International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

"A Hospital Based Study on Factors Influencing Iron Deficiency Anemia in 6 To 24 Months Aged Children, And Effectiveness of Iron Supplementation"

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Submitted: 20-02-2021 Revised: 05-03-2021 Accepted: 08-03-2021

ABSTRACT:Background: Iron deficiency is one of the major contributing factors to the worldwide burden of anemia in children, an indicator of poor nutrition and poor health. Evidence based studies show that Iron Deficiency Anemia (IDA) during early childhood can have long lasting detrimental effects on brain development, which can be prevented from hematological, non- hematological effects, and neurological effects in later parts of life with iron supplements

Objectives:
- Clinical and laboratory evaluation of IDA in children aged 6 to 24 months.
- Study the response to Iron supplementation in IDA, clinically and biochemical improvement.

Materials and methods:

During the two years study period, children between ages of 6 to 24 months with hemoglobin <10.9 g/dl and serum ferritin <10 ng/ml were included in our study. A total of 114 children were enrolled in our study, 24 cases were lost in follow up and 90 cases were followed.

Results.

In our study out of 90 children, 47.8% were in the age groups of 6 to 12 months. Out of 90 children of either sex, majority children had moderate anemia. Association of birth order, maternal anemia with IDA was not significant Majority of lower Socioeconomic Status cases (SES) 48.9% were associated with IDA.

Our study showed significant baseline changes of mean hemoglobin, MCV and MCHC after oral iron supplementation of 6mg/kg ($P < 0.0001$)

Mean changes in serum ferritin after iron supplementation was found to be statistically significant ($p < 0.05$) but weak correlation ($R = 0.05$, $p = 0.555$)

Interpretation and Conclusion:
The study concluded that the age groups of 6 to 12 months are at high risk to develop IDA because improper complimentary feeding, poor SES and low maternal education.

Universal iron supplementation program should be started prophylactically in high risk group children, ideal time is during MMR vaccination.

KEY WORDS: Iron Deficiency anemia; Socio economic status; Breastfeeding; Iron supplementation.

I. INTRODUCTION

This plebian metal is vital to the function of a wide variety of critical enzymes to execute a number of chemical reactions essential for our survival. In addition, we depend on hemoglobin, another iron-containing protein to transport inhaled oxygen from the lungs to peripheral tissues.[1]

Adequate nutrition among infants among infants is essential for optimal growth and development. The later part of first year of life is when rapid growth and development bring additional demands, thus require attention.

Parameters like birth weight triples and birth height increases by 50% during first year end. The relative requirements concerning iron are highest in early child hood from 6months to 24months of age.

IDA is most common in the age group of 6 months to 3 years and the reported prevalence of nutritional anemia in pre-school children ranges from 44 to 74%.

Nutritional deficiency is most common among the children in the developing countries and Iron deficiency is the cause.[2] Varying degrees of anemia in young children are associated with poor cognitive outcomes.[3,4,5,6,7] Anemia diagnosed at 8 or 9 months of age has been associated with lower achievement scores and low esteem levels in second grade children,[8] with impaired motor development at 18 months.[9]

Need for this study is to find toddlers at risk for anemia which is more common in the age groups of 6 months to 24 months, and supplementing iron. Therefore these children can

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be prevented from hematological, non-hematological effects, and neurological effects in later parts of life. [10, 11] Further to improve behavior, activity wellbeing of the toddler, to prevent morbidity and long term sequel.

The nutrient needs of full term normal birth weight infants typically can be met by human milk alone for the first six months if the mother is well nourished. However, in certain circumstances, some of the micronutrients may become limiting before six months. In the case of iron, the infant's reserves at birth play a major role in determining the risk for anemia during infancy because the iron concentration of human milk is low. Normal birth weight infants whose mothers had good prenatal iron status usually have adequate liver iron reserves, and thus the risk of iron deficiency before six months is low.[10] Although the iron in human milk is highly bioavailable (50% absorption). 11,12,13,14

The iron content is at it is highest in early transitional milk and decreases steadily over the course of lactation.[15] By six months, complimentary foods are required to provide the iron and other nutrients necessary for infant development.16, 17

After six months of age, however, it becomes increasingly difficult for breast fed infants to meet their nutrient needs from human milk alone. Furthermore most infants are developmentally ready for other foods at about six months.[18]

Feeding patterns differ in families but are established during the first years and affect later feeding and overall health of the child. Hence rational complimentary feeding practices plays a very important role in preventing IDA.

Need for this study is to find toddlers at risk for anemia which is more common in the age groups of 6 months to 24 months, and supplementing iron. Therefore these children can be prevented from hematological, non-hematological effects, and neurological effects in later parts of life.[19,20] Further to improve behavior, activity wellbeing of the toddler, to prevent morbidity and long term sequel

II. OBJECTIVES

- Clinical and laboratory evaluation of Iron deficiency anemia in children aged 6 to 24 months.
- To study the response to Iron supplementation in IDA, clinically and biochemical improvement.

III. REVIEW OF LITERATURE

Prevalence of Anemia

Iron deficiency is the most widespread and common nutritional disorder in the world. Under nutrition is usually responsible for iron deficiency in children.

Even though the prevalence of anemia is estimated at 9% in countries with high development, the prevalence is 43% in developing countries.

The global anemia prevalence estimates show that, the prevalence of anemia is as high as 47% in children younger than 5 years, 42% in pregnant women and 30% in non-pregnant women of 15-49 years. [21]

IDA is most common in age group of six months to 3 years. The reported prevalence of nutritional anemia in preschool children varies from 44 to 74%. 22,23,24,25,26,27,28,29

According to recent NFHS-4 survey, the prevalence of anemia among children aged 6-35 months in Karnataka is 60.9%, which was > 70.3% during NFHS-3 survey. 30

In term infants, anemia is caused solely by inadequate dietary iron usually occurs at 9-24 months of age and is relatively uncommon thereafter.

Table 1- Prevalence of anemia in different groups as per surveys in India

Group	**Reference**	**Prevalence (%)**
Early childhood Pre-school children (6–35 months)	NFHS II, 1998-99 NFHS III, 2006-7	**74**
Adolescent girls	Seshadri, 1999, Rural Gujarat Seshadri, 1999, Urban affluent ICMR, 2001, Rural India	**62** **22** **90**
Abbreviation: ICMR, Indian Council of Medical Research		

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Table 2 - WHO criteria for hemoglobin below which person is anemic

Age/gender groups	Hb (g/dL)
Children 6 months–5 years	< 11
Children 6–14 years	<12
Adult males	<13
Females (Non-pregnant)	<12
Females (Pregnant)	<11

PHYSIOLOGIC CHEMISTRY OF IRON

1. Iron and oxidation: Iron exists in two stable oxidation states Fe 2+ (ferrous) or Fe 3+ (ferric). The unique property of iron permits it to act as redox catalyst by donating or accepting electrons. An example is electron transport of oxidative phosphorylation.
2. Iron protein complexes: Help in metabolic functions.

Heme proteins:
Haemoglobin, Myoglobin, Cytochrome a,b, c, Cytochrome P-450, Tryptophan 1,2-dioxygenase, catalase, Myeloperoxidase.
Iron dependent enzymes: Aldehyde oxidase, Reduced nicotinamide adenine dinucleotide dehydrogenase, Tyrosine hydroxylase, Succinate dehydrogenase, Prolyl hydroxylase, Tryptopahn hydrolase, Xanthine oxidase, Ribonucleotide reducatse, Aconitase, phosphoenolpyruvate carboxykinase. [31]

Iron in the Body:

- The foetus has high level of Hb in order to transport oxygen in utero, and the newborn has enough concentrations of storage iron.[32]
- Total iron at birth: 80 mg/kg[33] is relatively stable till 4- 6 months age.
- After 6 months of age, iron stores are exhausted during which iron requirement is estimated at 100 mcg/kg/day. [32]
- Iron is primarily stored in the liver. Macrophages carry out the iron recycling.

Iron homeostasis exists to maintain balance between dietary iron intake and losses.

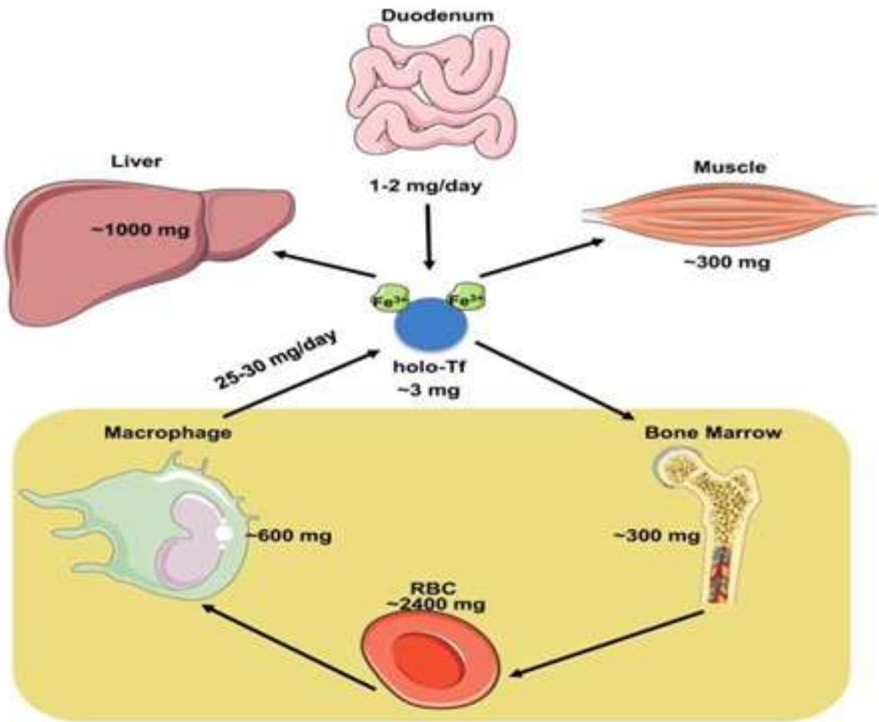

Fig.1 : Distribution of iron in body. [34]

Table 3 - Distribution of body iron

Hemoglobin	2.3 g
Storage form(Ferritin, Hemosiderin)	1.0 g
Essential tissue iron (myoglobin and enzymes of cellular respiration)	0.5 g
Plasma Iron(transport form)	3-4 mg
Total	**3.8 g**

Storage of iron occurs in two forms: [34]

Absorption of Iron: [35]

- Iron is mainly absorbed in the proximal duodenum. Non heme Iron arrives at the apical surface of the absorptive duodenal enterocyte in the ferric Fe3+ form. It's reduced through the action of a brush border ferric reductase. The ferrous iron is taken up by the enterocyte through the action of divalent metal transporter (DMT 1). After the iron enters the enterocyte, either it can be retained by the cell and subsequently be lost when the enterocyte dies and is sloughed into the intestinal lumen, or it can be transported across the baslolateral membrane to enter the body.
- -Iron in the enterocyte is used for cellular metabolism or incorporated into ferritin. Exported iron leaves the cell by way of a unique basolateral transmembrane iron transporter, ferroportin.

