necessary to rule out these conditions(93). The higher values of serum ferritin in our study may be because of the subclinical infections in the participants in the community. Non evaluation of these conditions and analysis of CRP is one of the limitations of our study.

In the study there was a significant difference in mean Hb level at enrolment between the groups after excluding the dropouts, however this did not affect the final outcome of the study.

This shows that liposomal iron improved Hb levels from a lower baseline among participants in that group with only prophylactic dose showing higher bioavailability as expected.

Secondary outcomes:

We observed an increase in mean weight, mean height, mean head circumference and mean MUAC in both the groups however no statistically significant difference was noted between and within the groups. Similar observations were made by Dossa et al. in their study where they reported no significant linear growth amongst participants after daily iron supplementation (85).

In our study, we observed that ferrous sulphate group has more number of side effects as compared to liposomal ferric pyrophosphate group . Most common side effect observed in liposomal ferric pyrophosphate group was flatulence (12.5% (n=5)). Ferrous sulphate group reported other side effects which were flatulence in 20%(n=8), diarrhea 10%(n=4) and diarrhea and flatulence in 7.5% (n=3). Most common side effect in both the groups combined was flatulence with incidence of 16.25%(n=13).

Gómez-Ramíreze et al. in their review on sucrosomial iron formulation which is similar to liposomal ferric pyrophosphate have also noted reduced risk of gastrointestinal side effects was associated with liposomal iron leading to increased treatment compliance. They have also explained that in this formulation ferric pyrophosphate is protected by a phospholipid bilayer membrane. Additional stability and coating is obtained by adding ingredients like tricalcium phosphate, starch. These form the “sucrosome” and allowing SI to be gastro-resistant and carried through the intestinal tract, without side effects from the interaction between iron and intestinal mucosa. The unique mechanism grants liposomal iron greater bioavailability, reduces the occurrence of gastrointestinal side effects, and safeguards against iron instability in the gastrointestinal tract, ensuring its direct absorption into the intestine and eventual liberation into the liver [9]. Visciano et al. in his explorative study on liposomal iron for treatment of anemia in chronic renal failure patients also highlighted its increased bioavailability and reduced gastrointestinal side effects. (58). Study by Parisi et al. reported poor compliance due to gastrointestinal side effects in both ferrous sulphate and liposomal iron group(92). However, the study done in pediatric population which compared ferrous sulphate and liposomal did not evaluate side effects amongst participants[88].

Compliance is a critical factor in achieving successful iron supplementation in children. We evaluated the compliance by number of doses consumed by the child as reported by the caretaker. We observed that a significant higher number of doses were taken by the children in liposomal ferric pyrophosphate group when compared to ferrous sulphate group (Group A:18.62±1.45;Group B:16.55±2.13, p value=0.0001).. We noted that in liposomal ferric pyrophosphate group where more number of doses were taken, there was a higher correlation with significant improvement in Hb values. Whereas, in ferrous sulphate group, where fewer number of doses were taken, there was less improvement in Hb values. This implies a potential relationship between the number of doses administered and the resulting change in Hb values, with liposomal iron showing a stronger correlation. The oral liposomal ferric pyrophosphate iron preparation is proven to have lesser side effects in our study and even in other studies testing its efficacy , leading to be the cause of a better compliance and better outcome to prevent iron deficiency especially in pediatric population. In a study from Cyprus amongst adult patients with heart failure who were administered oral liposomal iron for treatment of IDA reported a good compliance and higher tolerability(87). However Parisi et al. reported no difference in compliance between liposomal iron and ferrous sulphate preparations(92).

The study showed a total of 55% (n=44"Group A :22 ;Group B : 22)of the participants with mild to moderate anemia, with a mean hemoglobin level of 10.56±1.68 gm/dL. After excluding the dropouts ,a total of 58.6 % (group A : 19: group B : 15 n=34) prevalence was noted. In the liposomal ferric pyrophosphate iron group, 3 participants improved from mild to moderate anemic status to non anemic status i.e Hb>11gm/dL and in ferrous sulphate group only 1 participant showed this improvement. However, no statistically significant differences in the prevalence was noted at enrolment and follow-up in both the groups. Contrary to our study in the study Kılıç et al. reported a higher risk of iron deficiency in population who received liposomal iron as compared to ferrous sulphate(88).

Strengths of study

This was a first community-based randomized controlled trial to evaluate effectiveness of intermittent oral liposomal ferric pyrophosphate with ferrous sulphate for prevention of ID in 6-59 month aged children in Indian settings. Liposomal iron preparation was previously used in other studies only for treatment of IDA mostly in adult population and pregnant women and never it has been evaluated in this age group. The study design and statistical analysis are the other strengthens of the study.

Limitations

The limitations of the study are that it was a single centric study with a small sample size. Since it was a community level study ,a notable number of parents of the study participants did not give consent for blood tests at follow up due to cultural beliefs and local myths. Evaluation of C-reactive protein to validate the serum ferritin levels was not done due to limited resources.

Recommendations

Multicentric studies with a larger sample size in different socio-demographic settings is recommended to test the efficacy of oral liposomal pyrophosphate iron preparation in prevention of iron deficiency in children.

CONCLUSION

This community based randomized controlled trial (RCT) showed effectiveness of intermittent supplementation of oral liposomal ferric pyrophosphate when compared to oral ferrous sulphate for prevention of ID in 6-59 months age children with statistically significant improvement in hemoglobin and serum iron levels. Liposomal ferric pyrophosphate iron group showed statistically significant improvement in hemoglobin, serum iron, transferrin saturation, MCHC and RDW levels. Liposomal ferric pyrophosphate preparation showed lesser side effects with a greater compliance in the study with intermittent prophylaxis. However multicentric studies with large sample size, longer duration in different settings are recommended to generalize the observations of our study.

SUMMARY

The one year randomized control trial was conducted at the primary health center, Vantamuri along with its associated subcenters and Anganwadi centers of field practice areas of Jawaharlal Nehru Medical College, Belagavi. A total of 119 individuals were assessed, of whom 80 met the eligibility criteria and were included in the study. These 80 participants were evenly divided into two groups: Group A and Group B, with 40 participants in each group. Group A received oral liposomal ferric pyrophosphate, while Group B received oral ferrous sulphate as intermittent prophylaxis dosing. At the follow-up stage, 11 participants from each group withdrew their consent for follow-up blood tests, leaving data from 29 participants in each group available for analysis.

The data was analyzed and findings are summarized as below:

1) Socio-demographic data:

- In the present study, socio-demographic data namely age, birth weight, dietary preferences, father's education and occupation, mother's education and occupation along with socio economic status according to Modified Kuppuswamy scale were comparable between both groups and no significant difference between the groups were observed.
- The mean age(in months) of the participants in Group A was 32.82 ± 16.91 and Group B was 33 ± 13.97, and difference was not statistically significant (p value=0.957).
- The gender distribution in the groups showed that Group A had 42.5% (n=17) male and 57.5% (n=23) female participants, Group B had 70% (n=28) male and 30%(n=12) female participants, the difference was statistically significant ($p<0.05$).
- When the birth weight (in kg) was compared, Group A had mean weight of 2.78±0.45 and Group B 2.77±0.40 and the difference between the data was not statistically significant (p value=0.916).

- On comparing the diet preferences, Group A had 77.5% (n=31) with non-vegetarian diet and 22.5% (n=9) with vegetarian diet. In Group B, 85% (n=34) were non vegetarian diet and 15% (n=6) vegetarian diet, difference was not statistically significant (p value=0.389).
- Socio-economic status assessed using the Modified Kuppuswamy Scale showed that in Group A, the mean socio-economic status was 11.6 ± 2.1, while in Group B, it was 10.9 ± 1.2 suggesting that participants were from lower middle class. However, the difference in socio-economic status between the two groups was not statistically significant (p= 0.071).

