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Original Research Article

Clinical profile of hypochromic microcytic anemia in Chittoor district, India

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ABSTRACT

Background: Anemia is not a diagnosis by itself like fever but merely is an objective sign of the presence of disease. The correct diagnostic terminology for a child with anemia requires the detection of etiology, pathology, and pathogenesis of the anemia. To evaluate the role of therapeutic oral iron therapy as a diagnostic approach to hypochromic microcytic anemia.
Methods: The present study is a retrospective study conducted at the teaching hospital, Chittoor district from September 2019 to December 2019. A total number of 350 cases of anemia were studied from both inpatient and outpatient services in the age group 2 months to 12 years. Hemogram, Hb Electrophoresis, and bone marrow study as necessary based on individual cases.
Results: From the above analysis, the mean Hb% at the time of entry to study was 7.36gms%. The mean Hb% after the iron therapy was 11.8gms%. The mean increase in Hb was 4.4gms%. In this study, the average RBC count was 2.9 million cells/cumm.
Conclusions: A therapeutic trial of oral iron is an appropriate initial step in the diagnostic approach of hypochromic microcytic anemia. Costly investigations like Hb electrophoresis and bone marrow study are required only in selected cases.

Keywords: Hemoglobin, Iron deficiency anemia, Oral iron therapy, RBC Count

INTRODUCTION

Anemia is a major world health problem and is an important cause of morbidity and mortality much of which can be preventable. Man has only partially adapted to the rapid growth in the human population and environmental changes and anemia is one of the effects of these factors.[1] Thus still the most common cause of anemia in children is related to nutritional deficiency, especially iron deficiency. Initially, man depends mostly on animal food and as he learned agricultural practices, the contribution of animal food reduced drastically to less than 5%.[2] This profoundly affected the bioavailable iron and folate resulting in nutritional deficiency anemia. Anemia is defined as the reduction of RBC volume or hemoglobin concentration below the range of values for a particular age and sex.[3] The detection and diagnosis of anemia are frequently the focus of attention in the care of patients because accurate quantification and rational analysis of the problem is a must. Anemia is not a diagnosis in itself like fever but merely is an objective sign of the presence of disease.[4] A systematic approach through proper history, physical examination, and relevant investigations are very essential to diagnose the various causes of anemia.[5] Nutritional deficiency anemia particularly iron deficiency anemia is the most common type of anemia among these children. In countries like India iron deficiency anemia coexists with other types of anemia in almost every child with anemia.[6] This iron deficiency masks the underlying diseases especially thalassemia trait which cannot be diagnosed even by higher investigations like Hb electrophoresis unless the

iron deficiency is corrected before the electrophoresis.[7] Though thalassemia trait cases can lead a normal life, unless they are identified and genetic counseling has given, they will transmit the gene to next-generation leading to future thalassemia major cases which is a major burden to the family as well as the society, which is a preventable one.[8] Beta thalassemia is the most common single-gene disorder in this country. Beta thalassemia major is a homozygous severe transfusion-dependent condition with most of the children dying in childhood. Beta thalassemia trait is a heterozygous genetic disorder having normal growth and development and the individual may occasionally have mild anemia.[9]

METHODS

The present study is a retrospective study conducted at the teaching hospital, Chittoor district from September 2019 to December 2019. A total number of 350 cases of anemia were studied from both inpatient and outpatient services in the age group 2 months to 12 years. Hemogram, Hb Electrophoresis, and bone marrow study as necessary based on the individual.

Inclusion criteria

- The criteria used in the selection of children as those whose hemoglobin less than 11gm% in age group less than 6 years and whose hemoglobin less than 12gm% in age group 6 to 12 years along with peripheral smear showing hypochromic microcytic anemia.

Exclusion criteria

- This study had excluded the cases, who were already diagnosed elsewhere or who were on treatment before hospitalization or peripheral smear showing macrocytic and normochromic normocytic anemia or the neonates.