Haphaestin helps in changing the oxidation state of the iron on the basolateral side. Normally, only about 10% of dietary non-heme iron entering the duodenum is absorbed. However, this value increases significantly with iron deficiency.

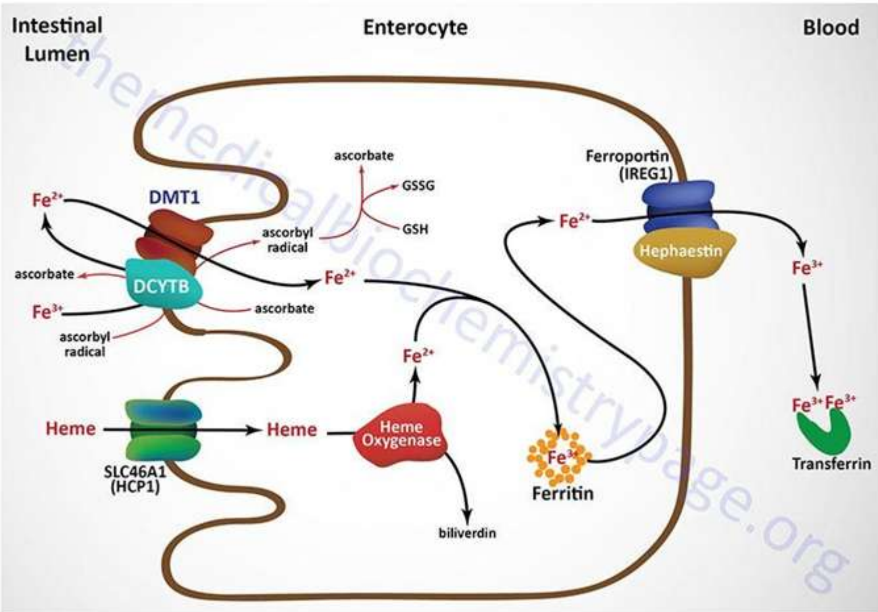

Fig. 2 Absorption of iron

Factors affecting iron absorption:[36,37,38,39,40,41,42]

- Promoters: Acidic Ph, ascorbic acid, citric acid.
- Inhibitors: phytates, calcium, metal ions Cd2+, C02+, Cu2+, Mn2+, Pb2+, Zn2+.
- Iron deficiency anemia and anemia associated with ineffective erythropoiesis causes a marked increase in iron absorption.
- Hepcidin, an iron-regulated peptide hormone produced in the liver which binds to the iron exporter ferroportin on the basolateral surface of absorptive enterocyte, causing internalization and degradation of ferroportin. Expression of hepcidin is induced in response to iron overload and inflammation and is repressed in response to increased erythropoietic activity and hypoxia. The inflammatory cytokine, IL-6 has been definitely shown to be involved in regulation of hepcidin expression. [43]

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Iron deficiency is the most frequent and wide spread nutritional deficiency in the world because it's common in developing and developed countries alike. [44]

Phases of development of Iron deficiency: [45]
Most of the iron in the body is utilized for the synthesis of haemoglobin, erythrocyte production. RBC production is among the first affected from iron deficiency. It actually represents late stage of iron depletion.

1. Prelatent iron deficiency:
It occurs when tissue stores are depleted, without a change in hematocrit or serum iron levels. This stage is detected by low serum ferritin levels.

2. Latent iron deficiency: It occurs when reticuloendothelial macrophage iron stores are depleted.

- Serum iron levels will drop
- TIBC increases
- No change in hematocrit.

This stage is detected by routine check of fasting, early morning transferrin saturation. The reticulocyte hemoglobin content decreases because newly produced erythrocytes are iron deficient.

3. Frank iron deficiency anemia:
It is associated with erythrocyte microcytosis and hypochromia. It is detected when iron deficiency has persisted long enough that a large proportion of the circulating RBC were produced after iron became limiting.

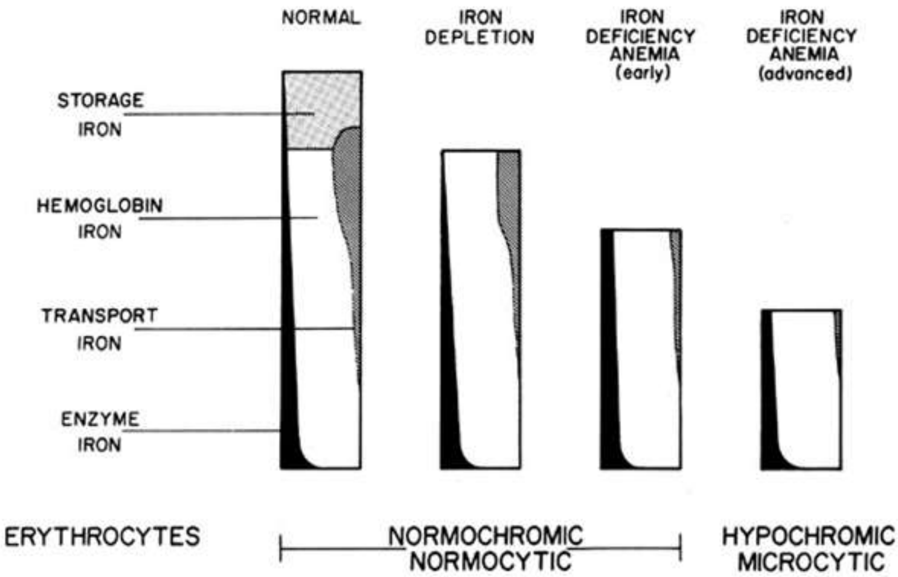

Fig. 3 - Stages of Iron Deficiency

INDICATORS OF IDA:
Various laboratory tests are performed in order to detect iron deficiency. No single test except for bone marrow can alone identify iron deficiency. Oski states that the most convincing evidence of iron deficiency is that hemoglobin increases after iron treatment. [46]
Looker et al suggest that two parameters or more indicating iron deficiency must be fulfilled in order to confirm the diagnosis. [47]

B-haemoglobin:
Haemoglobin in blood (B-Hb) is a transport protein for oxygen and a part of the RBC.
After birth when Hb levels are decreased the iron from the erythrocytes is reutilized. Synthesis of erythrocytes is dependent on iron and if iron stores are exhausted a decrease of Hb will occur. [48]

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Table 4 - Hemoglobin levels to diagnose Anemia (g/dl) [48]

Age	No anemia	Mild	Moderate	Severe
6-59m	>11	10-10.9	7-9.9	<7
5-11 years	≥ 11.5	11-11.4	8-10.9	<8
12-14 years	≥ 12	11-11.9	8-10.9	<8
15-49 years	≥ 12	11-11.9	8-10.9	<8
Pregnant	≥ 11	10-10.9	7-9.9	<7

S-ferritin: [48]
Serum ferritin is a protein which stores extra iron. One third of the total body iron is stored intracellularly in S-ferritin.
S-ferritin is found mainly in the bone marrow, the liver, the spleen and the muscles. These extra stores can be utilized when requirements are met.

A small amount circulates in the plasma, which makes it possible to measure in order to reflect body iron stores. S-ferritin is an acute-phase reactant and in the presence of an infection the value increases and therefore be falsely normal or high. The rise is about three times higher in the presence of an infection.

Newborn: 25-200 ng/ml

- Month age: 200 to 600 ng/ml
- 2-5 months: 60-200 ng/ml
- 6 months to 15 years: 7 to140 ng/ml

Serum Iron: [48]
Serum iron: 60–170 μg/dL (10–30 μmol/L)

Iron is transported within the body by a protein, transferrin. If iron is absent, transferrin can bind to other minerals. To measure the percentage of saturated transferrin, plasma iron is divided by plasma total iron binding capacity X 100. Transferrin saturation < 10% among infants and children is used as a criterion for iron deficiency. Serum iron concentrations vary during the day in the same individual. Which makes the transferrin saturation vary too.

S- Transferrin receptor: [48]

Almost all cells have transferrin receptors (TfR) on the surface, and the receptor is the gateway for the iron to be able to enter the cell. In the presence of iron need in the cell the number of transferrin receptors increases in order to optimize the iron uptake into the cell. A high level of TfR indicates iron depletion. Studies have suggested that serum transferrin receptor is a reliable and sensitive measurement of iron deficiency. TfR can distinguish iron deficiency anemia from anemia cause dby chronic diseases. [49,50]

Mean corpuscular volume:

When iron deficiency is developed the mean corpuscular volume (MCV) of the red blood cell decreases. If a combination of low MCV and low hemoglobin appears, thallasemia must be excluded.