2) Baseline growth parameters:

- On analysis of growth parameters, the mean weight (in kg) in Group A (10.74 ± 2.63) and Group B (11.25 ± 2.79) show no statistically significant difference (p value = 0.4655).
- The mean height (in cm) in Group A (86.72 ± 11.91) and Group B (87.50 ± 10) showed no statistically significant difference (p value = 0.9775).
- Mean head circumference (in cm) in Group A (46.38 ± 1.84) and Group B (46.76 ± 1.91) also demonstrates no statistically significant variation (p value = 0.5839)
- Mean mid upper arm circumference (in cm) of 12.59 ± 0.65 in Group A and 12.56 ± 0.60 in Group B reveals no statistically significant difference (p value > 0.99).

3) Baseline hematological parameters:

- On comparison of baseline hemogram values the mean Hb level at enrolment in Group A and Group B was 10.64 ± 1.32gm/dL and 10.98 ± 1.21 gm/dl respectively, difference was not statistically significant(p=0.4107).
- Mean haematocrit levels in Group A was 37.53±3.80% and in Group B was 38.38±3.50% at enrolment and the difference was not statistically significant(p=0.3141).

- Mean MCV levels at enrolment in Group A was 82.90±11.78fl and in group B was 85.45±7.90fl, the difference was not statistically significant(p=0.2586).
- Mean MCH level at enrolment in Group A was 23.68±4.01pg and in Group B was 24.67±3.08pg, the difference was not statistically significant(p=0.2181).
- Mean MCHC level at enrolment in Group A was28.46±1.28 g/dl and in Group B was 28.39±1.61g/dl, the difference was not statistically significant(p=0.9962).
- Mean RDW level in Group A at enrolment was 15.44±1.52% and in Group B was 15.83±1.41%, no statistical difference was noted(p=0.1826).
- Mean RBC counts in Group A at enrolment was 457125±42798.4 and inn Group B was 452775.0±40859.7, difference was not statistically significant(p=0.9463).
- Mean WBC counts in Group A at enrolment was 10.12±2.63 x 10^3 and in Group B was 10.57±2.49 x 10^3 difference was not statistically significant(p=0.3683).
- Mean Platelet count in Group A at enrolment was 390725.0±98934.6 and in group B was 382900.0±82330.7, difference was not statistically significant(p=0.9195).

4) Baseline iron profile:

- On comparison of baseline iron study values mean serum iron levels in Group A was 61.13±33.39 µg/dL and Group B was 56.03±26.86 µg/dL, difference was not statistically significant(p=0.5412).
- Mean TSAT level at enrolment in Group A was 19.63±16.66% and in Group B was 17.80±13.49%, difference was not statistically significant(p=0.9080).
- Mean TIBC in Group A was 366±86.92 µg/dL and in Group B was 368.33±88.91 µg/dL at enrolment, difference was not statistically significant(p=0.7558).

- Mean serum ferritin levels at enrolment in Group A was 58.44±56.78ng/dl and in Group B was 41.09±29.97 ng/dl, difference was not statistically significant(p=0.6755).

5) Primary outcomes:

- The mean Hb level at enrolment in Group A and Group B was 10.35 ± 1.28gm/dl and 11.02 ± 1.20gm/dl respectively. The follow-up mean Hb values of Group A and Group B were 11.10 ± 1.21gm/dl and 11.17 ± 1.52gm/dl respectively . The improvement in mean Hb levels were highly significantly within Group A compared to Group B (0.76 ± 0.67 vs 0.16 ± 0.60; P<0.0001*).
- At follow-up both groups showed a mean increase in mean Hb level (Group A: 0.76±0.67 and Group B showed 0.16±0.60), the difference in increment was statistically significant (p=0.0001).
- Comparison of the mean serum iron at enrolment and follow-up showed improved values in both groups but Group A observed statistically significant difference (58.28 vs 81.21;P<0.0001*), no significant differences were observed between enrolment and follow-up mean serum iron in Group B (57.10 vs 66.83; P=0.1766).The change in mean serum iron levels between the groups were compared which showed improved levels in both groups, but the increment at follow-up in Group A(22.93±29.51) as compared to Group B (9.72±27.37) was statistically significant(p-value=0.0177)
- The enrolment and follow-up mean transferrin saturation levels were compared within the groups. In group A, follow up mean TSAT levels were significantly higher than enrolment mean TSAT levels (22.97% vs 19.10%; P=0.0080*). In group B, no significant differences in the enrolment and follow-up mean TSAT levels were observed (19.21% vs 18.0%; P=0.2845)

- The difference between enrolment and follow-up values of mean TSAT in group A and B were 3.86 ± 10.15% and 1.21 ± 7.69% respectively with no significant differences in the improvement in mean TSAT levels between the groups A and B (P = 0.1687).
- The mean serum ferritin values when compared within the groups showed no significant difference in values were observed at follow-up in both groups , Group A(p=0.5705) and Group B (p value=0.5909). Similarly, no statistically significant difference was observed in mean serum ferritin at enrolment and follow-up between the groups A and B (7.45 ± 39.86 ng/mL vs -3.76 ± 28.65 ng/mL; P=0.4744)
- The mean MCHC levels within Group A showed a significant improvement at follow-up (28.80 vs 28.36; Diff: 0.45; P=0.0491*). However, the difference was not statistically significant in Group B(28.42 vs 28.43; p value=0.811) and comparison of the difference in mean MCHC levels at enrolment and follow-up levels between group A and group B was not statistically significant (0.45 vs 0.01; P=0.1417).
- Comparison of the mean RDW value at enrolment and follow-up within Group A was statistically significant (15.64 vs 15.83; Diff: 0.61, P=0.0225*). However no significant difference between was observed at enrolment and follow-up within Group B (14.72 vs 15.12; Diff = 0.39, P=0.5888) and on comparison of difference in mean RDW levels between both groups at follow-up it was noted that the difference in Group A (0.61±1.43) and Group B (-0.39±1.84) was not statistically significant(p value=0.0763)

6) Secondary outcomes:

- An increase in weight, height, head circumference and mid upper arm circumference is noted in most of the participants during follow-up in group A and group B following treatment. However, no significant differences are observed between the groups.

- The analysis shows lesser number of effects in Group A as compared to Group B. Most common side effect observed in Group A was flatulence in 12.5% (n=5) participants in the group .In Group B the side effects were flatulence in 20%(n=8), diarrhea 10%(n=4) and diarrhea and flatulence in 7.5% (n=3). Most common side effect in both groups was flatulence with incidence of 16.25%(n=13) combined in both groups.
- Compliance of medication was checked by the mean number of doses taken. The mean number of doses taken was higher in Group A(18.62±1.45) as compared to Group B(16.55±2.13) which was statistically significant ($p<0.05$).
- Group A, where more number of doses were taken, there was a higher correlation with significant improvement in Hb values. Whereas, in Group B, where fewer number of doses were taken, there was less improvement in Hb values. This implies a potential relationship between the number of doses administered and the resulting change in Hb values, with Group A showing a stronger correlation.
- The study revealed that 55% (n=44) of the participants exhibited mild to moderate anemia, with a mean hemoglobin level of 10.56±1.68 gm/dL. After excluding the dropouts ,a total of 58.6 % (group A : 19: group B : 15 n=34) prevalence was noted. At follow-up it was noted that in Group A, 3 participants improved from being mild to moderate anemic status to non anemic status i.e Hb>11gm/dL and in Group B only 1 participant showed this improvement. However, no statistically significant differences in the prevalence were noted at enrolment and follow-up in both the groups.

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ANNEXURE – I

INFORMED CONSENT FORM

"To compare the effectiveness of intermittent supplementation of oral liposomal ferric pyrophosphate with ferrous sulphate in children between 6-59 months in rural area Of Belagavi, Karnataka- A Randomised Control Trial"

NAME OF PARTICIPANT-__________________________

Name of Student/Principal Investigator:

Dr.

