

A STUDY OF CLINICAL AND HAEMATOPATHOLOGICAL CORRELATION OF HAEMOLYTIC ANAEMIAS IN CHILDREN

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ABSTRACT

Anaemia is a manifestation of disease, not a disease in itself. Anaemia is a frequent laboratory abnormality in children. As many as 80 children in developing countries will be anaemic at some point by the age of 18 years. Most children with anaemia are asymptomatic, but have abnormal lab data on routine screening. Physical examination is also many a times normal. Detection and diagnosis are essential for rational analysis and management. Among the anaemias, Haemolytic anaemias are unique. The aetiology is diverse and many hereditary and acquired disorders play a role. Clinical presentation depends on the onset of erythrocyte destruction. The morbidity depends on the aetiology of haemolysis. This study focuses on the prevalence, age of presentation and clinical profile of haemolytic anaemia in children and will help in early diagnosis and planning of appropriate treatment.

AIMS AND OBJECTIVES OF STUDY

To study the prevalence of various types of Haemolytic anaemia in children admitted in Paediatric wards at a tertiary care Hospital. To study the clinical profile, age at first presentation and the aetiology of the hereditary haemolytic anaemia and to study the utility of laboratory procedures in the diagnosis of hereditary haemolytic anaemia. To study the complications, treatment protocols and the response to treatment in hereditary haemolytic anaemia.

METHODOLOGY

Study Design: Prevalence study, Study Place: Department of Paediatrics, Coimbatore Medical College, Coimbatore, Study Period: 18 months (Nov 2012 - April 2014).

INCLUSION CRITERIA

The sample consisted of children aged 1 month to 17 years, presenting with clinical symptoms and signs suggestive of haemolytic anaemia and those with peripheral blood smear suggestive of haemolysis.

EXCLUSION CRITERIA

Neonates were excluded from the study.

MANOEUVRE

In the present hospital-based study, the prevalence of various types of haemolytic anaemia in children attending Coimbatore Medical College and Hospital was studied. In children diagnosed with hereditary haemolytic anaemia the clinical profile, complications, utility of the diagnostic procedures, treatment protocols and the response to the treatment were studied.

RESULTS/CONCLUSION

In the present hospital-based prevalence study, 52 children were diagnosed as having Haemolytic anaemia. In those children diagnosed as hereditary haemolytic disorders, the age at first presentation, clinical profile, complications, treatment protocols and response to the treatment were studied. In our study, the youngest child was 3-month-old female and the oldest was 3-year-old male. Most of the children were presented in the age group between 3 months to 12 months - 8 cases (66.66%). Mean age at presentation is 9 months. In the present study, the frequency of Hb-S related disorders was high constituting 57.57% followed by Thalassemia syndromes constituting 39.36%. Average age at presentation of Thalassemia major was 9 months; Sickle cell anaemia 6 yrs.; Sickle cell trait 4 yrs. and Sickle thalassemia 5.5 yrs. Male: Female ratio for Thalassemia major was 2:1; Male: Female ratio for Sickle cell anaemia was 26:1. The common mode of presentation/complication for Thalassemia major was anaemia with congestive cardiac failure; vaso-occlusive crisis for sickle cell anaemia and anaemia for sickle cell disease. Family history of consanguinity was positive in 69.69% of cases. When growth parameters were studied in children with beta thalassemia major, growth retardation was observed in 75% of cases; and in sickle cell disorders 78.4% of children had growth retardation. Peripheral smear evidence of haemolysis was positive in 90.9% cases suggesting that as the most useful method for screening. In children diagnosed as having Thalassemia major, 72% received 15 blood transfusions at the age of 0-2 yrs. and in children diagnosed as having Sickle cell disorders 50% received 1st blood transfusion at the age of 3-5 yrs. In those children receiving chelation therapy, side effect reported was neutropenia.

KEYWORDS

Anaemia, Thalassemia, Haemolytic, Sickle Cell.