Ethics committee approval was obtained. Informed consent was obtained from all parents. All the 350 cases of anemia were studied by taking a detailed history and thorough clinical examination with meticulous care and the findings were recorded in the predesigned proforma annexed in the last few pages.

Hemoglobin estimation and peripheral smear study were done in all cases. All children in the study group of more than one year of age and those with less than one year of age with no hepatosplenomegaly or frontal bossing were dewormed by giving a single dose of Albendazole and were started on oral Iron therapy. Albendazole was given in a dose of 400mg for children more than 2 years of age and 200 mg for children less than 2 years of age. Oral iron preparations used in this study were Ferrous sulfate. Each ferrous sulfate tablet containing an elemental iron of 20 mg. Iron was prescribed at a dose of 3-6mg/kg/day in 2-3 divided doses. Drugs were given once in 2 weeks. During each visit, these children were followed up by Hb estimation and checked for compliance. At the end of 3 months' completion of iron, therapy repeats peripheral smear examination was done. Those cases improved with iron that is peripheral smear showing the normochromic normocytic type of RBC's were considered as Iron deficiency anemia and they were prescribed iron for one more month to replenish the stores and then iron therapy stopped. Those cases not improved with iron were further evaluated using automated. hemogram, Hb Electrophoresis, and bone marrow study as necessary based on individual cases. All children less than 1 year of age with severe pallor, hepatosplenomegaly, and frontal bossing were not given iron therapy. These children were evaluated using automated hemogram and Hb electrophoresis. A bone marrow study was done if necessary.

Statistical analysis

The information collected regarding all the selected cases were recorded in a master chart. Using this software frequency, percentage, mean, standard deviation, chi-square, and 'p' values are calculated. Kruskal Wallis chi-square test was used to test the significance of differences between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote a significant relationship.

RESULTS

In this study a total of 400 children were included. 350 cases turned up for regular follow up. 50 cases lost the follow-up. Out of 350 children in the study group, 205 (58.6%) were males and 145 (41.4%) were females. Of the above analysis, 142 cases of severe anemia, 188 cases of moderate anemia, and 20 cases of mild anemia were documented. Since this is a hospital-based study number of moderate to severe anemia cases are more (Table 1).

Table 1: Severity of anemia.

Degree of anemia	No.	%
Severe (<7mg%)	142	40.6
Moderate (7-9.9gm%)	188	53.7
Mild (10-10.9gm%)	20	5.7

The various modes of presentation of anemia were as follows. 331 cases had easy fatiguability. 66 cases had H/o pica, 9 cases had H/o passage of worms in stools, 340 cases had a fever, and 11 cases presented with breathlessness. Many cases had more than one complaint (Table 2).

In this study, the various findings among children with anemia were as follows. Pallor was present in almost all cases. Koilonychia in 47 cases, frontal bossing in 10 cases. Pedal edema in 1 case. Hepatomegaly in 69 cases and splenomegaly in 68 cases. Many cases had more than one sign (Table 3).

Table 2: Complaints.

Complaints	No.	%
Easy fatiguability	339	96.9
Pica	66	18.9
Passing worms in stools	9	2.6
Fever	340	97.1
Breathlessness	21	3.1

Table 3: Signs.

Signs	No.	%
Pallor	350	100
Koilonychia	47	13.4
Frontal bossing	10	2.9
Pedal edema	1	0.3
Hepatomegaly	69	19.7
Splenomegaly	68	19.4

In this study, splenomegaly was present in 68 cases (19.4%) Out of 68 cases, 51 cases (14.8%) of IDA had mild splenomegaly.

The remaining 17 cases belong to the Thalassemia group. Among them, 5 cases had mild splenomegaly. 10 cases had moderate splenomegaly and 2 cases had massive splenomegaly (Table 4).

Table 4: Splenomegaly and type of anemia.

Type of anemia	Splenomegaly		
	Mild <4cm	Moderate 4 to 7cm	Massive >7cm
IDA	51	0	0
Others	5	10	2

From the below analysis, the mean Hb% at the time of entry to study was 7.36gms%. The mean Hb% after the iron therapy was11.8 gms%. The mean increase in Hb was 4.4gms% (Table 5).