Name of Guide/Co Investigators:

Dr.

You have been asked to involve your child in the above said research to be conducted

at Primary health center, subcenters and Anganwadis in Vantamuri, District Belagavi, Karnataka base in KAHER JN medical college hospital, Belagavi by Dr. ******* *****, PG

student in the Department of Paediatrics at Jawaharlal Nehru Medical College, Belagavi.

Objective:

Primary Objective : To compare the effectiveness of Ferric Pyrophosphate with Ferrous Sulphate in Intermittent Oral Iron prophylaxis in children between 6 month to 59 months.

Secondary Objective : 1)To compare iron stores after 3 months of prophylactic Oral Iron therapy with Ferric Pyrophosphate Iron and Ferrous Sulphate formulations.

2)To compare growth in these children by anthropological measures.

3) To compare side effects and compliance of both compounds

Introduction: Participation of your ward will help us to Evaluate the iron stores after using Ferric Pyrophosphate Iron for 3 months, giving us valuable information about the compound so that it can help population at large to prevent iron deficiency anemia and early detection of anemia in your child.

Explanation of procedure: The child will be enrolled in the study after consent in given. Iron stores will be checked at enrollment and anthropometry will be done. After 3 months of compliant drug usage iron stores will be checked again and child will be evaluated for any signs or symptoms of iron deficiency in the body and anthropometry will also be done to see the growth pattern. Any new side effect with the compound will be noted and compliance will be compared to the older compounds.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are some risks which include diarrhea, vomiting and nausea involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

In case of any questions with regard to this study, you are free to contact:

Dr. *****************

Post Graduate, Dept of Pediatrics, J.N. Medical College, Belagavi

Contact number. *************

Dr. *****************, M.D., D.C.H.

Professor, Dept of Pediatrics, J.N. Medical College, Belagavi

Contact number ***************

If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "To compare the effectiveness of Liposomal Ferric Pyrophosphate in oral formulation with Ferrous Sulphate oral formulation given as intermittent prophylactic therapy in children between 6month to 59 months in Rural area of Belagavi- A Randomised Controlled Trial". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of parent/guardian:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator

ANNEXURE- II

PROFORMA

SCREENING PROFORMA
BASIC DETAILS

SCREENING NUMBER

DATE OF SCREENING

NAME OF THE PARTICIPANT:

FIRST NAME

MIDDLE NAME

LAST NAME

AGE-

GENDER –

ADDRESS-H.NO.

STREET

TALUKA

DISTRICT

INCLUSION CRITERIA

1. Children in age group of 6 months to 59 months.	YES		NO	
2. Parents who consent for the trial	YES		NO	
3. Children started on complementary feeds with exclusive breast feeding	YES		NO	
4. Children enrolled in Anemia Mukt Bharat Program	YES		NO	

EXCLUSION CRITERIA

1. Diagnosed case of Iron deficiency anemia	Yes		No	
2. History of blood transfusion.	Yes		No	
3. Children diagnosed with chronic illnesses	Yes		No	

ELIGIBLE-

YES ☐ NO ☐

ENROLMENT FORM

PARTICIPANT DETAILS

- AGE AT ENROLMENT –YEAR / MONTHS
- DATE OF BIRTH
- BIRTH HISTORY
  - BIRTH WEIGHT
  - PERIOD OF GESTATION
  - MODE OF DELIVERY
  - INDICATION
  - PLACE OF DELIVERY
  - HISTORY OF NICU ADMISSION
  - PEDIGREE CHART

- HISTORY AND CLINICAL EXAMINATION

HISTORY OF HOSPITAL ADMISSION

RECENT HISTORY OF ANY ACUTE ILLNESS

- WEIGHT AT SCREENING
- HEIGHT AT SCREENING (CM)
- HEAD CIRCUMFERENCE AT SCREENING (CM)
- MUAC AT SCREENING (CM)

- EXAMINATION-
  - GENERAL
  - SYSTEMIC

DIETARY PREFRENCES

FAMILY-
CHILD-

- **FATHER'S DETAILS**
- NAME
- OCCUPTION
- EDUCATION
- **MOTHER'S DETAILS**
- NAME
- OCCUPATION
- EDUCATION
- CONTACT NUMBER OF PARENT (FATHER/MOTHER)

RANDOMIZATION FORM

1. RANDOMIZATION ID-
2. TRAIL ARM
   i. GROUP I
   ii. GROUP II

Q.4 DOSAGE GIVEN mg

- FORM COMPLETED BY

NAME

DESIGNTION

DATE

DISPENSING FORM

- RANDOMIZATION ID-
- TRAIL ARM
  - GROUP I (FERRIC PYROPHOSPHATE)
  - GROUP II (FERROUS SULPHATE)

Q1. PARTICIANT GIVEN DEWORMING RECENTLY

a. YES
b. NO

Q2. GROUP I ARM RECEIVED SYRUP

a. Yes NUMBER OF BOTTLES RECEIVED -
b. No

Q.3 GROUP II ARM RECEIVED SYRUP

a. Yes NUMBER OF BOTTLES RECEIVED -
b. No

CENTRAL LABORATORY FORM

RANDOMIZATION ID:

1ST VISIT			FOLLOW UP VISIT		
1.	Hb measurement :	____ G/dL	1.	Hb measurement :	____ G/dL
2.	Serum iron level:	____ μg/dL	2.	Serum iron level:	____ μg/dL
3.	Total iron-binding capacity (T1BC):	____ μg/dL	3.	Total iron-binding capacity (T1BC):	____ μg/dL
4.	Serum transferring saturation (TSAT) level:	____ %	4.	Serum transferring saturation (TSAT) level:	____ %
5.	Serum ferritin	____ ng/mL	5.	Serum ferritin	____ ng/mL
6	Complete Hemogram		6	Complete Hemogram	
	a. WBC	____ 10^3 / μl		a. WBC	____ 10^3 / μl
	b. RBC:	____ 10^6 / μl		b. RBC:	____ 10^6 / μl
	c. Hematocrit (HCT)	____ %		c. Hematocrit (HCT)	____ %
	d. MCV	____ fl		d. MCV	____ fl
	e. MCHC:	____ pg		e. MCHC:	____ pg
	f. MCHC:	____		f. MCHC:	____
	g. RDW	____ %		g. RDW	____ %
	h. Platelet count	____ 10^3		h. Platelet count	____ 10^3

SIDE EFFECTS FORM

Randomization ID: _______________

1. History of any allergy: a. Yes b. No

a. If Yes, Specify-______________

2.Date of starting |__|__|-|__|__|-|__|__|__|__|

3. Symptoms

a) Diarrhoea	YES	NO
b) Rashes/ redness of skin	YES	NO
c) Itching	YES	NO
d) Flatulence	YES	NO
e) Angioedema	YES	NO
f) Facial edema	YES	NO
g) Malaise	YES	NO
h) Headache	YES	NO
i) Fever	YES	NO
j) Throat itching , dysphonia	YES	NO

PATIENT FOLLOW UP CARD

- RANDOMIZATION ID-
- TRAIL ARM
  - GROUP I (SUCROSOMIAL IRON) ☐
  - GROUP II (FERROUS SULPHATE) ☐

DATE STARTED- ☐

	FIRST DOSE	SECOND DOSE
WEEK 1	☐	☐
WEEK 2	☐	☐
WEEK 3	☐	☐
WEEK 4	☐	☐
WEEK 5	☐	☐
WEEK 6	☐	☐
WEEK 7	☐	☐

	FIRST DOSE	SECOND DOSE
WEEK 8	☐	☐
WEEK 9	☐	☐
WEEK 10	☐	☐
WEEK 11	☐	☐
WEEK 12	☐	☐

ANNEXURE-III

Normality of pretest and posttest scores of all parameters in Group A and Group B