- 1-3 days: 108- 95 fl
- 3-6 months: 91-74 fl
- 7-24 months: 78-70 fl
- 1-6 years: 81-75 fl

MCV less than 70 fl with low serum iron levels, and low serum ferritin levels indicate IDA.

Factors Contributing to IDA:

1) Exclusive breast feeding:
WHO (2002) recommends exclusive breast feeding for the six months and demand feeding is recommended.
Breast milk is poor sources of Iron. Breast milk during first month contains 0.5mg/litre. During 4 to 6 months age breast milk contains 0.3 mg/litre. Cow's milk contains 0.5 to 1 mg/litre of iron.
The reason for low iron is not known but low protein and low calcium levels and high concentration of **lactoferrin** have been suggested to play a role.
EBF for 6 months confers several benefits.

1. Protection against gastrointestinal infections
2. Digestion and **absorption** of nutrients.
3. Modulate the composition of the indigenous intestinal microbes.
4. Provides all the nutrients a baby needs for the first 6 months of life.
5. Breast milk is clean, safe and cheap
6. Breastfeeding provides a perfect opportunity for building a close bond between mother and baby

Nutritional Composition of Breast Milk:
Fats: The mature human breast milk contains 3.2–3.8 g/dL of fats. Fats provide 50% of the total energy content of the breast milk.
Breast milk fat in the immediate postpartum period contains fat needed for **gray matter development** and in later months, fat which is needed for myelination.

Carbohydrates:
Lactose is the main carbohydrate in human breast

milk and provides about 50% of its energy content. Breast milk also contains oligosaccharides such as glucose, galactose, N-acetyl glucosamine and sialic acid

Proteins:
Mature breast milk contain 0.9 g/dL of protein while colostrum contains 2.3 g/dL. Whey protein consists of anti-infective proteins, which help to protect a baby against infection.
The anti-infective proteins in human milk are Lactoferrin, Lysozyme and Antibodies

Dynamic Composition of Breast Milk:

- **Colostrum:** A special, thick, sticky, bright lemony yellowish fluid. It is secreted in small quantities for first 3–4 days of life. Colostrum contains more protein than later milk. Colostrum is considered the first immunization for newborn. Colostrum contains more epidermal growth factors in comparison to mature breast milk, which help a baby's immature intestine to develop after birth.
- **Transitional Milk:** During the transition from colostrum to the mature milk, the amount of immunoglobulin, proteins, vitamin A and vitamin E decreases, and amount of lactose, fats, energy and water-soluble vitamins increases. The iron content is at its highest in early transitional milk and decreases steadily over the course of lactation. [51]
- Mature milk: Mature milk is in large amounts and the breasts feel full, hard and heavy.
- Foremilk is the bluish milk that is produced early in a feed, produced in larger amounts, and it provides plenty of protein, lactose and other nutrients. Baby gets all the water that he or she needs from it.

- Hindmilk is the whiter milk that is produced later in a feed. More fat than foremilk provides much of the energy of a breastfeed. According to the official NFHS-4 statistics, 56.4% of children under the age 3 years were breast fed within one hour of birth which has increased from 35.6%.

Evidence suggests that infants with adequate birth weight born to a anemic mothers who are EBF have low iron stores and are more likely to develop anemia.
52,53,54,55

Previous studies demonstrated that term normal birth weight infants who are exclusively breast fed beyond 6 months of age have a higher rate of iron deficiency anemia than infants fed iron fortified formula. [57,58,59] Maternal confidence is shown to be a significant predictor of breastfeeding duration.[60] High maternal education is found to improve the duration of breastfeeding. [61] Factors influencing the duration of breastfeeding negatively are the amount of formula given at the maternity ward[61] and use of a pacifier [62]

Complementary feeding [10]

Introduction of complimentary foods is complex and dependent on the availability of food, nutritional knowledge and social support. According to WHO report and UNICEF the recommended age for introducing complimentary food is approximately 6 months. Malnutrition starts in many children due to a discrepancy between the content of the complimentary food and the estimated requirements which makes this period a vulnerable one.

WHO guidelines prescribe responsive feeding i.e applying the principles of psycho-social care. Specifically: a)feed infants directly and assist older children when they feed themselves, being sensitive to their hunger and satiety clues; b)feed slowly and patiently, encourage children to eat ,but do not force them)if children refuse many foods, experiment with different food combinations; d) minimize distractions during meals if the child loses interest easily: e)remember that feeding times are periods of learning and love-talk to children during feeding ,with eye to eye contact.

Start at six months of age with small amounts of food and increase the quantity as the child gets older, while maintaining frequent breastfeeding. Breastfed infants self-regulate their total energy intake when complementary foods are introduced.[63]

Recommended intakes of iron, and to a lesser extent Zinc, are unlikely to be provided by these diets. [10]
When foods of appropriate consistency are offered, the child may be unable to consume more than a trivial amount, or may take so long to eat, that food intake is compromised. Thus although it may save time to continue feeding semi-solid foods, for optimal child development it is advisable to gradually increase food consistency with age. [10]

In most developing countries, complimentary foods donot provide sufficient iron. Even in the U. S, iron, zinc were identified as problem nutrients in the first year of life, despite the availability of iron fortified products [10]
Several studies have shown a negative correlation between cow's milk and iron status.
64,65,66,67,68,69,70,71
Thorsdottir et al concluded that a daily cow's milk

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intake above 500 g/day among one year old children should be avoided. [69]

Kwiatkowski et al found that 2-year old children with severe anemia had a mean intake of cow's milk exceeding 0.95 litres. [70]

Potential allergic reactions related to consumption of certain high-protein foods during infancy have been a concern in some developed countries. For example the American Academy of Pediatrics recommends that infants with a family history of allergies or food sensitivities should not receive cow's milk until 1 year of age, eggs until 2 years, and peanuts, nuts and fish until 3 years of age. [71]

Maternal Anaemia:

According to the cohort study done by Jareen et al, EBF more than 6 months, but not EBF for 4 to 6 months, was associated with increased risk of infant anemia compared with EBF less 4 months. Maternal anemia was independently associated with a 3-fold increased risk of infant anemia. By linear regression, a lower infant Hb at 9 months was associated with increased EBF duration among mothers who had a history of anemia, but not among mothers with no history of anemia. [72]

Frequently, the anemia is severe in degree and it coexists with maternal malnutrition. Under these situations, the competing demands of mother and fetus may disturb the normal maternal-fetal iron homeostasis. [73]

A RCT by Zhang et al on maternal hemoglobin which included 17, 193 women concluded that low maternal Hb concentration during 24-28 weeks of gestation was associated with an increased risk of anemia in infancy. [74]

A case-control study conducted by Kilbride J et al on relation between maternal anemia and IDA in infancy concluded that infants appear to be at a greater risk for developing IDA. [75,76]

Suyinf Chang et al did a study to determine the impact of IDA in pregnancy n young child development found that prenatal-IDA group had a significantly lower mental developmental index compared to prenatal non-IDA group. [77]

A study done by Amina et al in children aged 12 to 24 months, prevalence of anemia was 77% under 2 years age. Found that socio economic factors, faulty weaning and feeding practices are the contributing factors of anemia among children under 2 years age. [78]

A cross-sectional study conducted by Gisela et al in children aged 6 months to 5 years in 2005, 2018 and 2011 concluded that prevalence of anemia was more in the children aged between 6 to 23 months than those between 24 to 59 months. [79]

A community based study done by D. Schellenberg et al in Tanzania showed anemia increased with decreasing socioeconomic status. [80]

Iron supplementation:

Daily iron supplementation is recommended as a public health intervention in infants and young children aged 6–23 months, living in settings where anaemia is highly prevalent,[1] for preventing iron deficiency and anaemia (strong recommendation, moderate quality of evidence).[81]

A study done by Killip et al showed that, in pakisthan among children aged 5 months to 5 years, 62.3% were anemic (Hb less tha 11 g/dl) while 33.2% had iron deficiency anemia (Hb less than 10g/dl, ferritin levels less than 12 ng/l). [82]

The administration of oral iron is a convenient, inexpensive, and effective means of treating stable patients. 3 to 6 months of treatment are required for the repletion of iron stores and the normalization of serum ferritin levels. [83]

Although hemoglobin levels usually respond rapidly to oral iron therapy, repletion of iron stores and normalization of serum ferritin levels may require 3-6 months of treatment. [84]

The new American Academy of Pediatrics (AAP) 2011 recommendations for prevention of iron deficiency and iron-deficiency anemia conclude that –exclusively breastfed term infants should receive an iron supplementation of 1 mg/kg per day, starting at 4 months of age. [85]

IV. METHODOLOGY

Source of data: In our study, children aged between 6 to 24 months who visited SSIMS & RC, on outpatient and inpatient children, and who met the inclusion criteria were included.

Type of study: A hospital study, Prospective study

Duration of study: August 2017-August 2019

Method of collection of data

Children enrolled in the study group were checked for iron deficiency anemia based on clinical presentation, baseline Hemoglobin, MCV, MCHC and serum ferritin levels during first visit. The children who were given iron supplements (6mg/kg) were followed up after three months and rechecked for serum Hemoglobin, MCV, MCHC and serum ferritin levels along with clinical improvement. Follow up Hemoglobin and ferritin levels were correlated after iron supplementation.

A total of 114 anemic children with hemoglobin less than 10.9 g/dl, were enrolled. Out of 114 children enrolled, 24 children didn't follow up, were excluded from the study.