Table 5: Hemoglobin percent.

Hb%	Range	Mean	SD
Initial Hb	3.2-10.5	7.36	1.31
Repeat Hb	5.4-12.8	11.8	0.79
Increase in Hb	0-8	4.4	1.4
% of increase	0-250	64.5	32.3

Table 6: Response to iron.

Response to Iron	Cases	
	No.	%
Positive	333	95.1
Negative	7	2
Iron not given	10	2.9%
Total	350	100

In this study, 333 cases improved with oral iron therapy, 7 cases not improved with iron, and 10 cases do not receive iron therapy (Table 6).

From the below analysis, Iron deficiency anemia is the major cause which constitutes about 95% (333 cases). The other causes were 7 cases of Thalassemia major, 5 cases of Thalassemia trait; thalassemia intermedia one case; Hb variant E one case; unstable hemoglobinopathy one case and alpha thalassemia two cases (Table 7).

Table 7: Diagnosis.

Diagnosis	Cases	
	No.	%
Iron deficiency anemic	333	95.1
Alpha Thalassemia	2	0.6
Thalassemia intermedia	1	0.3
Thalassemia major	7	2.0
Thalassemia trait	5	1.4
Hb variant E	1	0.3
Unstable Haemoglobinopathy	1	0.3
Total	350	100

From the bbelow analysis, in case of IDA, the mean rise in Hb% after oral iron therapy was 4.46gm% whereas in the other types the mean rise in Hb% was only 1.81% Thus the type of anemia and Hb% changes after oral iron therapy was statistically significant (Table 8).

Table 8: Type of anaemia and Hb% changes.

Hb	Types of anemia				p-value
	IDA		Others		
	Mean	SD	Mean	SD	
Inial Hb	7.42	1.29	6.12	1.12	0.0001 significant
Repeat Hb	11.89	0.41	7.7	2.29	0.001 significant
Increase	4.46	1.34	1.81	1.97	0.0012 significant
% of increase	65.2	31.9	30.6	34	0.0028 significant

Table 9: Type of anemia and response to iron.

Types of anemia	Response to iron					
	Positive		Negative		Not given	
	No.	%	No.	%	No.	%
IDA	333	100	0	0	0	0
Others (17)	0	0	7	41.2	10	10
p	0.0001 Significant					

From the above analysis, it is seen that all cases of IDA, 333 cases improved with iron, and among the other types of anemia 7 cases not improved and 10 cases were not started on iron therapy. p-0.0001. Thus the relation

between the type of anemia and responds to iron is statistically significant (Table 9). From the below analysis, the mean rise in Hb% in cases improved with iron was 4.45gm% whereas only 1.45%, in cases with no response to iron therapy. Thus the response to iron and the rise in Hb% are statistically significant (Table 10).

Table 10: Response to iron and Hb% changes.

Parameter	Response to iron				p
	Positive		Negative		
	Mean	SD	Mean	SD	
Initial Hb	7.4	1.3	6.68	0.87	0.118 not Significant
Repeat Hb	11.87	0.53	7.75	1.16	0.0006 Significant
Increase	4.45	1.35	1.45	0.21	0.0012 Significant
% of increase	65.15	32	23.12	1.91	0.003 Significant

DISCUSSION

In this study, the incidence of hypochromic microcytic anemia is more common in males (58.6%) than female children (41.4%). But this is not statistically significant. Thus the most common age group affected is in between 1-3 years of age. This is similar to Fairbanks VF. et al, study which states that the peak incidence of nutritional anemia in children occurs between 6 months to 3 years of age. In this study, the presenting complaints of hypochromic microcytic anemia include easy fatiguability (96.9%), Pica in 18.9%, worm infestation in 2.6%, fever in 97.1% and breathlessness in 3.1%. Fever is the most common presenting complaint. Since this is a hospital-based study, most of the cases who came for upper respiratory tract infection and viral fever are incidentally found to be anemic and included in the study. Hence fever is present in the majority of cases.[10] In this study, PICA is present in 66 cases (18.9%). This symptom is found in 50% of children in a study conducted by Gomber S et al. Worm infestation is present only in 2.6% of cases. The low prevalence of parasitism in this study may be because of the widespread use of anthelminthic drugs by health officials. In this study, Pallor is present in all cases. Out of 350 cases, 47 cases (13.4%) have koilonychia. 2.9% of cases have frontal bossing. Malar prominence along with frontal bossing is even present in severe iron deficiency anemia.