Parameters	Times	Group	Shapiro-Wilk	p-value
Hb	Pretest	Group A	0.9630	0.3800
		Group B	0.9640	0.4060
	Posttest	Group A	0.9710	0.5920
		Group B	0.9770	0.7580
	Difference	Group A	0.7380	0.0001*
		Group B	0.8620	0.0010*
S. IRON	Pretest	Group A	0.8630	0.0010*
		Group B	0.9370	0.0840
	Posttest	Group A	0.9560	0.2610
		Group B	0.8640	0.0020*
	Difference	Group A	0.9550	0.2520
		Group B	0.8140	0.0001*
TIBC	Pretest	Group A	0.9650	0.4360
		Group B	0.9770	0.7670
	Posttest	Group A	0.9530	0.2140
		Group B	0.9760	0.7320
	Difference	Group A	0.9560	0.2590
		Group B	0.9460	0.1420
TSAT	Pretest	Group A	0.7600	0.0001*
		Group B	0.8190	0.0001*
	Posttest	Group A	0.8560	0.0010*
		Group B	0.8950	0.0070*
	Difference	Group A	0.9170	0.0250*

		Group B	0.9480	0.1650
S. FERRITIN	Pretest	Group A	0.7860	0.00001*
		Group B	0.8660	0.0020*
	Posttest	Group A	0.8230	0.0001*
		Group B	0.7610	0.0001*
	Difference	Group A	0.8400	0.0001*
		Group B	0.8970	0.0080*
WBC	Pretest	Group A	0.9620	0.3590
		Group B	0.9800	0.8250
	Posttest	Group A	0.8980	0.0090*
		Group B	0.9440	0.1290
	Difference	Group A	0.8750	0.0030*
		Group B	0.9750	0.6920
RBC	Pretest	Group A	0.9830	0.9120
		Group B	0.9510	0.1950
	Posttest	Group A	0.9400	0.0990
		Group B	0.9140	0.0220*
	Difference	Group A	0.9260	0.0440*
		Group B	0.9540	0.2280
HCT	Pretest	Group A	0.9790	0.8130
		Group B	0.9580	0.2900
	Posttest	Group A	0.9750	0.6910
		Group B	0.9560	0.2620
	Difference	Group A	0.8540	0.0578
		Group B	0.9730	0.6360
MCV	Pretest	Group A	0.9470	0.1540
		Group B	0.9500	0.1840
	Posttest	Group A	0.9700	0.5580

		Group B	0.9720	0.6140
	Difference	Group A	0.9430	0.1220
		Group B	0.9560	0.2580
MCH	Pretest	Group A	0.9560	0.2680
		Group B	0.9700	0.5730
	Posttest	Group A	0.9670	0.4880
		Group B	0.9570	0.2800
	Difference	Group A	0.9360	0.0780
		Group B	0.9860	0.9520
MCHC	Pretest	Group A	0.9820	0.8860
		Group B	0.8890	0.0050*
	Posttest	Group A	0.9070	0.0150*
		Group B	0.8190	0.0001*
	Difference	Group A	0.9810	0.8550
		Group B	0.9490	0.1680
RDW	Pretest	Group A	0.9720	0.6270
		Group B	0.9460	0.1470
	Posttest	Group A	0.9290	0.0500*
		Group B	0.9140	0.0210*
	Difference	Group A	0.9490	0.1750
		Group B	0.9240	0.0380*
PLT COUNT	Pretest	Group A	0.9370	0.0840
		Group B	0.9260	0.0430*
	Posttest	Group A	0.9520	0.2100
		Group B	0.9750	0.7140
	Difference	Group A	0.8600	0.0010*
		Group B	0.9770	0.7470

