



ETIOPATHOLOGICAL EVALUATION OF ANAEMIA IN CHILDREN – A HOSPITAL BASED STUDY.

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ABSTRACT

Introduction:- The present study was undertaken to evaluate clinical, haematological and biochemical parameters to aid in understanding and to determine the etiopathological patterns of anaemia and their causes and various morphological types of anaemias in children.

Materials and methods:- The present study is a cross sectional study, conducted on 600 hospitalised patients in the age group of 6 months to 12 years with anaemia and also those who presented with other complaints incidentally had haemoglobin values less than 12gm/dl. All required haematological, biochemical tests, bone marrow examination; radiological tests were done to see the etiological and morphological type of anaemia in the study group.

Results :- In the present study, pre-school children were found to be the most affected (45%). Nutritional diseases were seen to be most commonly associated with anaemia, followed by infectious diseases. The most common morphological type of anaemia was microcytic hypochromic anaemia (63.3%). Iron deficiency anaemia (43.3%) was the most common etiological type. HbE predominated among the haemoglobinopathies (22 out of 60) in children in this region. Iron deficiency anaemia is predominantly seen in the school going children (119 cases out of 260, i.e. 45.8%) Anaemia due to infections is seen more in the pre-school children (53 out of 104 cases i.e. 51%) followed by infants (33.6%). Haemoglobinopathies are more predominant in the pre-school children (50%). Leukemia is seen more commonly in the pre-school children (30 cases out of 50 cases i.e. 60%).

Conclusion:- In our study nutritional deficiency diseases are found to be the most common causes of anaemia in paediatric age group and infectious diseases are also found more commonly associated with anaemia in children. Preschool children were found to be most commonly affected, hence a compulsory screening strategy is recommended to detect anaemia in children and evaluate the aetiology to treat it early and give them a better healthy life.

KEYWORDS :

INTRODUCTION:

Anaemia in children is one of the major social health problems in India and in many parts of the world, since anaemic children have reduced exercise capacity, slower rate of growth, impaired cognitive development, and delayed wound healing and are also at a risk of dying due to complications associated with malnutrition and infection. As many as 20% of the children in USA and 80% of the children in the developing countries, are anaemic at some point by the age of 18.2 Because of these factors, the study of the etiopathogenesis of anaemia in infancy and childhood has attracted wide attention in the recent years in India.¹

Anaemia is defined as decreased concentration of haemoglobin and RBC mass as compared to the values in age and sex matched controls.² Most children with anaemia are asymptomatic. Infrequently, a child with anaemia may have pallor, fatigue and jaundice, but may or may not be critically ill.

A newborn reclaims and stores iron as the haematocrit levels decrease during the first few months of life. Therefore in full term infants iron deficiency is rarely a cause of anaemia until the age of six months. In premature infants iron deficiency can occur only after the birth weight has been doubled. Other causes like X-linked - glucose-6-phosphate dehydrogenase (G6PD) deficiency, Autosomal recessive - Pyruvate kinase deficiency.

Recurrent diarrhoea raises malabsorption, haematocasia in inflammatory bowel disease, and presence of occult blood due to upper gastrointestinal bleed may lead to the cause of anaemia.

In screening situations, when anaemia is found, the patient should undergo a complete blood count (CBC) examination to see the type - microcytic, normocytic, or microcytic followed by diagnostic workup according to the type.

The next step of anaemia work-up should include a peripheral blood smear examination and measurement of the reticulocyte count. Pathologic findings in the peripheral smear can indicate the aetiology of the anaemia based on the red cell morphology. Basophilic stippling in thalassemia syndromes, iron deficiency and lead poisoning; Howell-jolly bodies in asplenia, pernicious anaemia and severe iron deficiency anaemia; Cabot's ring bodies in lead poisoning, pernicious

anaemia, and hemolytic anaemias; Heinz bodies in thalassemia, asplenia and chronic liver disease.²

Reticulocyte count helps to distinguish a hypoproliferative anaemia from increased RBC destruction. The corrected reticulocyte count is a more accurate indicator of erythropoietic activity. A corrected reticulocyte count above 1.5 suggest increased RBC production.²

Other tests for evaluation of the cause of anaemia are - serum iron level, total iron binding capacity (TIBC), lead level, serum ferritin level, direct Coombs test, G6PD assay, haemoglobin electrophoresis, lactate dehydrogenase (LDH), haptoglobin, vitamin B12, folate assay, thyroid stimulating hormone, osmotic fragility, bone marrow aspiration or biopsy may be indicated.^{2,3}

The clinicopathological patterns of anaemia in children are often reflected by their underlying etiopathologic factors and the investigation of anaemia is mainly haematological. A thorough history elicitation, physical examination, complete hemogram including examination of peripheral smear and the required biochemical investigations would be the starting point of evaluation. The present study was undertaken to evaluate haematological and biochemical parameters to aid in understanding the clinicopathological patterns of anaemia and their causes in children. The main aim of the study was to determine the prevalence, patterns, and various morphological types of anaemias in children.