Hepatomegaly is present in 69 cases (19.7%) and splenomegaly is present in 68 cases (19.4%). In this study, hepatosplenomegaly is seen in 14.8% of the cases of IDA. A mild degree of hepatosplenomegaly is present in iron deficiency anemia.[11] Goodnough et al, state that a mild degree of hepatosplenomegaly is not uncommon in IDA. In this study, all cases of hypochromic microcytic anemia are given Oral iron in the form of ferrous sulfate tablets containing 20 mg elemental iron at a dose of 3-6 mg/kg/day in 2-3 divided doses. Oral iron therapy is given for 3 months. At the end of 3 months, cases improved with iron are those with true iron deficiency anemias. Only those cases not improved with iron therapy are further investigated. Thalassemia is the next most common cause of hypochromic microcytic anemia. It is an inherited genetic disorder causing a real burden to the family and the society.[12] Thalassemia trait cases have to be detected to prevent future homogenous thalassemia major cases. Hb electrophoresis is the investigation of choice. If there is coexisted iron deficiency in the thalassemia trait case, even by Hb electrophoresis it cannot be detected. It has to be corrected before Hb electrophoresis. This emphasizes once again that oral iron has to be given to all cases of hypochromic microcytic anemia as done in this study.[13] This concept is supported by Johnson CS et al. The pediatrics clinics of North America that the patient should not be iron deficient at the time of electrophoresis as iron deficiency depresses delta globin synthesis, obscuring a rise in HbA2. Iron deficiency causes reduced levels of HbA2. Elevated levels cannot be demonstrated until the iron deficiency is corrected. Nelson states that thalassemia trait is frequently misdiagnosed as an iron deficiency in children. A short course of iron and reevaluation is all that is required to identify children who will need further evaluation.[14] The most common cause of hypochromic microcytic anemia in this study is Iron deficiency anemia. This finding is similar to the studies conducted by Kapoor D et al. Automated hemogram was done in all these 7 cases to demonstrate low MCV (less than 75fl) even after 3 months of iron therapy. An automated hemogram was done to confirm the findings on the peripheral smear.[15] Out of 7 cases, 5 cases of thalassemia trait (1.4%) were detected by Hb electrophoresis. Among the 10 cases, 7 cases are diagnosed as Thalassemia major. It showed elevated HbF and low HbA. One case of unstable hemoglobinopathy was diagnosed. He is a 1-year-old boy presented with severe pallor, fever, and hepatosplenomegaly. Peripheral smear showed severe hypochromic microcytic anemia. Hb electrophoresis showed decreased HbA, Normal HbA2, HbF not elevated and unidentified Peak was present.[16] The child became more pallor and sick during intercurrent illness and was symptomatically treated.[17] In between the illness, the boy was normal without pallor. Of the remaining 2 cases, one was that of a 4 months old female child and another that of a 7 months old female child both of whom presented with severe pallor and hepatosplenomegaly. Peripheral smear showed severe hypochromic microcytic anemia.[18] Hb electrophoresis was normal in both cases. Both were subjected to bone marrow smear study. In both cases, erythroid hyperplasia was seen. These 2 cases could be that of Alpha thalassemia. Hb electrophoresis by the HPLC method could not detect alpha thalassemia. Genetic studies are further required to confirm the diagnosis.[19]

CONCLUSION

A therapeutic trial of oral iron is an appropriate initial

step in the diagnostic approach of hypochromic microcytic anemia. Costly investigations like Hb electrophoresis and bone marrow study are required only in selected cases.

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