ANNEXURE-IV

MASTERCHART

RD. NO.	AGE(m)	SEX	BIRTH WT(kg)	POG	M.O.D	NICU ADMISSION	PEDIGREE	HISTORY HOSPITAL ADMISSION	H/O ACUTE ILLNESS	Wt(kg)	Wt follw-up(kg)	Ht(cm)	Ht follow-up (cm)	HC(cm)	HC Follow-up(cm)	MUAC(cm)	MUAC follow-up(cm)	DIET FAMILY	DIET SELF	FATHER'S OCCUPATION	FATHER EDUCATION	MOD. KUPPUSWAMY SCALE	MOTHER OCCUPATION	MOTHER'S EDUCATION	DEWORMING (<6MT)	Side effects	DOSES T
A1	18	M	3.3	FT	LSCS	NO	1ST CHILD	NO	NO	8	9	78	78	46	46	13	13.5	VEG	VEG	ENGINEER	MSC	15	HOUSEWIFE	BE	YES	NIL	20/24
A2	14	M	3.1	FT	NVD	NO	2ND CHILD	NO	NO	8	9	72	72	43	43	13.5	14	NON VEG	VEG	COOLIE	10TH	10	HOUSEWIFE	10TH	NO	FLATULENCE	19/24
A3	42	F	3	FT	NVD	NO	4TH CHILD	NO	NO	10		94		47		11.8		NON VEG	NON VEG	FARMER	8TH	10	HOUSEWIFE	6TH	YES		
A4	57	M	3	FT	NVD	NO	2ND CHILD	NO	NO	11	11	108	109	48	48	12.5	12.5	NON VEG	NON VEG	COOLIE	8TH	11	HOUSEWIFE	6TH	YES	NIL	18/24
A5	58	F	3	FT	NVD	NO	4TH CHILD	NO	NO	12	13	100	101	48	49	12	12.5	NON VEG	NON VEG	FARMER	8TH	10	HOUSEWIFE	8TH	NO	NIL	19/24
A6	34	F	2	FT	NVD	NO	3RD CHILD	NO	NO	8.5	10	86	86	46	47	12	12	NON VEG	NONVEG	LABOUR	6TH	10	HOUSEWIFE	6TH	YES	NIL	19/24
A7	57	F	3.5	FT	LSCS	NO	2ND CHILD	NO	NO	12	12.5	97	97	46.5	47	11.7	12	NON VEG	NON VEG	FARMER	6TH	10	HOUSEWIFE	6TH	YES	NIL	19/24
A8	39	F	2.5	FT	NVD	NO	3RD CHILD	NO	NO	9	11	90	90	46	46	11.8	12	NON VEG	NON VEG	COOK	10TH	11	HOUSEWIFE	6TH	YES	NIL	16/24
A9	58	M	2.5	FT	NVD	NO	3RD CHILD	NO	NO	14		99		48		12		NON VEG	NON VEG	DRIVER	5TH	12	HOUSEWIFE	8TH	YES		
A10	30	M	3	FT	LSCS	NO	1ST CHILD	NO	NO	12	14	84	84	46	46	12	13	NON VEG	NON VEG	FARMER	5TH	11	HOUSEWIFE	12TH	YES	NIL	19/24
A11	10	M	3.1	FT	LSCS	NO	2ND CHILD	NO	NO	7		67		43		12		NON VEG	NON VEG	ARMY	12TH	18	HOUSEWIFE	D.Ed	NO		
A12	39	F	3.5	FT	NVD	NO	1ST CHILD	NO	NO	11	13	90	90	47	48	12	12.5	NON VEG	NON VEG	FARMER	8TH	11	HOUSEWIFE	8TH	NO	NIL	18/24
A13	26	F	3	FT	NVD	NO	1ST CHILD	NO	NO	9		80		46		12		NON VEG	NON VEG	FACTORY WORKER	10TH	10	HOUSEWIFE	6TH	NO		
A14	20	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	8.9	10	76	76	44	44	12	12.5	NON VEG	NON VEG	FARMER	8TH	11	HOUSEWIFE	8TH	YES	FLATULENCE	20/24
A15	21	M	3	FT	LSCS	NO	1ST CHILD	NO	NO	10	11	80	80	45	45	12.5	13	NON VEG	NON VEG	FACTORY WORKER	10TH	12	HOUSEWIFE	6TH	YES	NIL	18/24
A16	36	F	4	FT	NVD	NO	3RD CHILD	NO	NO	11	10	89	89	47	47	12	12.5	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	6TH	YES	NIL	20/24
A17	25	F	3	FT	NVD	NO	3RD CHILD	NO	NO	9	9	81	81	46	46	12	12	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	8TH	YES	NIL	19/24
A18	36	M	3	FT	MVD	NO	3RD CHILD	NO	NO	11.1	12	88	88	46	46	12.5	13	NON VEG	NON VEG	COOLIE	8TH	10	HOUSEWIFE	6TH	YES	NIL	18/24
A19	55	F	2.5	FT	NVD	NO	4TH CHILD	NO	NO	11.1	12	105	105	48	48	13	13	NON VEG	NON VEG	DRIVER	10TH	11	HOUSEWIFE	6TH	YES	FLATULENCE	19/24
A20	12	F	2.5	FT	NVD	YES (SEPSI	3RD CHILD	NO	COLD	7	8	69	69	44	44	12	12	NON VEG	NON VEG	LABOURER	10TH	10	HOUSEWIFE	6TH	NO	NIL	19/24
A21	35	F	2.8	FT	NVD	NO	2ND CHILD	NO	NO	11	10	90	90	47	44	12.5	13	NON VEG	NON VEG	SECURITY	10TH	12	TEACHER	B.Ed.	YES	NIL	20/24
A22	35	F	2.5	FT	LSCS	NO	1ST CHILD	NO	NO	12	12	90	90	48	49	13	13.4	NON VEG	NON VEG	POLICE	B.A.	16	HOUSE WIFE	B. Com.	YES	NIL	18/24
A23	16	F	2.5	FT	NVD	NO	4TH CHILD	NO	NO	8	9	78	78	46	46	12	12.5	NON VEG	NON VEG	SHOPOWNER	10TH	12	HOUSEWFE	10TH	YES	NIL	18/24
A24	58	F	2.5	FT	NVD	NO	3RD CHILD	NO	NO	15	16	100	100	49	49	13.5	13.8	NON VEG	NON VEG	SHOPOWNER	10TH	12	HOUSEWIFE	10TH	YES	NIL	19/24
A25	10	M	3.5	FT	LSCS	YES (NNH)	3RD CHILD	NO	NO	8	9	70	70	44	44	12.5	13	VEG	VEG	FACTORY WORKER	10TH	13	HOUSEWIFE	8TH	YES	FLATULENCE	13/24
A26	37	M	2.75	FT	NVD	YES (NNH)	2ND CHILD	NO	NO	13		93		48.5		13		NON VEG	NON VEG	SHOPOWNER	10TH	11	HOUSEWIFE	8TH	YES		
A27	23	F	3	FT	LSCS	NO	1ST CHILD	NO	NO	10	10	79	79	46	46	13	13	VEG	VEG	COMPANY WORKER	B.Com.	15	HOUSEWOFE	B.A.	NO	NIL	20/24
A28	16	F	2.5	FT	NVD	NO	4TH CHILD	NO	NO	10	10	78	78	45	45	13	13.5	NON VEG	VEG	LABOURER	10TH	10	HOUSEWIFE	8TH	NO	FLATULENCE	19/24
A29	11	M	2.6	FT	NVD	NO	3RD CHILD	NO	NO	9		72		45		12		NON VEG	VEG	DRIVER	12TH	11	HOUSEWIFE	8TH	NO		
A30	38	F	2.25	FT	LSCS	NO	1ST CHILD	NO	NO	13.5		94		48		13.5		NON VEG	NON VEG	AST MANAGER	M.Sc.	16	HOUSEWIFE	M.A.	NO		
A31	16	M	3	FT	LSCS	NO	2ND CHILD	NO	COLD	9.5	10	77	77	45	45	12.5	13.5	NON VEG	NON VEG	ENGINEER	B.E.	15	HOUSEWIFE	B.Ed.	NO	NIL	18/24
A32	56	F	2.8	FT	NVD	NO	1ST CHILD	NO	NO	16		105		49		13		NON VEG	NON VEG	DRIVER	12TH	10	HOUSEWIFE	10TH	YES		
A33	57	M	2	FT	LSCS	NO	2ND CHILD	NO	NO	16	17	104	104	50	50	14	14	NON VEG	NON VEG	LABOURER	8TH	9	HOUSEWIFE	6TH	NO	NIL	20/24
A34	49	M	1.7	PT	NVD	YES(NNH)	1ST CHILD	NO	NO	15	15	99	99	49	49	13.5	13.2	VEG	VEG	COMPANY WORKER	B.E.	12	HOUSEWIFE	10TH	YES	NIL	17/24
A35	15	F	2.5	FT	NVD	NO	1ST CHILD	NO	NO	8	9	76	77	44.5	45	12.5	12.8	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	8TH	NO	NIL	19/24
A36	10	M	2.2	FT	NVD	NO	2ND CHILD	NO	NO	7		69		43		12		VEG	VEG	FACTORY WORKER	12TH	11	HOUSEWIFE	8TH	NO		
A37	54	F	2.5	FT	NVD	NO	3RD CHILD	NO	NO	15		104		49		13.5		NON VEG	NON VEG	FARMER	8TH	11	HOUSEWIFE	6TH	YES		
A38	22	F	3	FT	NVD	NO	2ND CHILD	NO	NO	9	11	80	80	45	45	13	13	NON VEG	NON VEG	FARMER	8TH	9	HOUSEWIFE	8TH	NO	NIL	20/24
A39	12	M	3.3	FT	NVD	NO	2ND CHILD	NO	NO	9	10	73	74	45	45	13.5	13.5	VEG	VEG	FARMER	8TH	9	HOUSEWIFE	6TH	NO	NIL	19/24
A40	56	F	2.6	FT	LSCS	NO	2ND CHILD	NO	NO	16		105		49		14		NON VEG	NON VEG	FARMER	8TH	9	HOUSEWIFE	6TH	NO		