MATERIALS AND METHODS:-

The present study is a cross sectional study, conducted on 600 patients in the age group of 6 months to 12 years, who were admitted in pediatric and haematology ward with anaemia and also those who presented with other complaints incidentally had haemoglobin values less than 12gm/dl.

EXCLUSION CRITERIA: Recent blood or blood product transfusion recipients and recent treatment that leads to haematological alteration like chemotherapy, radiotherapy.

A detailed history was elicited, a thorough clinical examination undertaken and the data recorded in the performa. The required quantity of venous blood was collected in EDTA tubes. The collected

blood was analysed by using SYSMEX XS800i auto analyser, having three part differentials, from which the following parameter were obtained:- HB%, TC, DLC, PCV, MCV, MCH, MCHC, RBC COUNT, RDW, platelet count, BT: CT, Reticulocyte count, Peripheral Blood Smear, Bone marrow aspiration cytology, urine examination, stool examination, chest X-RAY, USG abdomen, Hb electrophoresis, Osmotic fragility test, Sickling test, COOMBS test(Direct,Indirect), iron studies, tuberculin test. Biochemical investigations: blood glucose, blood urea, Serum creatinine, S. electrolytes, LFT.

OBSERVATIONS AND RESULTS:-

In the present study, pre-school children were found to be the most affected constituting 45%, followed by 33% of school going children and 22% of infants.

In this study, nutritional diseases were seen to be most commonly associated with anaemia, followed by infectious diseases, gastrointestinal diseases, respiratory diseases and CNS diseases.

Table 1: Associated general and systemic diseases

General and systemic diseases	No of cases	Percentage
Nutritional diseases	230	38.3%
Infectious diseases	180	30%
Gastrointestinal diseases	100	16.7%
Respiratory diseases	70	11.7%
CNS diseases	20	3.3%

In the present study, the most common morphological type of anaemia was microcytic hypochromic anaemia(63.3%) followed by normocytic normochromic anaemia(18.3%), dimorphic anaemia (13.4%). Macrocytic anaemia(5%) was the least common type.

Table 2: Distribution of various morphological types of anaemia

Morphological types	No of cases	Percentage
Microcytic hypochromic anaemia	380	63.3%
Normocytic normochromic anaemia	110	18.3%
Dimorphic anaemia	80	13.4%
Macrocytic anaemia	30	5%
Total	600	100%

In this study, iron deficiency anaemia (43.3%) was the most common etiological type, followed by anaemia due to infections(17.3%), anaemia due to chronic diseases(11.7%), haemoglobinopathies(10%), leukemia (8.3%), combined iron and vitB12 deficiency(1.7%) and megaloblastic anaemia(0.7%) with least common type being autoimmune hemolytic anaemia(0.3%).

Table 3: Distribution of anaemia based on etiology

Etiology	No of cases	Percentage
Iron deficiency anaemia	260	43.3%
Anaemia due to Infections	104	17.3%
Anaemia due to chronic disease	70	11.7%
Haemoglobinopathies	60	10%
Leukemias	50	8.3%
Anaemia of unknown etiology	40	6.3%
Combined iron and vit B12 deficiency	10	1.7%
Megaloblastic anaemia	4	0.7%
Autoimmune hemolytic anaemia	2	0.3%

In this study, it was observed that out of 60 haemoglobinopathies, HbE disorders constitute most predominant type comprising of 22 cases (15 cases of HbE trait & 7 cases of HbE diseases). 19 cases of thalassemia were found, out of which 14 cases were β -thalassemia trait & 5 cases were β -thalassemia major. Compound heterozygous HbE- β thalassemia were found in 13 cases, sickle cell trait was seen in 3 cases & a single case of sickle cell disease was found.

Table 4: Spectrum of haemoglobinopathies

Haemoglobinopathies	No of cases	Percentage
Heterozygous HbE	15	25%
Homozygous HbE	7	11.7%
Compound heterozygous HbE B thalassemia	13	21.7%
Homozygous HbS	1	1.7%

Heterozygous HbS	5	8.3%
B Thalassemia major	5	8.3%
B Thalassemia trait	14	23.3%
Total	60	100%

In this study iron deficiency anaemia is predominantly seen in the school going children (119 cases out of 260, i.e. 45.8%) followed by pre-school children (36.9%) and infants(17.3%). Anaemia due to infections is seen more in the pre-school children (53 out of 104 cases i.e. 51%) followed by infants (33.6%). Haemoglobinopathies are more predominant in the pre-school children (50%). Leukemia is seen more commonly in the pre-school children (30 cases out of 50 cases i.e. 60%).