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INTRODUCTION

Anaemia is a frequent laboratory abnormality in children. As many as 80% children in developing countries will be anaemic at some point by the age of 18 years.^[1] Most children with anaemia are asymptomatic and have an abnormal value or haematocrit level on routine screening.

The physical examination is important, but will be unremarkable in most children with anaemia. Detection and diagnosis of anaemia are frequently the focus of attention in the care of the patients, because accurate quantification is not difficult to achieve and rational analysis of the problem is possible. Anaemia is a manifestation of disease, not a disease in itself.^[2]

The term "Haemolytic Anaemia" is limited to conditions in which the rate of red cell destruction is accelerated and the ability of the bone marrow to respond to the stimulus is unimpaired. The aetiology of haemolysis is diverse and it is the final event triggered by a number of hereditary and acquired disorders. Clinical presentation depends on whether the onset of haemolysis is gradual or abrupt and on the onset of

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erythrocyte destruction. The morbidity is dependent on the aetiology of haemolysis and the underlying disorder. This study focuses on the prevalence, age of presentation and clinical profile of haemolytic anaemia in children and will help in early diagnosis and planning of appropriate treatment.

AIMS AND OBJECTIVES OF STUDY

Primary Objective

To study the prevalence of various types of Haemolytic anaemia in children admitted in Paediatric wards at a tertiary care hospital.

Secondary Objective

To study the clinical profile, age at first presentation and the aetiology of the hereditary haemolytic anaemia and to study the utility of laboratory procedures in the diagnosis of hereditary haemolytic anaemia and to study the complications, treatment protocols and the response to treatment in hereditary haemolytic anaemia.

METHODOLOGY

Study Design: Prevalence study.

Study Place: Department of Paediatrics, Coimbatore Medical College, Coimbatore.

Study Period: 18 months (Nov 2012-April 2014).

STUDY POPULATION

Inclusion Criteria

The sample consisted of children aged 1 month to 17 years, presenting with clinical symptoms and signs suggestive of haemolytic anaemia and those with peripheral blood smear suggestive of haemolysis.

Exclusion Criteria

Neonates were excluded from the study.

In these children further investigations for the aetiological diagnosis of haemolytic anaemia was done and prevalence of various types was studied. In the children diagnosed as having hereditary haemolytic disorders, the clinical profile, complications, treatment protocols and the response to the treatment were studied.

MATERIALS AND METHODS

In the present hospital-based study, the prevalence of various types of haemolytic anaemia in children attending Coimbatore Medical College and Hospital was studied. In children diagnosed with hereditary haemolytic anaemia, the clinical profile, complications, utility of the diagnostic procedures, treatment protocols and the response to the treatment were studied.

The children attending the hospital with hereditary haemolytic anaemia were included in the study. The clinical and laboratory findings were analysed; new-born were excluded children.

The Data Obtained were Analysed in SPSS Version 16 Software as follows

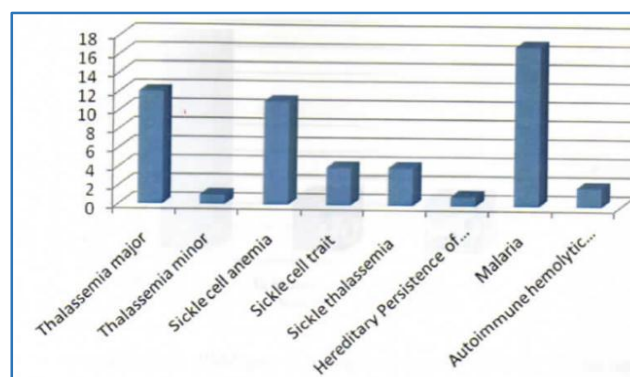
- Features of study population (Age, sex).
- Percentage of types of Haemolytic Anaemia.
- Age at first presentation of Thalassemia major.

- Mode of presentation of Thalassemia major and Sickle cell anaemia.
- Quantification of Haemoglobin variants based on HPLC analysis.
- Age distribution of children at 1st transfusion.
- Distribution of patients according to number of transfusions and clinical data of Thalassemia major.