AKEN

Hb	Hb F/U	S. IRON	S. IRON F/U	TIBC	TIBC F/U	TSAT	TSAT F/U	S. FERRITIN	S. FERRITIN F/U	WBC	WBC F/U	RBC	RBC F/U	HCT	HCT F/U	MCV	MCV F/U	MCH	MCHF/U	MCHC	MCHC F/U	RDW	RDW F/U	PLT COUNT	PLT COU
9.6	10.5	38	42	440	439	9	10	11.7	15.2	7.09	6.6	460000	470000	33.6	32	77	78.1	21.6	22	28.1	27.2	15.5	16	269000	281000
9.8	10.8	35	45	516	455	7	6	16	18	9.6	8	560000	568000	36.2	38	64	68	17.4	20	27.2	28	18.2	19	239000	275000
12.5		57		234		24		45.1		12.07		442000		41.1		93		28.2		30.3		13.7		418000	
11.3	12.1	61	65	384	424	16	9	19	43.5	14.6	15.74	507000	511000	39.5	42.8	78	83.7	22.3	23.7	28.5	28.3	16.7	17.3	350000	334000
9.6	10.8	36	89	491	396	7	15	12.1	10.63	9.5	7.8	463000	478000	33	34	71.3	72	20.7	22.1	29.1	28.9	17.5	15	436000	469000
9.9	10.5	38	51	377	480	10	10	11.5	14.6	18.5	15.38	440000	443000	34.3	34.2	77.5	78.9	22.4	22.2	29	28.1	16.9	15.8	612000	626000
12.3	13.5	133	149	226	259	59	60	86.6	86.9	11.09	9.65	456000	485000	41.6	40.6	91.1	85.6	26.9	25	29.5	28.6	13.8	14	358000	365000
9.3	10.6	50	84	317	296	16	30	42.8	39.16	12.19	8.9	463000	478000	32.8	35.2	70.8	72.6	20	22	28.2	30.2	14.5	12.6	414000	395000
13.4		156		250		62		77.5		9.86		532000		44.9		84.4		25.3		29.9		16.2		379000	
9.1	10.5	34	69	411	327	8	15	6.48	47.4	8.37	7.26	508000	560000	33.4	35.6	65.7	63.6	18	18.8	27.3	29.5	17.3	16	535000	283000
11		44		401		11		14.7		12.24		488000		37.1		76		22.5		29.6		14.2		358000	
11.6	12.4	126	162	163	233	77	79	72.3	65.23	8.6	7.8	376000	389000	37.5	36	99.8	85.4	30.7	28.6	30.8	29	13.1	13	238000	248000
11.3		80		368		22		33.45		10.3		434000		38.9		89.5		26		29		15.5		358000	
11	11.4	45	72	326	399	14	18	32.3	18.7	13.56	15.82	412000	413000	37	38.6	89.9	93.5	26.7	27.6	29.7	29.5	14.4	13.8	510000	365000
8.5	9	21	37	444	487	5	8	8.03	17.9	10.02	8.69	476000	393000	31.1	31	65.4	70.8	17.8	19.5	27.2	27.5	16.4	16	373000	423000
12	13	63	133	356	322	18	30	105.3	149	9.73	9.89	404000	454000	39.6	39.9	98	87.9	29.6	28.6	30	32.6	13.8	13.5	363000	455000
10.9	11.9	51	122	451	506	11	24	31.14	44.4	9.19	6.5	425000	482000	37.7	38.7	88.8	80	25.7	24.7	29	30.7	15.8	16	409000	410000
8.3	9	32	81	435	216	7	38	21.76	15.27	9.77	9.8	427000	428000	31.1	30.5	72.7	83	19.4	22.4	26.7	28	17	14	409000	218000
10	10.6	118	120	387	215	30	33	36.43	85.8	6.73	9.6	471000	407000	43.7	39.1	92.8	96	27.8	26.1	29.8	27.2	14.7	14	219000	360000
10.4	11.6	79	115	355	455	22	25	169.3	68.2	6.56	5.82	422000	463000	36.5	37.9	86.5	81.9	24.7	22.9	28.6	28	17.4	18	511000	484000
7.1	8.5	25	30	470	455	5	8	5.66	15	9.48	10.8	437000	450000	28.2	29	64.5	70.2	16.2	18	25.2	26	17.4	18	400000	420000
10.3	10.8	43	45	454	399	9	10	19.68	13.3	5.31	7.3	466000	448000	36.5	36.5	78.4	81.6	22.1	23.5	28.1	28.8	15.4	13.6	353000	365000
9.9	11.2	39	126	321	369	12	34	227.8	127	8.46	7.28	513000	473000	36	36.6	70.1	77.4	19.3	21.6	27.6	27.9	16.9	15.6	697000	301000
10.7	11.8	127	147	258	336	49	45	145.7	141	10.46	15.8	530000	588000	37.2	36.4	70.2	83.5	20.1	27.6	28.6	29.64	15.3	12.4	453000	448000
11.8	9.9	60	15	348	392	17	4	46	7.9	13.08	12.58	446000	450000	41.4	33.9	92.9	75.3	26.4	22	28.5	29.2	15.3	14.4	319000	330000
11.4		46		318		14		80		8.15		425000		40.8		95.9		26.8		27.9		14.9		232000	
11.4	10.8	90	50	229	390	39	13	91.1	25.3	10.14	12.7	437000	452000	41.3	37	94.5	81.9	26.1	23.9	27.6	29.2	14.4	14.2	356000	384000
11.9	12.8	87	92	288	296	30	35	161.7	59.63	11.96	10.89	377000	382000	42.5	43.6	113	106	31.5	32.6	27.9	28	14	14	356000	320000
9.1		37		526		7		28.82		7.41		438000		34		77.5		20.8		26.8		16.7		427000	
10.4		49		382		13		31.67		5.94		434000		39.2		90.3		23.8		26.4		14.6		245000	
9.8	10.8	58	89	502	455	11	19	33.92	26.98	11.02	7.5	506000	489000	38	39	75.1	78.6	19.4	20.9	25.8	27	18.5	15	519000	489000
12.4		105		384		27		133.3		12.03		455000		42.8		94.1		27.2		28.9		14.6		404000	
11.9	12.9	69	120	225	310	31	39	80.1	87.5	12.03	10.44	396000	454000	39	39	98.6	85.9	30.2	28.4	30.6	33.1	12.4	13	365000	553000
10.6	10.9	44	62	342	404	13	15	13.9	48.4	7.76	6.36	456000	420000	36.9	37.5	80.8	89.3	23.2	26	28.7	29.1	15.4	14.3	360000	342000
8.8	10	20	69	450	410	4	15	8.45	29.4	13.3	9.6	475000	485000	31.8	32	67	72	18.5	20	27.6	28	16.6	15	374000	289000
11.4		50		363		14		13.8		10.23		524000		40.7		77.6		21.8		28.1		16.7		459000	
11.8		70		347		20		128		10.55		408000		39.6		97.1		28.8		29.7		13.2		398000	
10.4	11.3	23	24	388	388	6	5	18	18	8.45	17.9	462000	451000	36.9	38.7	79.9	85.6	22.5	25	28.2	29.1	15	18.5	422000	635000
11.9	12.1	45	50	360	355	12	14	39.6	19	12.87	15	495000	497000	40.6	40	81.9	79	24	24	29.3	29	14	14	402000	396000
10.8		61		355		17		177		6.72		439000		37		84.4		24.7		29.2		13.5		330000	