Table 5: Age distribution in different etiology of anaemia

Etiology	Age groups						Total
	6 months to 1 year		1 to 5 years		5 to 12 years		
	No	%	No	%	No	%	
Iron deficiency anaemia	45	17.3%	96	36.9%	119	45.8%	260
Infections	35	33.6%	53	51%	16	15.4%	104
Anaemia of chronic disease	10	14.3%	34	48.6%	26	37.1%	70
Haemoglobinopathies	12	20%	30	50%	18	30%	60
Megaloblastic anaemia	0	0	0	0	4	100%	4
Leukemia	10	20%	30	60%	10	20%	50
Anaemia of unknown etiology	17	42.5%	20	50%	3	7.5%	40
Combined iron and VitB12 deficiency	3	30%	5	50%	2	20%	10
Autoimmune hemolytic anaemia	0	0	2	100%	0	0	2

DISCUSSION:-

Paediatric anaemia is an important universal problem.³¹ It is a critical issue which needs to be addressed on a priority basis especially in the developing countries.¹⁷ Nutritional anaemia is a recognized public health problem worldwide.⁷ In India, anaemia is the most common nutritional problem affecting more than half of the total population, particularly the children and the pregnant women.¹⁸

Iron deficiency anaemia is the commonest form of nutritional deficiency in the world responsible for the staggering amount of ill health, cost productivity, increased mortality and morbidity. Even in the developed countries, iron deficiency with or without anaemia is still prevailing in infants, toddlers, adolescent females and women of the child bearing age. It remains the most common hematologic disease in infants and children.¹⁹

Given the detrimental long term effects and high prevalence of iron deficiency, its prevention in early childhood is an important public health issue.¹³ Patients with hemoglobinopathy syndromes are commonly encountered in hematologic clinics. Of these, the commonest disorder in India is thalassemia.²⁰

The clinicopathological patterns, the morphological and the etiological types of anaemia as analyzed in the present study of 600 pediatric anaemia cases were compared with the other similar studies.

In the present study, preschool children were found to be maximally affected contributing to 45% which is in concurrence with the study done by Sahu T et al.⁸ (94%) and Divya A.²¹ (48%) Whereas, in a study by Adewuyi JO et al.⁴, the school going children were maximally affected. (70%).

In this study the second most common age group affected by anaemia was school going children (33%) followed by infants with prevalence of 22%. Similarly, Sahu T et al.⁸ found 59.4% were moderately anaemic and 5.4% were severely anaemic in the children of age group 5-14 years.

Similarly, Divya A. found 27% of school going children were affected followed by infants with prevalence of 25%.²¹

In the present study, microcytic hypochromic anaemia (54%) was the most common type. Similar findings is in concurrence with the study done by Saba F et al.⁷(48%), Verma M et al.⁵(55.4%), Kamil KH et al.¹² (60.7%) Molla A et al.¹⁴ (61%), Vinukumar V et al.¹⁵ (58.9%)& Agravat AH et al.¹¹

In the present study, second most common type was normocytic normochromic anaemia (13%), followed by dimorphic anaemia (8%) and macrocytic anaemia (3%).

In contrast, Agravat AH et al.¹¹ found second most common type was dimorphic followed by macroovalocytic and hemolytic.

Kamil KH et al.¹² also found second most common type was normocytic (26.7%) followed by macrocytic (12.6%), hemolytic anaemia (18.6%), followed by thalassemia syndromes (16.6%), anaemia of chronic disease (15.5%), acute leukemia (2.7%), liver diseases (1%), megaloblastic anaemia (0.6%), acute blood loss (0.6%), aplastic anaemia (0.3%) and anaemia of undetermined cause (1.5%).

It was observed in the present study, the most prevalent etiological type was iron deficiency anaemia (43.3%).

Similar findings were found with the study done by Gomber S et al.⁷ (41.05%), Kumar R et al.¹⁰ (45%) Kamil KH et al.¹² (42.6%) & Miller CJ et al.⁶ (9.9%)

In the present study the second most common etiological type was anaemia due to infections (17.3%) followed by anaemia due to chronic diseases (11.7%), haemoglobinopathies (10%), leukemia (8.3%), combined iron and vitB12 deficiency (1.7%), megaloblastic anaemia (0.7%) and autoimmune hemolytic anaemia (0.3%).

