

Original Research Article

An observational study of childhood iron deficiency anaemia and the factors affecting the outcome of oral iron therapy

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ABSTRACT

Background: Iron deficiency is the most common cause of anaemia worldwide. In-depth studies examining facilitators and barriers to oral iron therapy are lacking. The aim of our study is to determine the factors affecting the outcome of oral iron therapy in iron deficiency anaemia.

Methods: This is an observational study conducted in a tertiary hospital in Mumbai in children in the age group of 12 to 60 months. Out of a total of 416 children screened, 208 were eligible for oral iron therapy and were given oral iron in the dose of 3 milligrams per kilogram per day and reviewed after two months. A comprehensive questionnaire was given to parents after the completion of therapy to study the factors affecting iron therapy. The details were then analysed using Excel sheets, and correlation was calculated using SPSS program version 20.0.

Results: After 2 months of oral iron therapy, IDA was corrected in 68.98%. Factors that led to an unsatisfactory outcome with iron therapy were, history of low birth weight, past hospital admissions, gastrointestinal side effects, malnutrition, and children who had tea, milk, or food with iron therapy. In contrast, children who took iron on an empty stomach and along with vitamin C-rich foods had a significant increase in haemoglobin levels.

Conclusions: Various modifiable factors affect adherence and outcome of oral iron therapy. Tea and Coffee are to be avoided when the child is on iron therapy. Meticulous counselling of parents and children is pivotal for the successful management of IDA with oral iron therapy.

Keywords: IDA, Iron Therapy, Tea

INTRODUCTION

Iron deficiency anaemia (IDA) is the most common cause of anaemia worldwide.¹ As per Indian National Family Health Survey-5 (NFHS 2019-21), the prevalence of anaemia has increased from 59% to 67% in the last five years.² Anaemia is still highly prevalent even with the existing National Anaemia Control Programs and treatment guidelines. Multiple factors affect the absorption and metabolism of iron. Food items like meat, fish, lemon, and orange juice are enhancers of iron absorption while Tea, Phytates, and Polyphenols inhibit absorption.³ In-depth studies examining facilitators and barriers to oral

iron therapy are scanty. The present study was designed to study the various non-modifiable and modifiable factors that affect the outcome of oral iron therapy despite having good compliance.

Aim and objectives

Aim of current study was to determine the factors affecting the outcome of oral iron therapy in iron deficiency anaemia. Objectives: were to estimate the prevalence of iron deficiency anaemia in children between 1 to 5 years coming to OPD, Casualty, and In-patients in the Department of Paediatrics at Jagjivan Ram Hospital and to

determine the factors associated with iron deficiency anemia

METHODS

Study location and duration

This was a hospital-based observational study carried out in the Paediatrics department of Jagjivan Ram Hospital, Mumbai. Study was conducted from December 2020 to May 2022.

Study population

Children of age group 1-5 years attending our hospital with symptoms suggestive of Iron deficiency anemia.

Sample size, sample size calculation and sampling technique

Total 416 participants were included in the study. Sample size was calculated according to the study conducted by Inderpreet Santokh et al, the prevalence of iron deficiency anaemia in children aged 6 months to 60 months in a teaching hospital is 56%.⁴ The formula used was;

$$n = z^2pq \div d^2$$

Where; n is sample size: $z=1.96$ (at 95% confidence interval), $p=\text{prevalence}=56\%$, $q=100-p=44\%$, $d=\text{precision}=5\%$. Therefore, $n=\text{sample size for this study}=378$. By adding a 10% loss to follow up total sample size becomes $378+38=416$. Consecutive sampling, a type of convenience sampling is followed in the selection of cases till the desired sample size is achieved

Inclusion criteria

Children in the age group of 1 to 5 years coming to OPD, Casualty, and In-Patient departments at Jagjivan Ram railway hospital, Mumbai from October 2020 till the desired sample is achieved and Children whose parents or guardians give consent to participate in the study were included.