RD. NO.	AGE(m)	SEX	BIRTH WT(kg)	POG	M.O.D	NICU ADM	PEDIGREE	HISTORY OF HOSPITAL ADMISSION	H/O ACUTE ILLNESS	WT.(KG)	Wt f/u (kg)	HT(CM)	Ht f/u (cm)	HC(CM)	HC f/u(cm)	MUAC(CM)	MUAC f/u (cm)	DIET FAMILY	DIET SELF	FATHER'S OCCUPATION	FATHER EDUCATION	MOD. KUPPUSWAMY SCALE	MOTHER OCCUPATION	MOTHER'S EDUCATION	DEWORMING (<6MT)	ADR	DOSES T
B1	36	F	2.7	FT	NVD	NO	1ST CHILD	NO	NO	13	15	90	90	45	45	13	13	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	Bed.	YES	NIL	14/24
B2	44	M	2.5	FT	NVD	NO	2ND CHILD	NO	NO	11	13	96	97	48	48	12	12.5	NON VEG	NONVEG	POLICE	PUC	16	HOUSEWIFE	10TH	YES	NIL	17/24
B3	56	F	3	FT	NVD	NO	2ND CHILD	NO	NO	16	17	100	100	47	47	12	12.5	NON VEG	NON VEG	FARMER	6TH	10	HOUSEWIFE	6TH	YES	NIL	18/24
B4	33	F	3	FT	NVD	NO	1ST CHILD	NO	NO	8	10	85	85	46	46	11.5	12	NON VEG	NON VEG	FARMER	8TH	10	HOUSEWIFE	6TH	YES	NIL	16/24
B5	40	M	3	FT	NVD	NO	1ST CHILD	NO	NO	10	12	90	90	47	47	12	12	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	6TH	NO	NIL	19/24
B6	34	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	10	11	88	89	47	47	12	12	NON VEG	NON VEG	DRIVER	8TH	11	HOUSEWIFE	8TH	NO	FLATULENCE	18/24
B7	41	M	3	FT	NVD	NO	3RD CHILD	NO	NO	10	10	91	91	47	47	12	12	NON VEG	NON VEG	FACTORY WOR	10TH	13	HOUSEWIFE	10TH	YES	DIARRHOEA, FLATULENCE	14/24
B8	23	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	9		80		45		11.8		NON VEG	NON VEG	LABOUR	6TH	10	HOUSEWFE	8TH	YES		
B9	9	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	5.5	6	66	66	42	42	11.8	11.8	NON VEG	VEG	SECURITY	8TH	12	HOUSEWIFE	8TH	YES	DIARRHOEA	14/24
B10	58	M	4	FT	NVD	NO	1ST CHILD	NO	NO	16		100		49		12.5		NON VEG	NON VEG	POLICE	PUC	16	HOUSEWUFE	8TH	YES		
B11	15	F	2.9	FT	NVD	NO	2ND CHILD	NO	NO	7.5	8	71	71	43	43	11.8	11.8	NON VEG	VEG	FACTORY WOR	8TH	12	HOUSE WIFE	6TH	YES	DAIRRHOEA	15/24
B12	25	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	8	10	77	77	46	46	12.5	12.5	NON VEG	NON VEG	LABOURER	10TH	10	HOUSEWIFE	8TH	YES	FLATULENCE	18/24
B13	11	F	2.5	FT	NVD	NO	2ND CHILD	NO	NO	6	9	65	65	42	42	12	12	VEG	VEG	LABOURER	8TH	10	HOUSEWIFE	6TH	YES	FALTULENCE	18/24
B14	31	F	3	FT	NVD	NO	1ST CHILD	NO	NO	10	11	83	84	46	46	12.5	12.5	NON VEG	NON VEG	LABOURER	8TH	10	HOUSEWIFE	6TH	NO	FLATULENCE, DIARRHEA	14/24
B15	27	M	2.8	FT	NVD	NO	2ND CHILD	NO	NO	10	12	85	85	47	47	12.5	12.5	NON VEG	NON VEG	FARMER	8TH	11	HOUSEWIFE	6TH	YES	DIARRHOEA, FLATULENCE	13/24
B16	31	F	3	FT	NVD	NO	1ST CHILD	NO	NO	10	12	85	85	46	46	12	12	NON VEG	NON VEG	SECURITY	10TH	12	HOUSEWIFE	8TH	YES	NIL	18/24
B17	49	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	12	13	92	92	47	47	12.5	12.5	NON VEG	NON VEG	TEACHER	B Ed.	14	HOUSEWIFE	12TH	NO	FLATULENCE	18/24
B18	26	M	2.5	FT	NVD	NO	2ND CHILD	NO	NO	11	10	83	84	46	46	12	12	NON VEG	NON VEG	TEACHER	B Ed.	14	HOUSEWIFE	12TH	NO	NIL	15/24
B19	13	F	2.5	FT	NVD	NO	1ST CHILD	NO	NO	8	9	73	73	44	44	12.5	13	NON VEG	NON VEG	DRIVER	10TH	11	HOUSEWIFE	6TH	NO	NIL	15/24
B20	50	F	2.5	FT	NVD	NO	2ND CHILD	NO	NO	15	14	99		49		13		NON VEG	NON VEG	COOLIE	8TH	10	HOUSEWIFE	10TH	YES		
B21	43	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	13		97		48.5		12.5		NON VEG	NON VEG	FARMER	10TH	10	HOUSEWIFE	10TH	NO		
B22	11	M	3.5	FT	LSCS	NO	3RD CHILD	NO	NO	8	10	72	72	44	44	12	12.5	VEG	VEG	FARMER	10TH	11	HOUSEWIFE	6TH	NO	DIARRHOEA	13/24
B23	42	M	2.8	FT	NVD	NO	2ND CHILD	NO	NO	14		97		49		13		VEG	VEG	FACTORY WOR	12TH	12	HOUSEWIFE	12TH	YES		
B24	44	F	2.8	FT	LSCS	NO	1ST CHILD	NO	NO	14	16	96	96	47.5	47.5	13.5	14	NON VEG	NON VEG	FACTORY WOR	B.E.	12	HOUSEWIFE	B.Com	NO	NIL	18/24
B25	34	M	3.5	FT	LSCS	NO	1ST CHILD	NO	NO	13	15	91	91	47.5	47.5	13.5	13.5	VEG	VEG	FACTORY WOR	B.E.	12	HOUSEWIFE	12TH	YES	DIARRHOEA	18/24
B26	20	M	2.5	FT	LSCS	NO	3RD CHILD	NO	NO	10	11	82	82	47	47	12.5	13	NON VEG	NON VEG	LABOURER	10TH	11	HOUSEWIFE	6TH	YES	FLATULENCE	14/24
B27	39	M	2	FT	NVD	NO	3RD CHILD	NO	NO	14	16	95	95	49	49	13.5	14	NON VEG	NON VEG	CABLE OPERAT	12TH	12	HOUSEWIFE	8TH	YES	NIL	20/24
B28	18	M	2.6	FT	LSCS	NO	1ST CHILD	NO	NO	9		80		46		12.5		NON VEG	VEG	COMPANY WO	12TH	12	HOUSEWIFE	8TH	NO		
B29	18	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	9.5		79		46		12.5		NON VEG	NON VEG	FARMER	8TH	10	HOUSEWIFE	8TH	NO		
B30	16	M	2.5	FT	LSCS	NO	1ST CHILD	NO	NO	10	12	78	78	46	46	12	12	VEG	VEG	SHOPOWNER	12TH	12	HOUSEWIFE	6TH	NO	NIL	18/24
B31	22	M	2.5	FT	NVD	NO	2ND CHILD	NO	NO	10.5		82		47		13		NON VEG	NON VEG	FARMER	10TH	11	HOUSEWIFE	6TH	NO		
B32	56	M	3	FT	NVD	NO	1ST CHILD	NO	NO	15		104		49		13.5		NON VEG	NON VEG	FARMER	10TH	11	HOUSEWIFE	6TH	YES		
B33	43	M	4	FT	NVD	NO	2ND CHILD	NO	NO	14	16	98	99	49	49	13.5	14	NON VEG	NON VEG	FARMER	7TH	10	HOUSEWIFE	6TH	NO	FLATULENCE	19/24
B34	42	M	2.5	FT	NVD	NO	3RD CHILD	NO	NO	14	12	97	97	49	49	13.5	13.5	NON VEG	NON VEG	DRIVER	10TH	13	HOUSEWIFE	8TH	YES	NIL	15/24
B35	39	M	3	FT	NVD	NO	1ST CHILD	NO	NO	13	12	94	94	49	49	12.5	12.5	NON VEG	NON VEG	SHOPOWNER	10TH	13	HOUSEWIFE	10TH	YES	FLATULENCE	18/24
B36	52	M	2.5	FT	NVD	NO	1ST CHILD	NO	NO	16	16	101	101	49	49	13.5	13.5	NON VEG	NON VEG	NOT LIVING	NOT APPLI	10	FARMER	6TH	YES	NIL	19/24
B37	48	M	3	FT	NVD	NO	1ST CHILD	NO	NO	15		99		49		13.5		NON VEG	NON VEG	LABOURER	8TH	10	HOUSEWIFE	6TH	NO		
B38	30	F	2.5	FT	NVD	NO	2ND CHILD	NO	NO	11	13	88	88	47	47	12	12.5	NON VEG	NON VEG	LABOURER	8TH	10	HOUSEWIFE	8TH	NO	FLATULENCE	15/24
B39	32	M	3	FT	NVD	NO	2ND CHILD	NO	NO	12	14	92	92	48	48	13	13	NON VEG	NON VEG	NOT LIVING	NOT APPLI	9	FARMER	6TH	NO	NIL	19/24
B40	19	F	2.5	FT	NVD	NO	2ND CHILD	NO	NO	9		79		45		13		NON VEG	NON VEG	FARMER	8TH	10	HOUSEWIFE	6TH	YES		