RESULTS

In the present hospital-based prevalence study, 52 children were diagnosed as having haemolytic anaemia. In those children diagnosed as hereditary haemolytic disorders, the age at first presentation, clinical profile, complications, treatment protocols and response to the treatment were studied. In our study the youngest child was 3-month old female and the oldest was 3-year-old male. Most of the children were presented in the age group between 3 months to 12 months - 8 cases (66.66%). Mean age at presentation is 9 months.

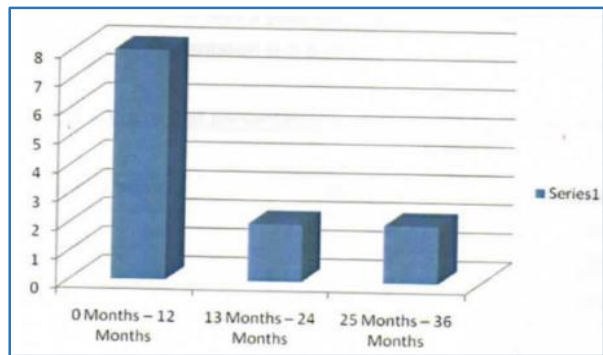
Types of Haemolytic Anaemia	No. of Cases	%
Hereditary Haemolytic Anaemia		
Thalassemia Major	12	23.07%
Thalassemia Minor	1	1.97%
Sickle Cell Anaemia	11	21.15%
Sickle Cell Trait	4	7.69%
Sickle Thalassemia	4	7.69%
Hereditary Persistence of Foetal Haemoglobin	1	1.92%
Acquired Haemolytic Anaemia		
Malaria	17	32.69%
Autoimmune Haemolytic Anaemia	2	3.84%



Types of Haemolytic Anaemia

Age in Months	No. of Cases	Percentage
0-12	8	66.66%
13-24	2	16.66%
25-36	2	16.66%

Age at First Presentation with Thalassemia Major



Age at First Presentation with Thalassemia Major

MODE OF PRESENTATION

Clinical Features	No. of Cases	Percentage
Pallor, Breathlessness (CHF)	8	66.66%
Pallor	3	25%
Chronic Cough	1	8.3%
Mode of Presentation - Thalassemia Major		

Clinical Features	No. of Cases	Percentage
Arthralgia	5	45.45%
Pallor	2	18.18%
Pallor Mass Per Abdomen	1	9%
Pallor, Breathlessness (CHF)	1	9%
Fever, Chest Pain	1	9%
Pallor, Arthralgia	1	9%
Mode of Presentation - Sickle Cell Anaemia		

Hb Variant	Thalassemia Major	Thalassemia Minor	Sickle Cell Anaemia	Sickle Cell Disease	HPFH
Hb A (%)	0.1-81.1	93.9	0.0-34.9	24.3-74.2	0.4
Hb A2 (%)	2-3.8	5.7	1.0-7.6	2.8-4.7	0.0
Hb F (%)	17.9-97.9	0.5	7.3-42.7	0.7-18.9	99.6
Hb S (%)	0.0	0.0	51.0-83.3	22.3-58.7	0.0
Quantification of Haemoglobin Variants Based on HPLC Analysis					

Age at 1 st Transfusion	0-2 yrs.	3-5 yrs.	6-13 yrs.
No of Children with Thalassemia	8	3	-
No. of Children with Sickle Cell Disorders	2	9	7
Age Distribution of Children at 1st Transfusion			

72% of children with Thalassemia major received 1st blood transfusion at the age of 0-2 yrs. and 28% at the age of 3-5 yrs.; 11.11% of children with sickle cell disorders received 1st blood transfusion at the age of 0-2 yrs.; 50% at the age of 3-5 yrs.; and 38.8% at the age of 6-13 yrs.