Inclusion criteria:

- Infants and toddlers aged 6 months to 24 months of all socio economic status.
- Hemoglobin levels less than 10.9 g/dl, MCV less than 70 fl and low MCHC and serum ferritin levels less than 10ng/ml
- Clinically suspected and hematologically proven children.
- After taking informed consent
- Parents willing to get ferritin levels for their children were enrolled

Exclusion criteria: Children

- Parents who are not willing to get their child into the study
- With any recent acute pediatric emergency admission
- Children with comorbidities (blood disorders, Liver, Kidney)
- Children on long term transfusion therapy
- Who received transfusion with in last 120 days
- Other types of anemia's excluded (Thalassemia, sickle cell, hemolytic anemia's)

INVESTIGATIONS:
Complete Hemogram and Serum Ferritin levels

INSTRUMENT
COMPLETE HAEMOGRAM done with **ABX Pentra XL 80 (HORIBA,**

Automatic calibrated)
Serum Ferritin levels estimated by Microplate chemi-luminescence immunoassay (CLIA) which is based on the principle of immune enzymometric sequential assay

Statistical analysis
The data was entered in the Microsoft Excel. Proportions and mean values with its 2 standard deviation was used to compare the differences between various groups.

Paired t test was used to analyze the differences between mean values of two groups. ANOVA (analysis of variances) test was used to analyze the differences between mean values of more than two groups. Two tailed P value of less than 0.05 was taken as statistically significant. Open Epi version 3.01 (Open source Epidemiologic Statistics for Public Health) statistical software was used for analysis.

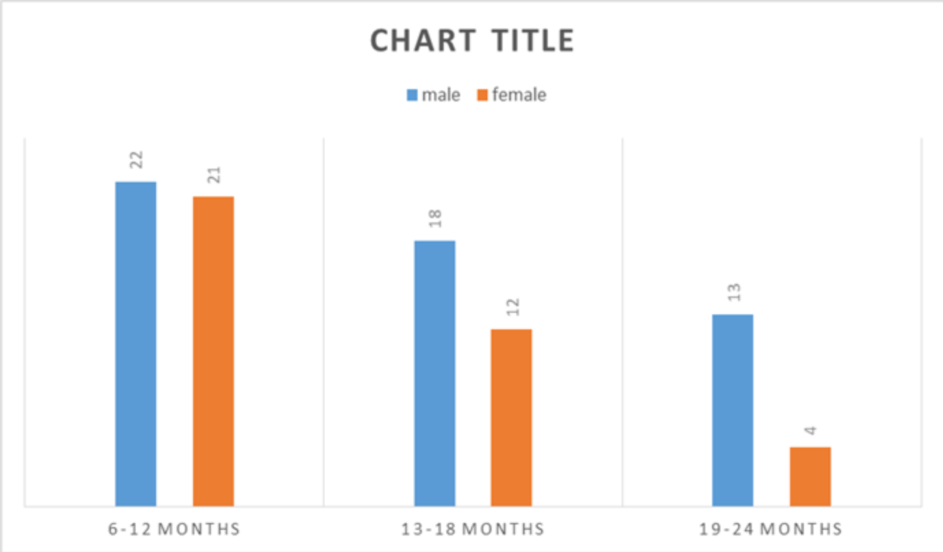
SAMPLE SIZE ESTIMATION
Sample size calculation
As per NFHS-3 data, the prevalence of anemia in children of age 6-24 months in Karnataka was 60.9%
Taking this as p for for the present study So q = 1-p = 39.1
d is absolute error, taken as 15% of p = 9.135
Putting these values in formula
Sample size = $4pq / d^2$
= 114
Out of these 114, 24 lost to follow up and the final sample that could be included in the present study was 90

V. RESULTS

Table 5: Distribution of study subjects as per age and sex

Age (months)	Male		Female		Total	
	Number	Percentage	Number	Percentage	Number	Percent age
6-12	22	51.2	21	48.8	43	47.8
13-18	18	60	12	40	30	33.3
19-24	13	76.5	04	23.5	17	18.9
Total	**53**	**58.9**	**37**	**41.1**	**90**	**100**

Majority of the study subjects were males i.e. 53 (58.9%) compared to females i.e. 37 (41.1%). Similar trend was seen in infants as well as children between 1-2 years of age. In males as well as in females children aged 6-12 months were more.

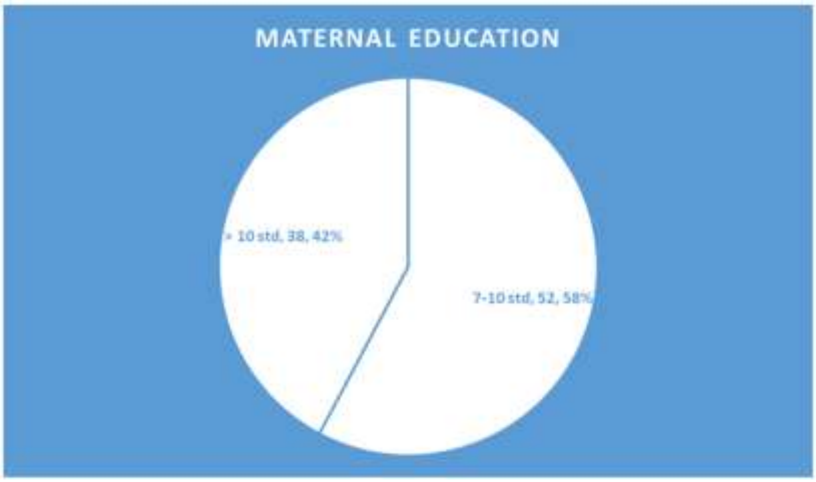


Graph 1: Distribution of study subjects as per age and sex

Table 6: Distribution of study subjects as per maternal education

Maternal education	Number	Percentage
Educated up to 10th standard	52	57.8
Educated more than 10th standard	38	42.2
Total	**90**	**100**

Majority of the mothers i.e. 57.8% were educated up to only 10th standard while 42.2% of the mothers were educated above 10th standard.

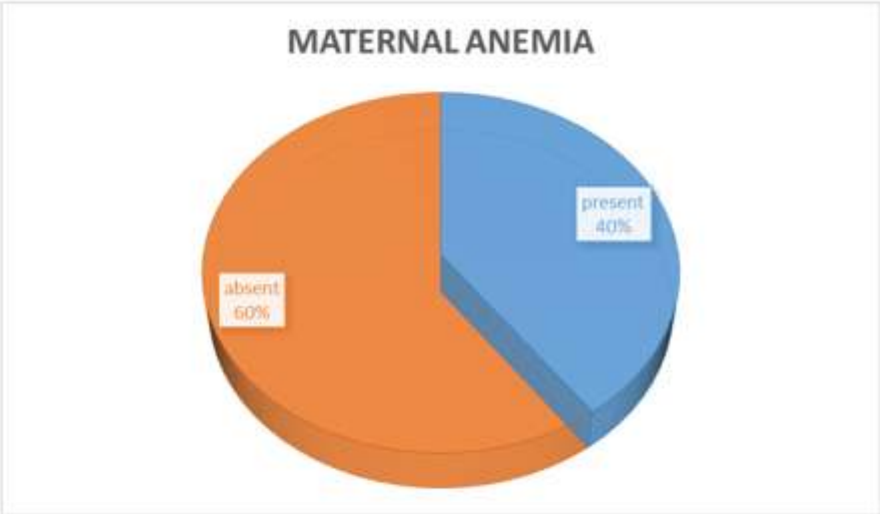


Graph 2: Distribution of study subjects as per maternal education

Table 7: Distribution of study subjects as per maternal anemia

Maternal anemia	Number	Percentage
Present	36	40
Absent	54	60
Total	**90**	**100**

36 i.e. 40% of the mothers were found to be anemic while more i.e. 54 (60%) of the mother's hemoglobin was in the normal range.



Graph 3: Distribution of study subjects as per maternal anemia during pregnancy

Table 8: Distribution of study subjects as per Socio-Economic status

Social class	Number	Percentage
Upper	24	26.7
Middle	22	24.4
Lower	44	48.9
Total	**90**	**100**

Majority of the children (48.9%) belonged to the lower social class. 26.7% were in the upper class while 24.4% were in the middle class Upper class (5357 & above)| Upper middle class (2652-5356) | Middle class (1570-2651)| Lower middle class (812-1569)| Lower class (<811)

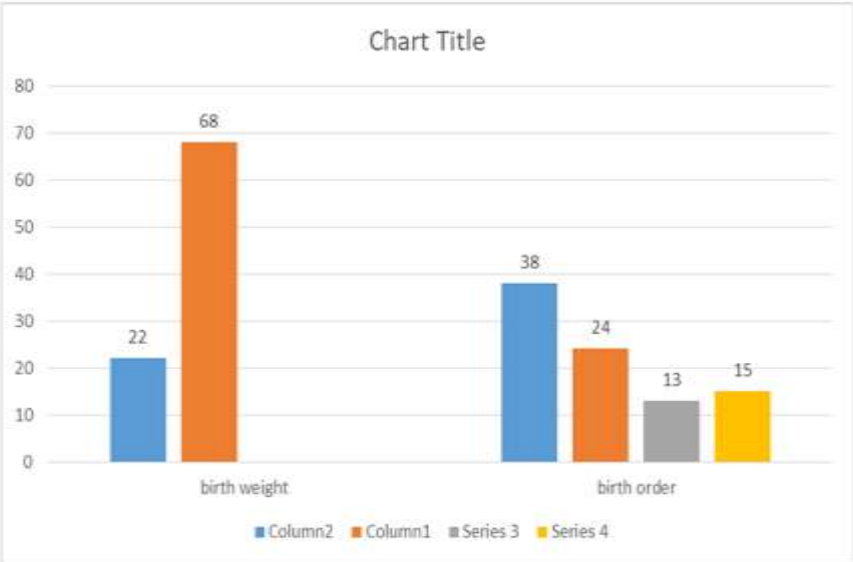
Graph 4: Distribution of study subjects as per socio economic status

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

Table 9: Distribution of study subjects as per their birth weight status and birth order

Variables		Number	Percentage
Birth weight status	Low birth weight	22	24.4
	Normal birth weight	68	75.6
Birth order	1	38	42.2
	2	24	26.7
	3	13	14.4
	4	15	16.7

Majority of the children i.e. 75.6% had normal birth weight above 2.5 kg at the time of birth but even 24.4% were reported that they had low birth weight. Majority of the children in the present study i.e. 42.2% belonged to first birth order followed by second i.e. 26.7%, third as 14.4% and 16.7% as fourth birth order.