Exclusion criteria

Children in the age group less than 1 year and more than 5 years and Children whose parents or guardians did not give consent to participate in the study,

Participants with iron deficiency Anaemia who were not eligible for Iron therapy

Lymphoreticular malignancy-blasts in Peripheral smear, Haemolysis-Increased reticulocyte count, Pancytopenia, Congenital heart disease, $\text{Hb} < 4 \text{ gm\%}$ needing blood transfusion, Gastritis, Persistent vomiting, Children already on iron therapy and Children with chronic diseases

Data management and analysis

The data collected through the questionnaires were entered in Microsoft Excel Home & Student 2019 and statistical analysis was done using Statistical Package for Social Sciences v 20.0. The chi-square test and Fisher's exact test were used to determine the significance of the association of various factors with IDA and the factors affecting iron therapy. Paired t-test was used to compare pre and post-treatment haematological parameters. A p value of <0.05 was taken as significant.

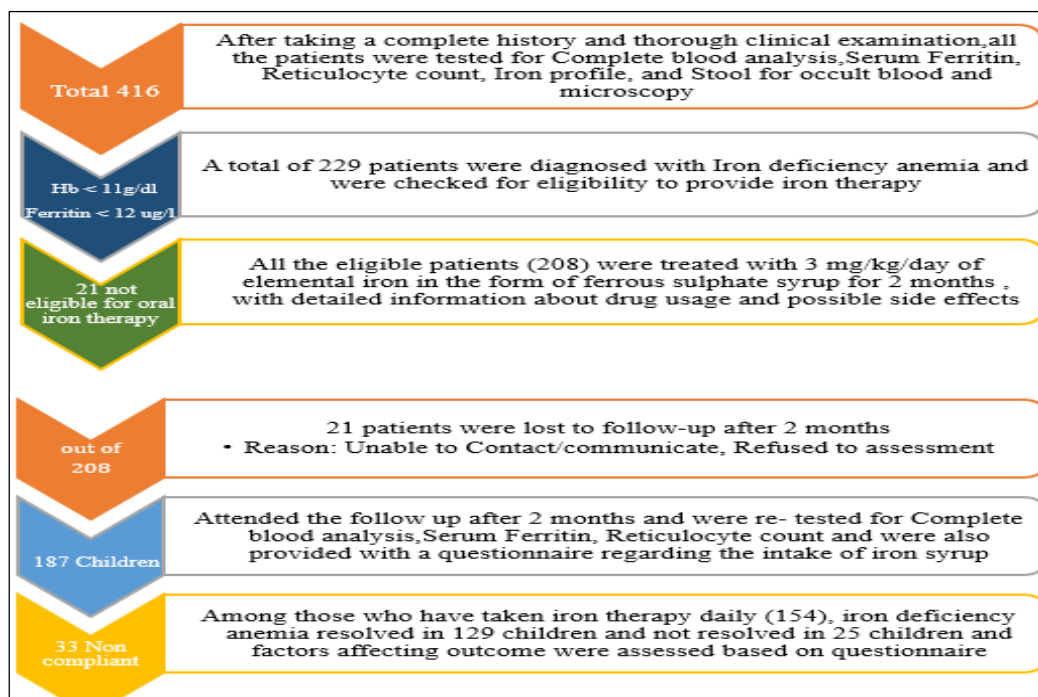


Figure 1: Study procedure.

RESULTS

Haemoglobin, MCV, MCH, Reticulocyte count, and Serum Ferritin levels increased after iron therapy, whereas RDW decreased after treatment. 17.65% (33 out of 187) of children did not take iron syrup daily (poor compliance) due to various reasons. Even with good compliance, some children (25) did not respond to oral iron therapy, the reasons being H/O Low birth weight, Nutritional status of the child, and not following advice regarding medications and gastrointestinal side effects (Table 2).

Iron taken along with food, tea, and milk has shown a significant negative effect in response to oral iron therapy. IDA is corrected in all 33 children (100%) who have taken iron syrup along with vitamin C-rich foods like lime, and orange. This shows a positive association between vitamin C and iron absorption ($p < 0.001$). History of hospital admission and having gastrointestinal side effects like vomiting and loose stools during the course of therapy has shown a significant negative association in the correction of IDA, whereas constipation, stomach pain, and dark stools have no association.

Table 1: Factors determining Iron deficiency anemia in Children (n=416).