No. of Transfusions	T1	T2	T3	T4	T5	T6	T7	T8 & More
No. of Patients	-	1	5	2	-	-	-	3
Hepatomegaly	-	1	4	2	-	-	-	3
Splenomegaly	-	1	4	2	-	-	-	3
Distribution of Patients According to No. of Transfusions & Clinical Data in Thalassemia Major								

In children diagnosed as having Thalassemia major, 90.9% had hepatosplenomegaly.

DISCUSSION

Prevalence of Various Types of Haemolytic Anaemia

In the present study, 12 children were diagnosed as having Thalassemia major (23.07%) and 1 child was diagnosed as having Thalassemia minor (1.92%). Chatterjee JB, et al reported the prevalence of Thalassemia as 3.5 to 14.9% in India.^[3] Banerjee et al reported that in India prevalence of Thalassemia minor varies between 1 and 17% in normal population.^[4] In the present study, 11 children were diagnosed as having Sickle cell anaemia (21.15%) and 4 children were diagnosed as Sickle cell trait (7.69%). R.S. Balgir reported the distribution of Sickle cell disorders in different states of India and in Andhra Pradesh; the distribution was reported as 1 to 35.7%.^[5]

In our study, 11 children were diagnosed as Sickle cell anaemia out of total 16 cases of Sickle cell disorders (68.75%) and 4 children were diagnosed as Sickle cell trait (36.36%). Kamble M et al reported similar findings - Sickle cell anaemia constituted 61.6% and Sickle cell trait constituted 38.4% in total Sickle cell disorders.^[6] In the present study, 17 children were diagnosed as having Malaria (32.69%).

The prevalence of Malaria was reported as 58.6% in India by Singh N et al.^[7] Mohapatra MK reported that severe anaemia was the presenting feature in 6.9% of patients suffering from Malaria.^[8] In our study, 2 children were diagnosed as having Autoimmune haemolytic anaemia (3.84%). One of the children was diagnosed previously as having Systemic lupus erythematosus. Sultan SM et al reported that 6.6% of children with SLE manifested with severe haemolytic anaemia.^[9]

Age at First Presentation

In the present study most of the children diagnosed as Thalassemia major, first presented at the age between 3 to 12 months. In our study in children with Sickle cell anaemia, 63.63% first presented below the age of 6 yrs. This is in accordance with the study results of Kamble M et al, who reported that 62% of children were presented below the age of 5 yrs. In our study, average age at first presentation in Sickle cell anaemia was 6 yrs. This is in accordance with the study result of Patel AB et al, who reported the average age at presentation was 7.05±3.26 yrs.^[10]

Sex Distribution

In the present study, in children diagnosed as having Thalassemia major, the Male:Female ratio was 2:1. The study of D. Shaligram et al showed the M:F ratio of 1.421.^[11] Sex distribution of Sickle cell anaemia in the present study showed the M:F ratio of 2.6:1. M:F ratio for Sickle cell trait was 1:1. Kamble M et al reported the M:F ratio of 1.65:1 in Sickle cell anaemia and 1.71:1 in Sickle cell trait.^[6]

Frequency of Complications

In the present study, the frequency of congestive heart failure in Thalassemia major is 66.66%. D. Shaligram et al reported that congestive heart failure due to Thalassemia and its treatment was present in 35.8% of children.^[11] In the present study, Growth retardation was reported in 75% of Thalassemia patients. Banerjee J. et al reported that 71% of children suffering from Thalassemia showed growth retardation.^[4] In the present study in children with Thalassemia major, Thalassemic facies was present in 9

children out of 12 [75%]. In the study of D. Shaligram et al, it was reported that Thalassaemic facies was present in 89.7% of children.^[11]

Comparison of Frequency of Complications in Children with Thalassemia Major

In this study, the frequency of vaso-occlusive crisis in Sickle cell anaemia was 54%. Kamble et al reported that vaso-occlusive crisis (23.2%) was the commonest crisis. Serjeant GR et al also reported that vaso-occlusive crisis is the most common and is the hallmark of patients with sickle cell disease.^[12] In the present study, the frequency of dactylitis was more in the age group of 1-5 yrs. constituting 62.5% of the children. This is in accordance with the study result of Stevens MCG et al who reported that dactylitis occurs almost entirely in the first 4 years of life with a peak incidence at approximately 1 year of age.^[13] In the present study, the mean values of Hb F in HPLC analysis for Sickle cell disorders were reported as follows: For Sickle cell anaemia - 19.8% for Sickle cell disease - 8.76%. R. S. Balgir reported the mean values of Hb F in Sickle cell anaemia as 10.4 and in Sickle cell disease as 6.6%.