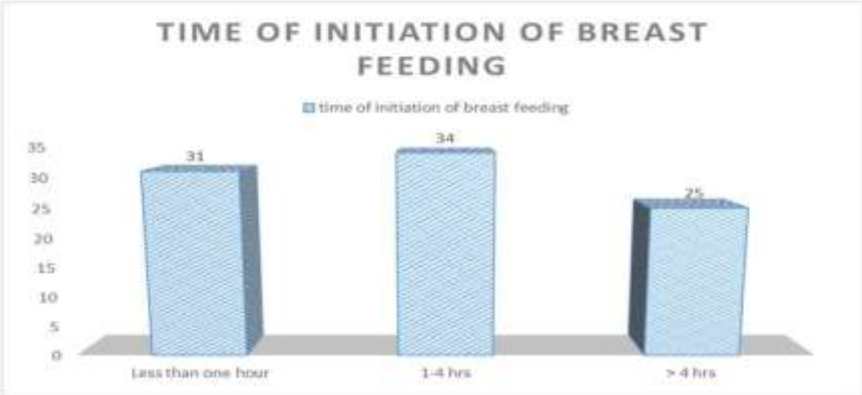


Graph 5: Distribution of study subjects as per their birth weight status and birth order

Table 10: Distribution of study subjects as per time of initiation of breast feeding

Time of initiation of breast feeding	Number	Percentage
Less than one hour	31	34.4
1 to 4 hours	34	37.8
More than 4 hours	25	27.8
Total	**90**	**100**

Majority of the mothers i.e. 37.8% initiated breast feeding after delivery in 1-4 hours and 34.4% initiated within one hour. But 27.8% of the mothers were unable to do so and they initiated the breast feeding after four hours of delivery.

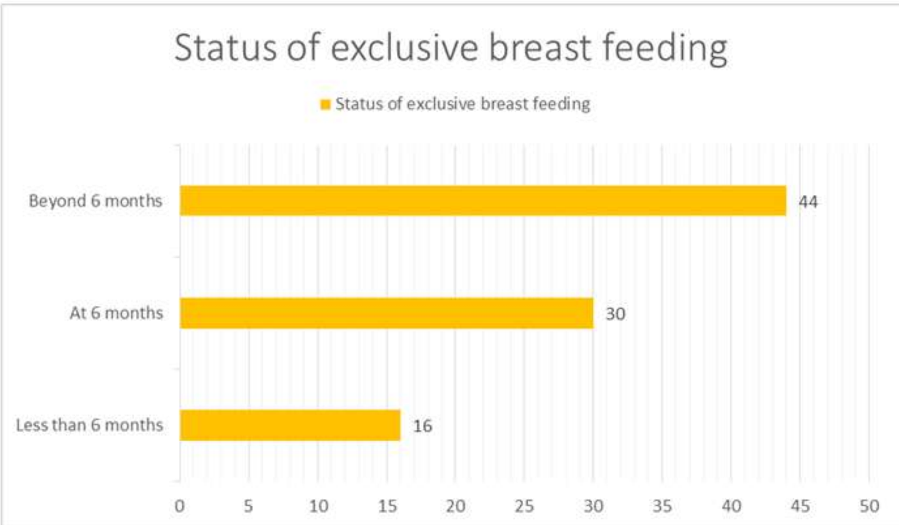


Graph 6: Distribution of study subjects as per time of initiation of breast feeding

Table 11: Distribution of study subjects as per status of exclusive breast feeding

Status of exclusive breast feeding	Number	Percentage
Less than 6 months	16	17.8
At 6 months	30	33.3
Beyond 6 months	44	48.9
Total	**90**	**100**

17.8% of the mothers were unable to give exclusive breast feeding till six months of the age of the baby but 33.3% of the mothers were able to do so while 48.9% of the mothers extended the exclusive breast feeding beyond six months of age.



Graph 7: Distribution of study subjects as per status of exclusive breast feeding

Table 12: Distribution of study subjects as per the age of initiation of complimentary feeding

Age of initiation of complimentary feeding	Number	Percentage
< 6 months	14	15.6
6-10 months	23	25.6
> 10 months	53	58.8
Total	**90**	**100**

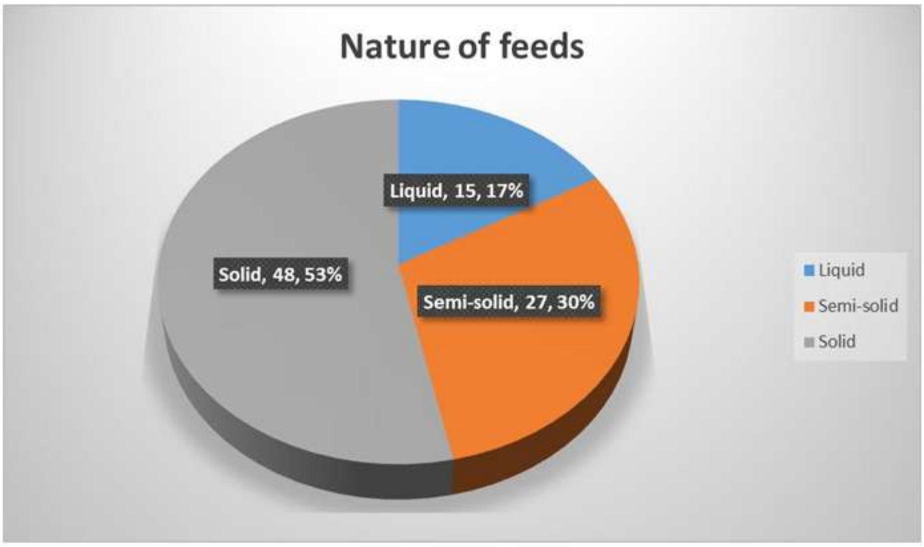
15.6% of the mothers hurried to initiate giving the complimentary feeding before six months of age of the baby while 25.6% of the mothers correctly started giving complimentary feeding between 6-10 months of age of the baby. But majority i.e. 58.8% could not start at correct age were able to start after the age of 10 months of the baby.

Graph 8: Distribution of study subjects as per the age of initiation of complimentary feeding

Table 13: Distribution of study subjects as per nature of feeds given as complimentary feeding

Nature of feeds	Number	Percentage
Liquid	15	16.7
Semi-solid	27	30
Solid	48	53.3
Total	**90**	**100**

16.7% of the mothers correctly started giving liquid first while 30% of the mothers started giving semi solid foods as complimentary feeding. But majority of the mothers i.e. 53.3% started giving directly solid foods as complimentary feeding.



Graph 9: Distribution of study subjects as per nature of feeds

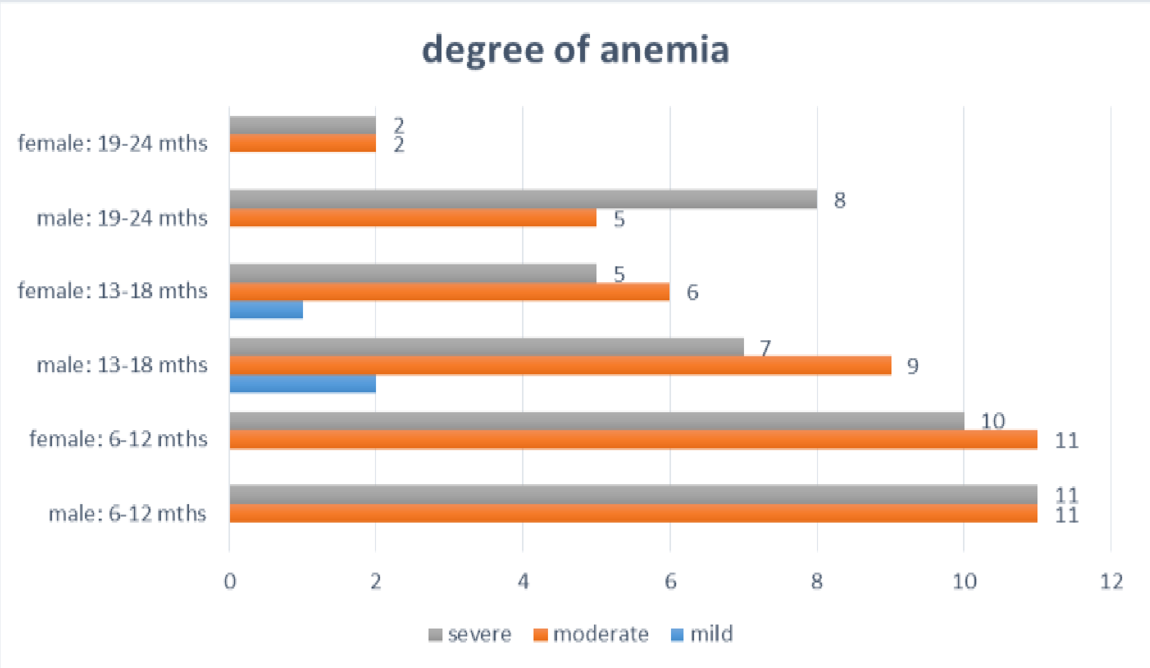
International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

Table 14: Various factors with baseline status of severity of anemia (mild, moderate and severe)