.AKEN

Hb	Hb F/U	S. IRON	S. IRON F/U	TIBC	TIBC F/U	TSAT	TSAT F/U	S. FERRITIN	S. FERRITIN F/U	WBC	WBC F/U	RBC	RBC F/U	HCT	HCT F/U	MCV	MCV F/U	MCH	MCH F/U	MCHC	MCHC F/U	RDW	RDW F/U	PLT COUNT	PLT COU
10.9	11	42	49	500	359	8	6	11.6	16.95	11.39	10.35	505000	521000	38.8	38.6	77	78	21.6	21.6	28.1	28.3	15.5	14	478000	360000
12.2	13.3	109	206	170	396	64	52	64.9	137	9.1	7.2	417000	413000	40.9	46.1	98	96	29.4	32.2	30	28.9	13.3	15	310000	258000
13.3	14.2	89	102	196	200	47	44	103	45.1	9.3	12.2	437000	525000	42.4	41.5	96.9	86.3	30.6	32.5	31.5	28.9	13.5	13	389000	482000
13.1	13.5	82	86	278	289	29	30	33	36.21	6.16	8.2	467000	490000	44.1	45	94.4	89.6	28.1	27.6	29.8	28.9	13.7	13	380000	389000
10.5	11.2	57	65	466	412	12	18	34.6	52.36	13.09	10.23	439000	440000	36.2	38	82.4	79.2	24	26	29.1	28.6	15.2	14	289000	315000
11.9	12.4	65	82	279	379	23	38	65.8	81.3	12.5	9.52	407000	501000	38.9	38.6	95.7	84.2	29.2	24.8	30.5	29.4	13.2	12.5	337000	281000
11	10.6	45	32	409	486	11	9	13.7	26.39	10.7	9.65	496000	389000	39	36	78.7	74.6	28.3	26.9	22.3	20	14.6	16	431000	321000
11.8		53		329		16		36.4		5.7		486000		40.5		83.5		24.4		29.2		15.3		292000	
11.3	10.8	70	45	261	346	27	16	27.7	56.54	8.18	9.6	474000	389000	38.8	40.2	81.8	79.6	23.9	22.4	29.2	30.2	14.4	18	522000	386000
12.8		117		233		50		106		9.92		439000		42.8		97.6		29.2		29.9		13.3		301000	
11.3	11	43	48	421	375	10	25	24.28	30.4	12.52	15	446000	414000	39.3	36.5	88.1	88.2	25.4	24.4	28.8	27.7	14.3	15	373000	206000
10.3	10.6	38	54	351	363	11	15	47.4	75.5	10.99	10.35	444000	430000	36.2	41	81.5	95.3	23.3	26.9	28.6	28.2	14.9	14.1	333000	334000
10.5	10.7	33	32	488	476	7	7	24.86	19	15.94	17.01	513000	517000	38.9	35.9	75.8	69.4	20.4	18.7	26.9	26.9	15.4	20	426000	479000
12.6	12	97	98	346	372	28	26	39.6	112	13.88	15.58	488000	439000	43.8	41.3	89.8	94.2	25.9	27.3	28.8	29	14.3	14	415000	380000
10.2	8.6	33	18	545	565	6	7	15.88	19.63	7	8.94	492000	397000	36.8	38.9	74.7	72.6	20.6	22.6	27.6	26.5	16.4	16.8	287000	310000
11.4	11.9	74	90	470	342	16	26	29.57	23.05	9.09	8.71	490000	462000	38.5	38.4	94.1	92	27.8	25.8	29.5	25.1	13.8	14	362000	303000
13.3	13.8	66	68	412	385	16	18	32.36	24.8	10.22	13.91	483000	492000	44.2	44.9	91.5	91.2	27.5	28.1	30.1	30.8	13.7	13.5	289000	334000
9.9	10.3	32	34	513	265	6	10	8.02	24.5	15.3	10.16	494000	529000	36.7	38.7	74.4	78.8	20	23.3	26.9	29.5	15.6	12.9	293000	305000
9.4	9.2	55	45	452	512	12	10	12.17	19.63	11.65	9.56	392000	389000	33.1	35.6	84.4	86.6	24.1	24	28.5	27.9	13.8	16	507000	470000
10.9		27		357		8		18.04		12.12		469000		38.4		81.9		23.2		28.3		16.3		550000	
12.7		55		213		26		518.8		8.12		483000		44.1		91.4		26.4		28.8		16		196000	
8.9	7.5	33	21	379	489	9	8	25.2	12.35	13.6	12.1	428000	386000	32.7	28.5	76.2	79.5	20.7	26.1	27.2	29.3	15.9	19.6	481000	381000
11.3		49		361		14		60.4		8.74		456000		40.4		88.6		24.9		28.1		16.3		404000	
10.2	10.6	43	60	403	483	11	12	82.1	31.4	9.13	10.81	455000	489000	37.4	37.3	82.1	76.3	22.3	21.7	27.2	28.4	16.5	17.8	298000	354000
11.7	12	63	147	363	493	17	30	48	44.6	10.53	11.96	463000	527000	41.9	41.6	90.7	78.9	25.4	22.8	28	28.8	14.6	16	354000	396000
9.6	9.6	50	46	366	436	14	11	25.8	21.5	6.46	9.5	398000	274000	34.3	34.9	86.2	74.7	24.1	20.6	27.9	27.5	15.5	19.6	380000	274000
11.9	12.1	106	71	292	392	36	18	77.7	24.2	11.24	11.52	482000	516000	43.6	39.6	89.3	76.7	24.7	23.4	24.7	30.6	14.2	13.9	432000	551000
10.5		95		336		28		148.1		11.91		399000		37.5		93.8		26.2		28		15.6		413000	
9.3		37		406		9		44.91		13.23		451000		33.6		74.6		20.5		27.5		18.6		433000	
10.9	11.3	97	110	301	286	32	35	44.49	36.25	12.78	10.5	487000	495000	38.9	39	80	82	22.4	24	28	26	17.1	16	515000	436000
8.6		34		372		9		38.22		11.82		509000		32.7		64.2		17		26.4		19		376000	
10.9		66		363		18		73.81		11.45		462000		39		84.6		23.5		27.8		14.6		470000	
12.2	12.7	45	58	297	353	15	16	36.7	28.5	11.62	11.35	476000	510000	42.4	41.2	89.2	80.2	25.6	24.9	28.7	30.8	13.9	13.8	274000	354000
10.2	10.5	22	30	479	450	5	9	14	26.35	10.66	8.5	412000	390000	36.2	38	87.9	85.6	24.7	26	28.1	29	14.7	13	493000	489000
11.3	11.8	86	82	305	401	28	20	21.2	19.1	9.5	10.18	420000	446000	38	37.3	90.3	83.6	26.9	26.5	29.8	31.6	13.1	12.7	415000	388000
10.1	10.5	34	55	353	396	10	14	19	10.9	6.04	6.88	370000	403000	34.3	35.2	92.8	87.3	27.2	26.1	29.3	29.8	13.7	12	303000	247000
10.5		22		405		5		27.7		10.3		401000		35.5		88.6		26.3		29.6		13.4		416000	
9.8	10	17	25	453	460	4	6	21.4	45.21	9.09	8.56	430000	456000	34.1	34.6	79.4	79	22.8	23	28.8	28.6	15.2	15.2	315000	365000
9.6	10.3	30	79	388	385	8	21	21.7	34.1	8.27	5.86	346000	428000	31.8	35.2	92	82.2	27.8	24.1	30.2	29.3	17	17	338000	377000
10.3		30		422		7		12.6		13.49		505000		37.4		74		20.5		27.7		15.8		446000	