Treatment Protocol

In the present study in children diagnosed as having Thalassemia major, 72% received 1st blood transfusion at the age of 0-2 yrs. The range of number of transfusions was 2-25. Mean age of patients was 1.3 yrs.; and in children diagnosed as having Sickle cell disorders 50% received 1st blood transfusion at the age of 3-5 yrs. The range of number of transfusions was 2-10. Mean age of patients was 5.5 yrs.^[14] in the present study. With blood transfusions, 17 children developed febrile reactions (58.62%), one child developed allergic reaction (3.4%).^[11] In the present study, 2 children with Thalassemia major were under chelation therapy (Oral Deferiprone).^[15] The complication of neutropenia was observed in one of them.^[16]

SUMMARY

In this study, 52 children aged from 1 month to 17 years presenting with clinical symptoms and signs suggestive of haemolytic anaemia were evaluated for the aetiological diagnosis of haemolytic anaemia. The children were diagnosed as having the following types of haemolytic anaemia: Thalassemia major constituted 12 cases (36.36%); Thalassemia trait, 1 case (3%); Sickle cell anaemia, 11 cases (3.33%); Sickle cell trait, 4 cases (12.12%); Sickle thalassemia, 4 cases (12.12%); Hereditary persistence of foetal haemoglobin, 1 case (3%); Malaria, 17 cases (32.69%); and Autoimmune haemolytic anaemia, 2 cases (3.84%). In those children diagnosed as having hereditary haemolytic anaemia the clinical profile, complications, treatment protocol followed and the response to the treatment were studied and the results were compared with those of similar studies. Age wise distribution of Thalassemia major. Most of the children first presented at the age of 3 months to 12 months - 8 cases (66.66%). Average age at presentation is 9 months. Average age at presentation of Sickle cell anaemia is 6 years. For Thalassemia major, Male:Female ratio is 2:1; for sickle cell anaemia, 2.6:1; for Sickle cell trait, 1:1 and for Sickle thalassemia, 1:3.

CONCLUSION

In the present hospital-based prevalence study, 52 children were diagnosed as having haemolytic anaemia and in those 33 were diagnosed as having hereditary haemolytic anaemia. The results were compared with those of similar studies. The following conclusions are drawn from the study:

- In the present study, the frequency of Hb-S related disorders was high constituting 57.57% followed by Thalassemia syndromes constituting 39.36%.
- Average age at presentation of Thalassemia major was 9 months; Sickle cell anaemia 6 yrs., Sickle cell trait 4 yrs. and Sickle thalassemia 5.5 yrs.
- Male:Female ratio for Thalassemia major was 2:1; Male:Female ratio for Sickle cell anaemia was 26:1.
- The common mode of presentation/complication for Thalassemia major was anaemia with congestive cardiac failure; vaso-occlusive crisis for sickle cell anaemia and anaemia for sickle cell disease.
- Family history of consanguinity was positive in 69.69% of cases.
- When growth parameters were studied in children with beta thalassemia major, growth retardation was observed in 75% of cases; and in Sickle cell disorders 78.4% of children had growth retardation.
- Peripheral smear evidence of haemolysis was positive in 90.9% cases suggesting that as the most useful method for screening.
- In children diagnosed as having Thalassemia major, 72% received 15 blood transfusions at the age of 0-2 yrs. and in children diagnosed as having Sickle cell disorders 50% received 1st blood transfusion at the age of 3-5 yrs.
- In those children receiving chelation therapy, side effect reported was neutropenia.

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