Variables		Baseline status of anemia						Total	
		Mild		Moderate		Severe			
		No.	%*	No.	%*	No.	%*	No.	%#
Age (months)	6-12	0	0	22	51.2	21	48.8	43	47.8
	13-18	3	10	15	50	12	40	30	33.3
	19-24	0	0	7	41.2	10	58.8	17	18.9
Sex	Male	2	3.8	25	47.2	26	49.1	53	58.9
	Female	1	2.7	19	51.4	17	45.9	37	41.1
Mother education	7-10 std	3	5.8	22	42.3	27	51.9	52	57.8
	> 10th std	0	0	22	57.9	16	42.1	38	42.2
Social class	Upper	0	0	7	29.2	17	70.8	24	26.7
	Middle	2	9.1	14	63.6	6	27.3	22	24.4
	Lower	1	2.3	23	52.3	20	45.4	44	48.9
Initiation of breast feeding	< 1 hr	0	0	17	54.8	14	45.2	31	34.4
	1-4 hrs	3	8.8	17	50	14	41.2	34	37.8
	> 4 hrs	0	0	10	40	15	40	25	27.8
Exclusive breast feeding	< 6 months	0	0	8	50	8	50	16	17.8
	6 months	0	0	10	33.3	20	66.7	30	33.3
	> 6 months	3	6.8	26	59.1	15	34.1	44	48.9
Age at initiation of complimentary feeding	< 6 months	0	0	7	46.7	8	53.3	15	16.7
	6-10 months	1	3.7	10	37	16	59.3	27	30
	> 10 months	2	4.2	27	56.3	19	39.6	48	53.3

#Percentages are row percentages; *These percentages are column percentages

In the age group of 19-24 months, 58.8% had severe anemia, in the age group of 6-12 months, 48.8% had severe anemia while 40% had severe anemia in the age group of 13-18 months. Severe anemia was more in males (49.1%) compared to females (45.9%). Severe anemia was more in children with maternal education of 7- 10 standard (51.9%) compared to 42.1% in children with maternal education of more than 10th standard. Severe anemia was found more in upper class children (70.8%) compared to 45.4% in lower class children and lowest of 27.3% in the middle class children. 45.2% of the children had severe anemia when breast feeding was initiated within one hour of delivery, 41.2% when it was 1-4 hours and 40% after four hours. Severe anemia was more (66.7%) in children given exclusive breast feeding up to six months of age compared to 50% before six months of age and 34.1% beyond six months of age. Severe anemia was more (59.3%) when Age at initiation of complimentary feeding was 6-10 months, 53.3% when Age at initiation of complimentary feeding was up to six months and 39.6% when Age at initiation of complimentary feeding was beyond 10 months.



Graph 10: Age and sex specific distribution of study subjects as per their baseline status of anemia

In the age group of 6-12 months, 11 males and 11 females had moderate anemia and 11 males and 10 females had severe anemia but no one was having mild anemia. In the age group of 13-18 months, 2 males and one female had mild anemia, 9 males and six females had moderate anemia and seven males and five females had severe anemia. In the age group of 19-24 months, five males and two females had moderate anemia, eight males and two females had severe anemia while no one had mild anemia.

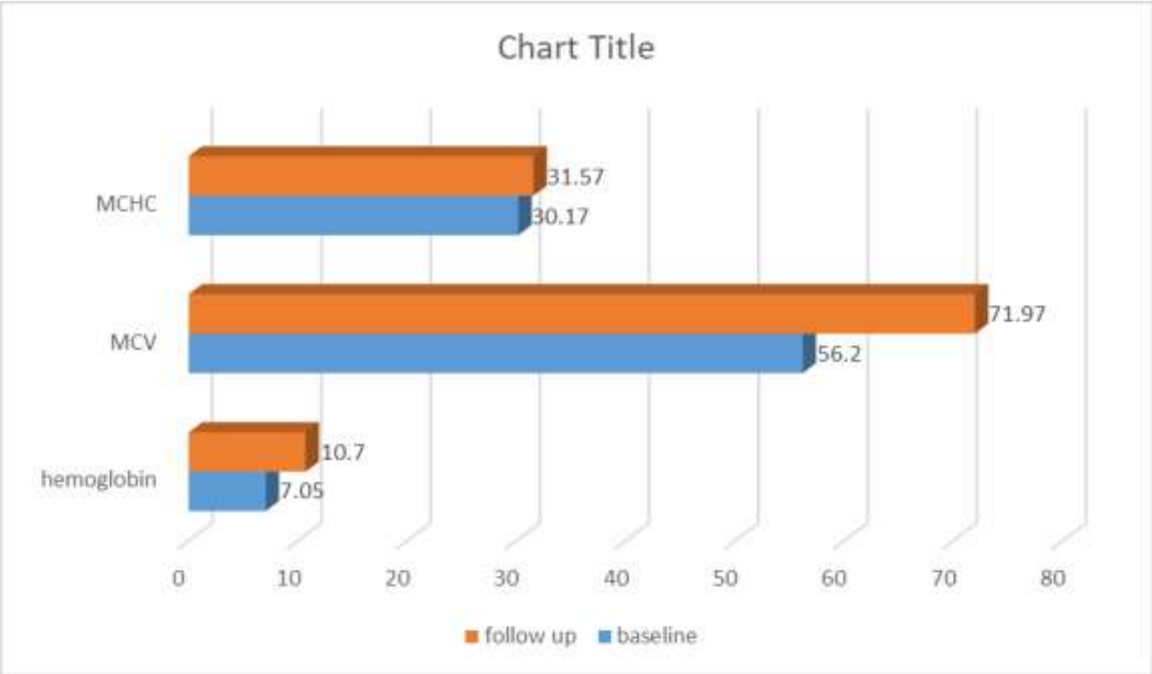
Table 15: Effect of iron supplementation on hemoglobin, MCV and MCHC (mean±SD)

Variable	Number	Baseline value	Value after supplementation	T value	P value	Interpretation
Hemoglobin	90	7.05±1.21	10.70±1.28	27.08	< 0.0001	Highly significant
MCV	90	56.2±5.04	71.97±7.73	28.49	< 0.0001	Highly significant

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

MCHC	90	30.17±0.65	31.57±1.07	81.604	< 0.0001	Highly significant

After iron supplementation, mean hemoglobin increased from 7.05 gm/dl to 10.70 gm/dl and this increase was statistically significant ($p < 0.05$). Similarly MCV also increased from 56.2 to 71.97 significantly ($p < 0.05$) and MCHC also increased from 30.17 to 31.57 significantly ($p < 0.05$).



Graph 11: Effect of iron supplementation on hemoglobin, MCV and MCHC (mean±SD)

Table 16: Distribution of study subjects as per the clinical improvement after iron supplementation

Clinical improvement	Number	Percentage
Yes	72	80
No	18	20
Total	**90**	**100**

The clinical improvement was seen in 80% of the children after iron supplementation while it was not seen in 20% of the children.

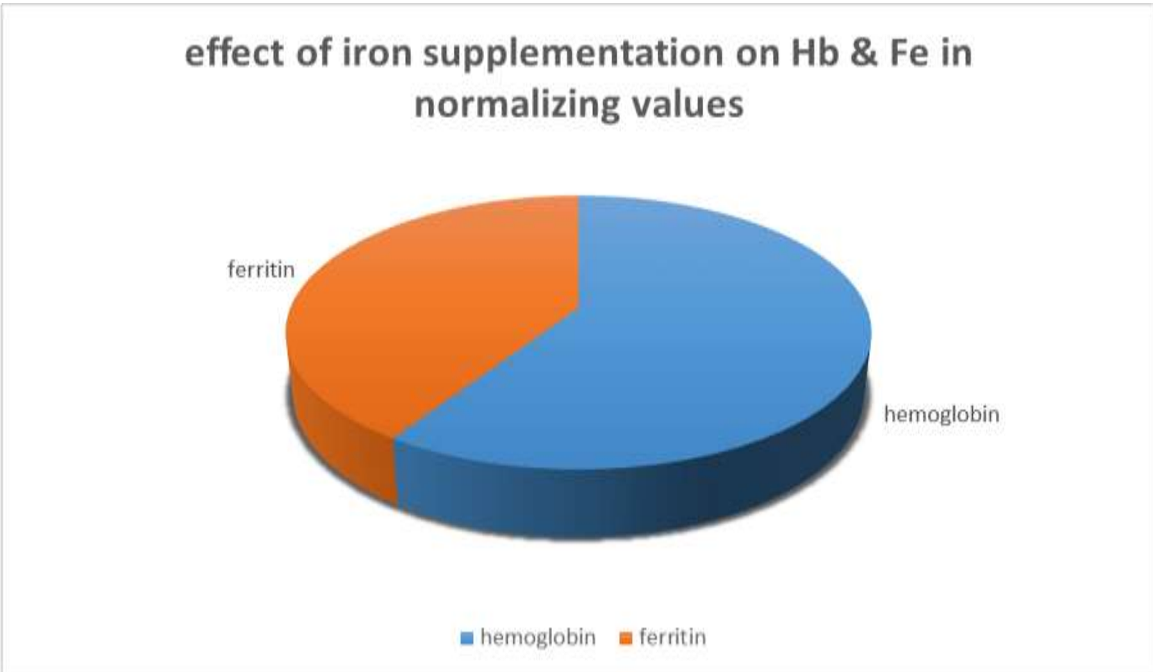
International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

Graph 12: Distribution of study subjects as per the clinical improvement after iron supplementation

Table 17: Response of hemoglobin and ferritin after iron supplementation in terms of normalizing to normal values

Variable		**Number**	**%**
Hemoglobin	Normalized to normal value	45	50
Ferritin	Normalized to normal value	31	34.4

Hemoglobin normalized to normal value in 50% of the cases while ferritin normalized to normal value in 34.4% of the cases. (Table 13 and figure 13)