Parameters, N (%)	Yes, N=229	No, N=187	P value
Females	114 (50)	85 (45)	0.38
Socio economic status			
Lower	38 (17)	18 (9.6)	<0.001
Lower middle	76 (33)	29 (16)	
Upper middle	91 (40)	134 (72)	
Upper	24 (10)	6 (3.2)	
Birth weight, mean (SD)	2.47 (0.48)	2.31 (0.52)	0.001
Exclusive breastfed, yes	167 (73)	164 (88)	<0.001
Cow milk intake before 1yr, yes	155 (68)	123 (66)	0.68
Daily calorie intake (%), Mean (SD)	82 (8)	81 (7)	0.15
Pica, yes	70 (31)	21 (11)	<0.001
Blood in stools, yes	36 (16)	7 (3.7)	<0.001
Worms in stool, yes	55 (24)	25 (13)	0.006

Table 2: Factors affecting Iron therapy outcome among those who took daily iron therapy (n=154).

Parameters N (%)	IDA corrected		P value
	Yes, N=129	No, N=25	
Low birth weight	41 (32)	13 (52)	0.053
Weight for height	4 (3.1)	4 (16)	0.024
Time of iron therapy			
Morning	121 (94)	17 (68)	<0.001
Afternoon	4 (3.1)	0 (0)	
Night	4 (3.1)	8 (32)	
Empty stomach	76 (59)	8 (32)	0.013
With food	8 (6.2)	17 (68)	<0.001
With tea/milk	16 (12)	12 (48)	<0.001
With lime/curd/orange	33 (26)	0 (0)	0.004
Nausea/vomiting	33 (26)	12 (48)	0.024
Constipation	17 (13)	4 (16)	0.75
Loose stools	8 (6.2)	9 (36)	<0.001
Stomach pain	21 (16)	5 (20)	0.77
Hospital admission	4 (3.1)	12 (48)	<0.001
Dark stools	50 (39)	9 (36)	0.80

DISCUSSION

Iron deficiency anaemia (IDA) is the most common anaemia worldwide. World Health Organization (WHO)

estimates that close to two billion people, or 25% of the world's population, are anaemic, and approximately half of them suffer from IDA.¹ As per the National Family Health Survey-5 (2019-21), Between 2015-16 and 2019-21, the

prevalence of anaemia among children aged 6-59 months increased from 59 percent to 67 percent and continued to be higher among rural children.² This indicates the increasing burden of this disease on our country and the need for effective preventive and treatment strategies. Risk factors associated with a higher prevalence of IDA include low birth weight, high cow's milk intake, low intake of iron-rich complementary foods, and low socioeconomic status. A lot of attention has focused on the prevention and early diagnosis of IDA, yet little research has assessed the treatment and follow-up of those children in whom IDA is diagnosed despite preventive strategies.⁸ In-depth studies examining barriers to oral iron therapy adherence in young children are lacking. Even fewer studies exist to assess facilitators of its adherence. In our study, 229 out of 416 children were diagnosed with iron deficiency anaemia. The prevalence of iron deficiency anaemia between 1 to 5 years of age is 55.02%. Out of 229 children with iron deficiency anaemia, 122 children are between 1 to 2 years of age, with a proportion of 53.28%.

LISBÔA et al in their cross-sectional study included a random sample of 725 male and female children aged less than 60 months.⁹ The prevalence of anemia in their study was 37.4%. The greatest prevalence occurred in ages 6 to 24 months (43.0%). It suggests that children under two years of age are more likely to develop IDA. This finding is consistent with other studies by Veira et al.¹⁰ This could be attributed to a higher need for iron in this age group due to rapid growth and development combined with a lack of iron intake.¹¹

Our study has 217 males and 199 females, out of which 115 (53%) and 114 (57.29%) had iron deficiency anaemia, respectively. There is no statistically significant association (p value 0.379) between the gender of children and iron deficiency anaemia. Based on haemoglobin levels, anaemia is divided into three categories, Mild (10 g/dl to 10.9 g/dl), moderate (7 g/dl to 9.9 g/dl), and severe (<7 g/dl). The majority of children come under moderate anaemia (62.01%), followed by mild (25.76%) and severe types (12.23%). These results were similar to a study by Santokh et al in Haryana, a cross-sectional study on Iron deficiency anaemia among hospitalized children between 6 to 60 months in a rural teaching hospital.⁴

Out of 100 children in that study group, 56 had iron deficiency anaemia, with a prevalence of 56%. IDA was most prevalent in the age group of 6 to 24 months (65%). Their study also showed no statistical significance (p value >0.05) of gender with iron deficiency anaemia. Most children (46%) suffered from moderate anaemia, 37% mild, and only 17% suffered from severe anaemia, similar to our study. Pica is compulsive eating of non-nutritious substances. There are many reports in the literature, both clinical cases and case series, on the association between Pica and iron deficiency.¹² Among 91 children with complaints of Pica, 71 were diagnosed with iron deficiency anaemia in our study with a p value of <0.001,

showing a significant association between Pica and iron deficiency anaemia, as reported by other studies.