In contrast, Kamil KH et al.¹² found second most common etiological type was hemolytic anaemia (18.6%), followed by thalassemia syndromes (16.6%), anaemia of chronic disease (15.5%), acute leukemia (2.7%), liver diseases (1%), megaloblastic anaemia (0.6%), acute blood loss (0.6%), aplastic anaemia (0.3%) and anaemia of undetermined cause (1.5%).

Miller CJ et al.⁶ found second most common etiological type was glucose-6-phosphate dehydrogenase (G6PD) deficiency (9.1%), sickle cell trait (4.6%) and beta thalassemia (8.7%)

Kumar R et al.¹⁰ & Gomber S et al.⁷ found pure or mixed B12 deficiency as the second following cause with prevalence 21% and 28.42% respectively.

In this study, it was observed that HbE disorders constitute most predominant type comprising of 36.7% of cases followed by β -thalassemia(31.6%), compound heterozygous HbE- β thalassemia (21.7%) and sickle cell anaemia(10%).

Similar findings is in concurrence with the study by Baruah et al.²² who studied to identify haemoglobinopathies and thalassemias in Upper Assam region of North East India and found the HbE gene was detected in 4315 patients of which HbE trait was seen in 2294 followed by HbE disease in 1892, 114 of HbE beta thalassemia & 15 double heterozygotes of HbE with HbS or HbD. He also found beta thalassemia trait in 313 patients and beta thalassemia homozygous in 32 patients.

In contrast, Chopra et al.²³ in 2008 found beta thalassemia to be most prevalent i.e. 17.4% followed by sickle cell disorders which constitute 4% of cases. HbE disorders contributed 1.4% of cases in this study.

Similarly, Mesbah Uddin et al.²⁴ studied pattern of β -thalassemia and other haemoglobinopathies in Bangladesh in 600 subjects and found the most common form of haemoglobin (Hb) formation disorder was β -thalassemia minor (21.3%) followed by E- β -thalassemia and HbE trait, (13.5 and 12.1%, resp.) Other forms of haemoglobin formation disorders observed were HbE disease (9.2%), Hb D/S trait (0.7%), β -thalassemia major (0.5%), and δ - β -thalassemia (0.5%).

Ambekar S S et al.¹⁶ in 2008, studied the Pattern of haemoglobinopathy

in Western Maharashtra, 891 cases from Pediatric age group and found thalassemia major in 76 (8.5%) subjects, β Thalassemia trait in 4 (0.5%), sickle cell disease in 16 (1.8%) HbE in 4 (0.5%) and HbD disease in 1 (0.1%).

The peripheral smear findings in HbE disease (EE) a microcytic hypochromic anaemia with anisocytosis, hypochromia and target cells was seen.

In thalassemia major, the peripheral smear showed marked degree of anisopoikilocytosis with hypochromia and polychromasia and a raised RDW. BTT in an asymptomatic individual with no or mild anaemia.

In HbE beta thalassemia, the PBS invariably showed anisopoikilocytosis with hypochromia and target cells depending on the severity of the anaemia with the red cell indices showing a microcytic hypochromic anaemia.

In HbSS, anaemia consisted of a microcytic hypochromic anaemia (48.7%) with the peripheral smear showing anisopoikilocytosis, hypochromia, target cells and polychromasia.

All this findings are found to be similar with the study by Baruah et al.²³ in Upper Assam region of North East India.

CONCLUSION :-

Nutritional deficiency diseases are the most common causes of anaemia in paediatric age group. Children being the most vulnerable group for nutritional deficiencies require early screening for anaemias and associated illnesses. Possibly the unawareness of the condition, illiteracy, poor socioeconomic conditions, poor hygiene, may be the root cause leading to high prevalence of anaemia in this age group.

In the present study, the preschool children were found to be the mostly affected. Hence, it is recommended that, this age group is compulsorily screened for anaemia. Initial screening and subsequent diagnostic tests enable early diagnosis and appropriate management. Prevention of infection, screening for asymptomatic nutritional deficiencies specially iron, Vit B12 and folate and haemoglobinopathies are mandatory. Use of prenatal diagnostic techniques and early detection of haemoglobinopathies would ensure effective management.

Steps need to be undertaken to educate the masses and improve their living standards, so that, the initial symptoms of illness are not ignored and the children are brought to the hospital at the earliest for timely diagnosis and effective management. One of the most important areas for scope in the improvement of primary health care is prevention of nutritional deficiency because it has been associated with delay in psychomotor development and increased morbidity and mortality in children. A uniform definition of screening and an effective system to respond to abnormalities is the need of the hour.

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