Graph 13: Response of hemoglobin and ferritin after iron supplementation in terms of normalizing to normal values

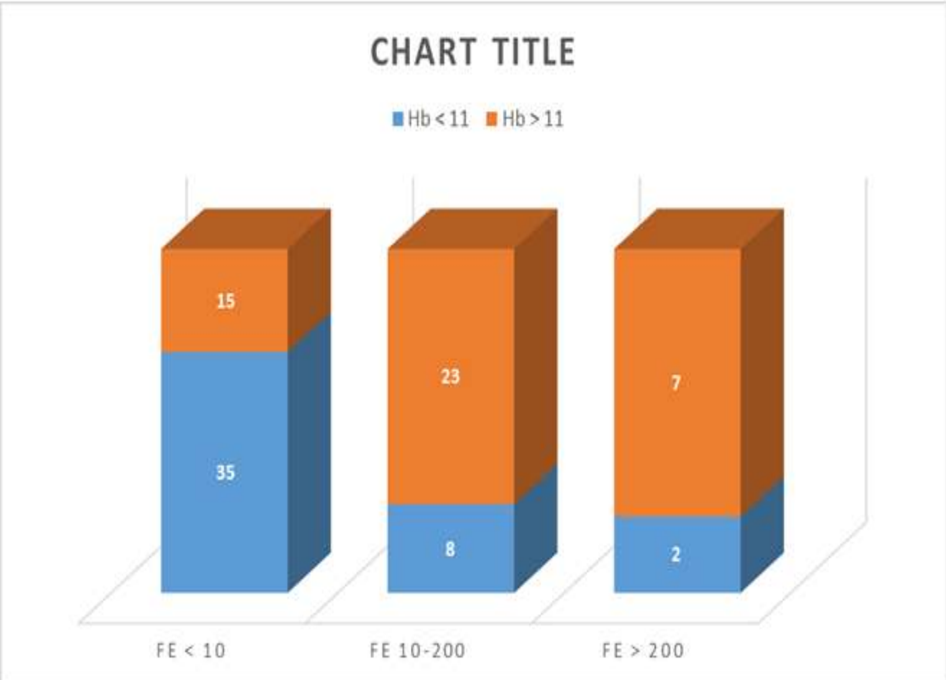
International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr 2021 pp 65-91 www.ijdmsrjournal.com ISSN: 2582-6018

Table 18: Relation between follow up Hemoglobin and follow up ferritin (N = 72)

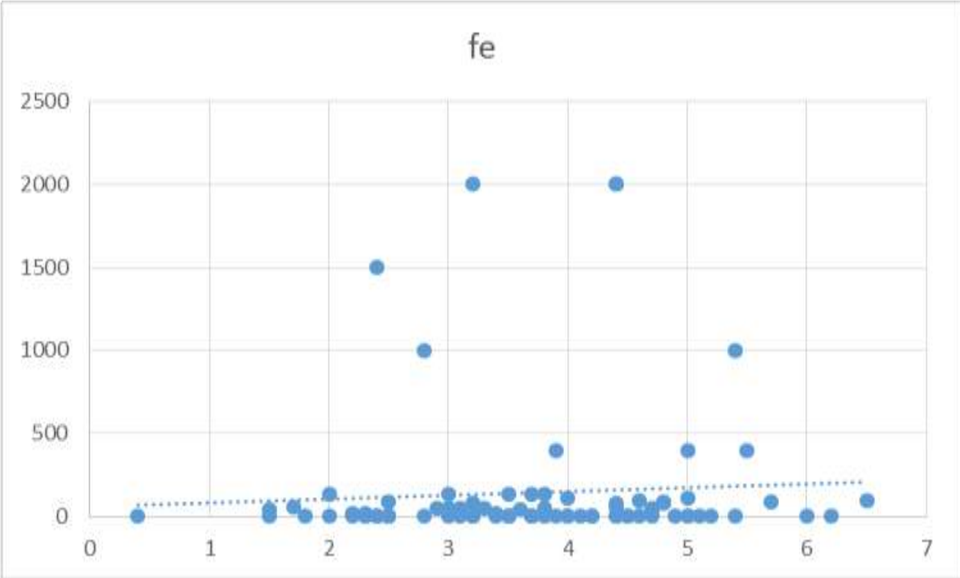
Follow up Hb (gm/dl)	Follow up Ferritin (ng/ml)						Total	
	< 10		10-200		> 200			
	Number	%	Number	%	Number	%	Number	%
< 11	35	77.8	8	17.8	2	4.4	45	50
≥ 11	15	33.3	23	51.1	7	15.6	45	50
Total	**50**	**55.6**	**31**	**34.4**	**9**	**10**	**90**	**100**

X^2 = 18.0358, p = 0.0001 (Highly significant)

Out of 45 children whose hemoglobin was less than normal even after iron supplementation, majority i.e. 35 (77.8%) ferritin levels were also less than normal, among these children, 8 (17.8%) were found to achieve normal ferritin levels while it was abnormally increased in only two cases. Out of 45 children whose hemoglobin became normal after iron supplementation, it was found that ferritin remained less than normal in 15 (33.3%) of the cases while in majority it became normal 23 (51.1%) and in 7 children it increased up to abnormal values.



Graph 14: Relation between follow up Hemoglobin and follow up ferritin (N = 72)



Graph 15: Relation between increased hemoglobin from baseline (x axis) with follow up ferritin (y axis)

R= 0.05, p = 0.555
he correlation between increased hemoglobin from baseline and follow up ferritin was found to be weak. Both were correlated with each other only at 5% level and it was not found to be statistically significant.

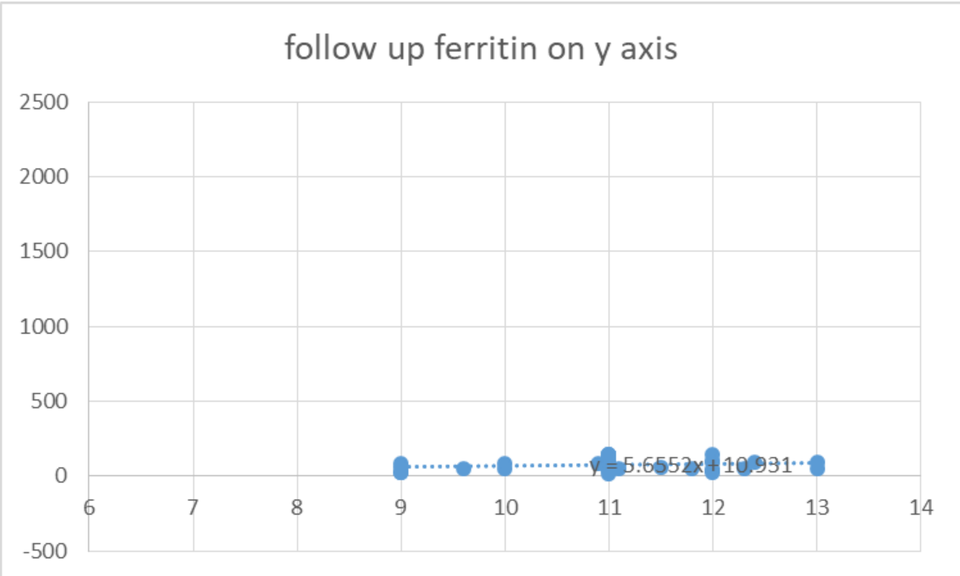
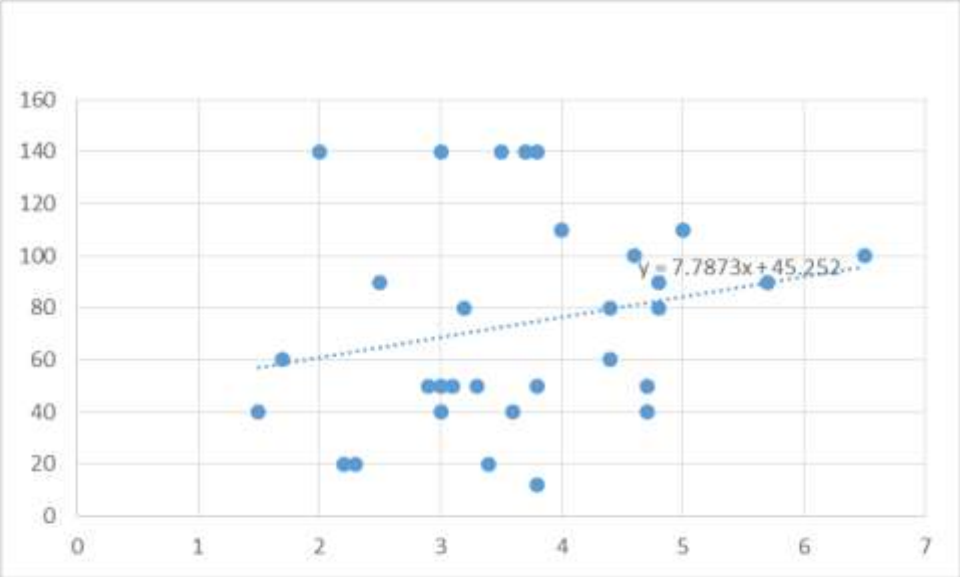


Figure 16: Relation between follow up hemoglobin (x axis) and follow up ferritin (y axis)

R = 0.20, p = 0.0518
he correlation between follow up hemoglobin and follow up ferritin was found to be weak. Both were correlated with each other only at 20% level and it was not found to be statistically significant.