Parents were questioned whether they had given exclusive breastfeeding (EBF) to children for the first six months of age. A total of 331 children received EBF, whereas 85 children were not breastfed exclusively for six months. 62 out of 85 children (72.94%) who did not receive exclusive breastfeeding for the first six months of life have developed iron deficiency anaemia, while 167 out of 331 (50.45%) who were given EBF developed IDA. This suggests that those who have not taken breastfeeding have a high risk of developing iron deficiency anaemia.

Human milk contains lower amounts of casein, phosphate, calcium, and factors thought to inhibit iron absorption. Enhancing compounds such as lactoferrin, ascorbic acid, lactose, cysteine, taurine, and inosine are in higher concentrations in human milk. However, some studies reported that exclusive breastfeeding beyond six months of age leads to the development of IDA, as human milk is a poor source of iron.¹³

Out of 278 children who had cow milk intake before 1yr of age, 155 children have iron deficiency anaemia (55.76%), and 134 children who did not take cow milk before one year, 74 children developed iron deficiency anaemia (53.62%) with a p value of 0.681, which is not statistically significant. Therefore, there is no relationship between cow milk intake before one year of age and the development of Iron deficiency anaemia in our study, contrary to many studies which show a significant association between cow milk intake and iron deficiency anaemia.⁵⁻⁷ This may be due to recall bias, smaller sample size, and children receiving cow's milk in different quantities, as the effect of cow's milk on iron absorption is not all or none. It is dose-dependent.¹⁴ Children in our study group were divided into different socioeconomic classes based on the Kuppuswamy scale, and the prevalence of iron deficiency anaemia was studied. 38 Out of 56 children in the lower class (67.86%) had IDA, 76 out of 105 in the lower middle class (72.38%) had IDA, 91 out of 195 children in the upper middle class (46.66%) and 24 out of 60 in upper class (40%) had IDA. There is a statistically significant association between different socioeconomic classes and iron deficiency anaemia (P value <0.001), with IDA being more prevalent in the lower middle and lower classes.

A stool examination was done for all the children in the study population for occult blood and microscopy. Out of 416 children in the study group, 43 children had a positive faecal occult blood test, out of which 36 had iron deficiency anaemia, suggesting a significant association between IDA and blood in stools with a p value of <0.001.

A stool for microscopy was sent for all children in the study group to look for eggs, cysts, and parasites in the children's faeces. Out of 229 patients with iron deficiency anaemia, 55 children have worms or eggs in the faeces

(24%), with a p value of 0.006. It suggests parasitic infestations are strongly associated with the development of iron deficiency anaemia. Out of 208 children who were started on daily oral therapy, only 187 children came for follow-up after two months.

Twenty-one children lost to follow-up due to various reasons (10.1%). Repeat CBC, Reticulocyte count, and Serum ferritin was done on these children, which shows improvement in mean haemoglobin levels from 8.64 g/dl to 11.14 g/dl, MCV from 65.44 fL to 72.97fL, MCH from 22.88 pg to 29.74 pg, Mean Reticulocyte count from 0.99 to 1.58 and mean Serum Ferritin levels improved from 9.65 mcg/lit to 24.05 mcg/lit. There is a significant fall in mean RDW from 18.52% to 14.76%. All the mean parameters before and after treatment have a p value of <0.001, which is significant statistically. Out of 187 children who came for follow-up after two months, 33 children did not take iron syrup daily as advised (17.65%). These children have poor compliance with iron therapy, the reasons being refusal by the child, lack of awareness of parents, and Gastrointestinal side effects. IDA is not corrected in all of these thirty-three children.

Powers et al in their study on deficiencies in the management of iron deficiency anaemia during childhood, stated that Sixty-four patients (33%) exhibited poor adherence to oral iron as manifested by: taking less than prescribed (38%), medication intolerance, and/or gastrointestinal upset (30%), never obtaining the prescribed medication (14%), and/or misunderstanding of the prescribed dose (7%). Low birth weight, defined as birth weight less than 2.5 kg, is a significant health problem. Children with low birth weights were more likely to develop IDA than those with normal birth weights. Most children born small for gestational age (SGA) catch up in weight and length within the first two years of life. As a result, the increased demand for iron during this period of rapid growth may result in IDA.