Graph 17: Relation between increased hemoglobin from baseline (x axis) with follow up normal values of ferritin (y axis)

R = 0.21, p = 0.252

The correlation between follow up hemoglobin and follow up ferritin was found to be mildly positive. Both were correlated with each other only at 21% level and it was not found to be statistically significant. (Figure 16)

VI. DISCUSSION

Adequate nutrition during the first 24 months of life is proportional to the proper breastfeeding and complimentary feeding practices. Children enter a particularly vulnerable period after 6 months of age when all nutritional requirements are not met through breast milk, during which they make a transition to eat normal home food. The period from 6 to 18 months of age, where during which the incidence of poor nutrition rises rapidly in most countries. Deficits acquired at this age are hard to compensate later in childhood.[7]

The most common macronutrient deficiency across the world and also in India is the iron deficiency anemia. Iron is of gre0ater significance during the first 2 years of life, as it is the period of rapid brain development and results in irreversible changes in the brain.[2]

Since iron deficiency is the most prevalent and preventable cause, aim of this study is to identify anemic children aged between 6- 24 months for 2 to 3 months and follow up for clinical response and laboratory changes with improvement in relation to baseline Hb and ferritin levels

In our study, out of 114 enrolled, and 24 were lost with follow up and 90 children were followed up. Out of 90 enrolled, 47.8% (43 children) belonged to age groups 6 to 12 months, 33.3% (30 children) belonged to 13 to 18 months, 18.9% (17 children) belonged to 19 to 24 months age. Predominantly children aged 6 to 12 months were found to have anemia in our study

A study done by Fajolu et al showed the prevalence of IDA in this study is high especially before the age of 12 months, which correlates to our study. [86]

Our study showed that out of 90 children, (48.8%) 44 children had moderated anemia, out of which male predominance among groups of anemia is seen in our group.

It was found in our study that majority 75.6% (68 children) were term babies with birth weight of 2.5 kg or more, whereas only 24.4% (22 children) were low birth weights

The mean change of hemoglobin values from baseline to follow up was more in normal birth weight children but the difference was statistically not significant ($p > 0.05$).

Majority of the children were first born children i.e. 42.2% (38 children), second born children in 26.7% (24 children) of the cases. 14.4% (13 children) of the cases had birth order of 3. And 16.7% (15 children) were found belonging to birth order of 4.

However according to a study done by Amina et al,[78]birth order was not significantly associated with IDA which is similar to our study.

According to a cross-sectional hospital based study done by Sandip Ray et al on two hundred patients attending outpatient and in-patients, during the period of November 2010 to March 2012, found that increasing birth order was significantly associated with nutritional anemia both on univariate analysis (0.001 and multiple variable regression analysis (0.003) [87]

In our study, out of 90 mothers, majority i.e. 40% (36 cases) were found to have anemia during pregnancy, while 60% (54 cases) were found to have normal levels of hemoglobin.

A study done by Jareen et al, maternal anemia was independently (p = 0.03) associated with a 3-fold increased risk of infant anemia. [72]

In our study, the mean change of hemoglobin values from baseline to follow up after iron supplementation was slightly lesser in children with absence of maternal anemia but the difference was statistically not significant (p > 0.05).

In our study, out of 90 children, 57.8% (41.2%) of the mothers were educated up to 10th standard only and 42.2% (38 children) of the mothers were educated higher than that.

A study done by Amina et al,[78] found that about one third of the low educated mothers had anemic infants more than the highly educated ones (11.7%) with statistically significant difference (p < 0.0001). which correlates to our study.

In our study, the mean change of hemoglobin values from baseline to follow up after iron supplementation was slightly more in children with mother education of 7-10 standard but the difference was statistically not significant (p > 0.05).

But studies have found maternal education level to be positively related to better use of health services, lower fertility and, good nutritional status of children.

In our study out of 90 children, Majority i.e. 48.9% (44 children) belonged to lower class which is significant A study done by D. Schellenberg et al in mid 1999, showed the risk of severe anemia increased as the socioeconomic score decreased, which is in accordance to our study. [80]

In our study among 90 cases, 34.4% (31 cases) breastfeeding was initiated in less than one hour after delivery. In 27.8% (25 children) breast feeding was initiated after four hours.

According to NFHS-4, 2015-16, Karnataka around 57.7% of children are being breastfed in the first hour of life, up from 23.4% around 10 years ago and 35.6% in NFHS- 3(National family health survey (NFHS-4, Karnataka, 2015-16) [30], On contrary, institutional deliveries, have jumped from 38.7% to 78.9% between NFHS-3 and NFHS-4, indicating 40 percentage points (The DHS program, March 2017). [30]

However a study by Amina et al showed no significant differences between early and delayed breastfeed initiation. [78]

In our study Out of 90 children, 48.9% (44 children) , exclusive breast feeding was given for more than six months, while, 33.3.% (30 children) were breastfed up to six months of age.

In the recent NFHS-4, Karnataka around 54.2% were exclusively breast fed for 6 months, which has dropped from 58.6% in NFHS-3. [30]

According to a study done by Gisela et al children between 6 months for 5 years concluded that prevalence of breast feeding for six months, if increased and lack of breastfeeding was found to be associated with anemia, which is slightly more in our study, but not statistically not significant (P > 0.5). [79.] Our study slightly correlates the above study.

In our study out of 90 children, 58.8% (53 cases) were started on complimentary feeding after 10 months age, which is slightly high in our study. While 15.6% (14 children) were started on complimentary feeding either before 6 months age.

A study done by Banapuramath et al in central Karnataka 55% were initiated appropriate complementary feeds compared to 46% as per NFHS-4 survey, which is in contrary to our study. [30, 88]

Our study showed that age at complimentary feeding was found to be statistically significantly associated with mean change of hemoglobin values from baseline to follow up after iron supplementation. (p < 0.05)

In our study 90 children were sampled baseline hemoglobin. Hemoglobin, MCV, MCHC serum ferritin levels and were followed up in 90 children. Children who were enrolled were evaluated for proper history to find the cause of IDA.

Children were supplemented with 6 mg/kg of Iron supplementation based on the severity of anemia, with counselling about diet.

Our study showed majority of the children showed clinical improvement in terms of improved activity,appetite and alertness, decreased pallor, decreased irritability with adjusted normal sleep. Clinical response was noted in 80% (72 children) with the above improvement features.

Although hemoglobin levels usually respond rapidly to oral iron therapy, repletion of iron stores and normalization of serum ferritin levels may require 3-6 months of treatment. [83, 84]

After iron supplementation, mean

hemoglobin increased from 7.05 gm/dl to 10.70 gm/dl and this increase was statistically significant ($p < 0.05$). Similarly MCV also increased from 56.2 to 71.97 significantly ($p < 0.05$) and MCHC also increased from 30.17 to 31.57 significantly ($p < 0.05$). A similar studies showed same results as our study[83, 84]

Our study showed significant baseline changes of mean hemoglobin, MCV and serum ferritin values after oral iron supplementation for 3 months duration($P < 0.0001$)
Hemoglobin normalized to normal value in 50% of the cases while ferritin normalized to normal value in 34.4% of the cases.

A study done by Ahmad et al in 2018 showed Low ferritin levels are frequent among children starting first year of school life. Low ferritin levels are equally frequent among children with or without anemia. There is poor correlation between ferritin and hemoglobin levels. Our study also showed poor correlation between hemoglobin rise and rise in ferritin rise after iron supplementation [89]

Further, many studies to be done with a big sample size to find out other factors influencing iron deficiency anemia and response to iron supplementation over iron profile. Our study will be continued with further results in near future.

VII. CONCLUSION

Based on our study findings, it could be concluded that the anemia was higher among the

It is recommended that all efforts should be made to detect IDA in the children aged 6 to 24 months. Also initiation from the government and media, to have an active role in information, education and communication activities such as promoting breastfeeding for 6 months to maintain iron stores in children.

Efforts should be made to implement supplementation of prophylactic oral iron in age groups of 6 to 12 months universally, irrespective of anemic status in developing countries when infants come for MMR vaccination.

WHO Recommendation: Daily iron supplementation for 3 consecutive months in a year is recommended as a public health intervention in infants and young children aged 6–23 months, living in settings where anaemia is highly prevalent,1 for preventing iron deficiency and anaemia (strong recommendation, moderate quality of evidence). [81]

infants aged 6 to 12 months.

IDA is most common with delayed of complementary feeds for more than 6 months. Mothers with low education can have IDA children. Our study showed that maternal education and educating mothers ensured compliance with taking iron supplements and complimentary feeds at appropriate age.

Majority of the children were found to have moderate anemia with no symptoms which improved with iron supplementation alongside encouraging complimentary feeds at 6 months age.

Birth order and birth weight was not associated with IDA in children unlike other studies.

Breast feeding is ancient and unique. Inspite of well promotions and so much emphasis of breastfeeding, the rate of exclusive breastfeeding are below expected levels.

The present study has shown that exclusive breast feeding for six months and appropriate initiation of complementary feeds at 6 months age decreases the incidence of IDA. Our study showed significant improvement clinically and laboratory improvement after iron supplements.

Our study emphasize on early detection of IDA in children aged 6 to 24 months. Ideal time to screen children is during MMR vaccination at 9 months age, where children are more prone for IDA.

VIII. SUMMARY

Based on the presence of anemia, participated children were grouped as mild, moderate and severe anemia, based on baseline hemoglobin and available serum ferritin levels. Total of 114 children enrolled and 24 were lost in follow up.

- IDA is more common in the age groups of 6 to 12 months.
- Lower economic status is associated with IDA in children.
- Maternal education, contribute to IDA like in other studies. But maternal anemia in contrary to other studies didn’t contribute to IDA in our study.
- Delayed complimentary feeding is associated with IDA in our study. It should be ideally started at 6 months age
- Children aged between 6 to 12 months are at risk of IDA, and should be supplemented with iron for 3 consecutive months.
- Oral iron supplementation in anemic children showed statistically significant baseline improvement changes in hemoglobin, MCV,

MCHC. Serum ferritin were improved in only few cases and there is a poor correlation between hemoglobin and ferritin levels change after iron supplementation.

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