In Our study, 14 out of 55 children with Low birth weight (25.45%) failed to improve even with good compliance with iron. In contrast, in only 11 out of 99 children with a birth weight of more than 2.5 kg (11.11%), iron deficiency is not resolved despite good compliance with iron. The relationship is statistically significant with a p value of 0.02. This suggests that Low birth weight babies have difficulty improving IDA even with good compliance. Similar results were found in a study conducted by Thomson et al in Minnesota, USA, in 1 to 10 years old children who were anaemic, and birth weight was a major determinant in the outcome.¹⁵ Oral iron therapy is affected by the nutritional status of children. Malnutrition is a significant hurdle in the treatment of IDA. In our study, weight/height is taken as an indicator of acute malnutrition. 50% of children who have weight/height less than the 3rd percentile failed to improve with iron therapy. It suggests that the nutritional status of the child is very important in the improvement of Haemoglobin status during oral iron therapy.

Iron is best absorbed when taken on an empty stomach, ideally 1 hour before or 2 hours after eating, as suggested by many studies.^{16,17} Our study also had similar results; IDA corrected in 87.68% (121 out of 138) of children who have taken iron during the morning times while only 33.33% (4 out of 12) who have taken it during the night have corrected their IDA. In 17 out of 70 children (24.29%) who had taken iron syrup with a full stomach, IDA is not corrected despite good compliance. 90.48% of children who have taken iron with an empty stomach have improved IDA, but it is associated with gastrointestinal side effects. A total of 25 children have taken iron syrup along with food, and 129 children with empty stomachs or 1 hour after food. IDA was not corrected in 17 out of 25 children (68%) who have taken iron with food. This suggests that food inhibits the bioavailability of iron syrup.

Smith and Schultz et al found that feeding 30 mg iron as ferrous sulfate with 180 ml milk rather than water reduced average absorption (in children) from 15% to 5%.¹⁸ In our study, we found through the questionnaire that 28 children have taken tea, coffee, or milk along with or immediately after taking iron syrup, out of which 12 children (42.86%) have failed to improve IDA even after taking iron syrup daily as advised. These results are statistically significant, with a p value of <0.001. This shows the negative effect of tea, coffee, and milk on iron absorption.

IDA is corrected in all 33 children (100%) who have taken iron syrup along with vitamin C-rich foods like lemon and orange and in 96 children (79.34%) who have not taken it. This shows a positive association between vitamin C and iron absorption (p value 0.001). This is supported by various studies.¹⁹ Vomiting and Nausea are the common side effects of iron therapy. It is present in 26.67% of children who failed to respond to iron therapy which is significant (p value 0.024).

IDA is not corrected in 9 out of 17 children (52.94%) who had complaints of loose stools during iron therapy with a statistically significant relationship (p value=0.024). This suggests that gastrointestinal side effects have a prominent impact on iron therapy. However, stomach pain (p value=0.770) and constipation (p value=0.751) have no significant relationship in our study.

Intercurrent infections also play a role in iron absorption or utilization. The history of any hospitalization due to various reasons was a strong factor in deciding the outcome. A total of 125 out of 129 controls who improved did not have any history of hospital admission, while 12 out of 25 cases who did not improve had a history of hospital admission. This suggests frequent infections may be a factor in non-improvement despite regular iron intake.

Limitations

Limitations of the study are a smaller sample size and a hospital-based study.

CONCLUSION

This study highlights the significant prevalence of IDA among children 1 to 5 years of age. It identifies various risk factors, including young age, pica, lower socioeconomic status, and non-exclusive breastfeeding, contributing to the development of IDA. Additionally, dietary factors play a crucial role, with the consumption of tea, coffee, and milk alongside iron supplementation negatively impacting iron absorption and treatment outcomes. Conversely, the intake of Vitamin- C rich foods demonstrate a positive association with treatment response.

Recommendations

To ensure optimal treatment outcomes, it is recommended to avoid the consumption of tea, coffee, and certain foods in paediatric patients requiring iron supplementation. Educating parents about these dietary restrictions is essential to ensure better treatment outcomes in paediatric patients.

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