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Clinicopathological Study of Anemia Patterns in Children in Rural Area in a Tertiary Care Hospital

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ABSTRACT: Background And Objectives: Anaemia in children is one of the major health problems in India as well as in many parts of the world, since anemic children have reduced exercise tolerance, slow growth rate, impaired cognitive development and increased risk of complications associated with malnutrition and infection.

Objectives

1. To study the clinicopathological patterns of anaemia in children in the age group of 6 months to 14 years.
2. To detect the morphological and etiological types of anaemia among them.
3. To detect the degree of severity of the paediatric anaemias.

METHODOLOGY: The study was conducted on 100 patients in the age group of 6 months to 14 years. The children with Hb% lesser than the cut-off value for their age were included in the study. Detailed clinical history was elicited and thorough clinical examination was performed. Peripheral smears of these patients were examined. The complete haemogram including reticulocyte count was done. The special investigations like bone marrow study, Hb electrophoresis, iron studies and stool examination were done whenever required.

RESULTS: Male children were more affected than the female children and pre-school children were affected the most. The most common presenting symptom was acute
gastroenteritis followed by respiratory symptoms. Microcytic hypochronic anaemia was the most common morphological type and iron deficiency anaemia was the most common etiological type. Amongst the hemolytic anaemias, thalassemia major was most common. Electrophoretic analysis of thalassemia major showed that the mean value of HbF, HbA_2 and HbA were 92.5%, 2.59% and 3.61% and that of thalassemia minor were 31.66, 8.5
and 56.05 respectively.

Interpretation And Conclusion: Paediatric anaemias are very common since children are the most vulnerable population for occurrence of these anaemias. This necessitates prompt screening and early diagnosis through investigations by utilization of available advanced technical modalities in order to initiate timely treatment and appropriate management.

KEY WORDS: Complete hemogram; Iron deficiency anaemia; Vit. B12; Folic acid; Thalassemia; Hb electrophoresis

I. INTRODUCTION

Anaemia is defined as a decreased concentration of hemoglobin and RBC mass as compared to the values in age-matched controls. Anaemia in children is one of the major social health problems in India and in many parts of the world, since anemic children have reduced exercise capacity, slower rate of growth, impaired cognitive development, and delayed wound healing.[1]

Anemic children are also at an increased risk of dying due to complications associated with malnutrition and infection. Prevalence rate of anaemia is an important indicator of the nutritional status within the pediatric population. As many as 20 percent of the children in the United states and 80 percent of the children in the developing countries are anemic 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.[3]

Most children with anaemia are asymptomatic and have abnormal hemoglobin or hematocrit levels on routine screening. Infrequently, a child with anaemia may have pallor, fatigue, and jaundice, but may or may not be critically ill. Thorough elicitation of history and findings on physical examination can reveal the underlying cause of anaemia.[2]

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II. OBJECTIVES

1. To study the clinicopathological patterns of anaemias in children in the age group ranging from 6 months to 14 years.
2. To detect the morphological and etiological types of anaemias prevalent among children in the age group of 6 months to 14 years.
3. To detect the severity and degree of anaemia among these children.

III. METHODOLOGY

The present study is a cross sectional, descriptive study conducted on 100 patients in the age group of 6 months to 14 years, who were admitted to the pediatric ward of Maharajah's Institute of Medical Sciences, Vizianagaram, with anaemia and also those who presented with other complaints and were incidentally found to have anaemia. The children with hemoglobin values of less than 11 gm/dl in the age group of 6 months to 6 years those with hemoglobin values of less than 12 gm/dl in the age group of 6 to 14 years, were included in the study which was conducted from November 2018 to November 2019.

IV. METHOD OF STUDY

A detailed history was elicited, a thorough clinical examination undertaken and the data recorded in the proforma. The required quantity of venous blood was collected in EDTA tubes. The collected blood was analyzed using **Sysmex KX-21 autoanalyser**, having three part differentials.

Peripheral smears were prepared on glass slides and stained with Leishman's stain. The reticulocyte count was done by the supravital staining technique using Brilliant cresyl blue.

Among the microcytic hypochromic anaemia cases, iron deficiency anaemia was diagnosed by serum ferritin estimation and also by iron storage assessment of bone marrow examination using Perl's stain.

Among the macrocytic anaemias, suspected cases of megaloblastic anaemias were confirmed by bone marrow examination, serum B12 and folate estimations.

The hemolytic anaemia cases which were suspected on clinical and peripheral blood examination, were takenup for a complete hematological work up including Hb electrophoresis, osmotic fragility and Coomb's test depending on the specific requirement.

Other ancillary tests including stool examination, urine examination, liver function tests, renal function tests, Mantoux test, radiological investigations like x ray, ultrasonography and CT scan were done whenever required.

In the present study, WHO criteria was employed to

1. **Define** anaemias as

Hb% < 11gm/dl-among children between 6 months to 6 years Hb%< 12 gm/dl – among children between 6 years to 14 years.

2. **Grade** anaemias as

Mild – Hb% between 10- 12 gm% Moderate – Hb% between 7 – 10 gm% Severe – Hb% < 7 gm%

The categorization of RBCs as microcytic, normocytic and macrocytic based on the MCV values was as follows:

Microcytic when

MCV was < 70fl among children < 1 year

MCV was< 73fl among children between 1 year to 5 years MCV was < 75fl among children > 5 years.

Normocytic when MCV was within the normal range

Macrocytic when MCV was > 100 fl.

Reduced Hb% and RDW > 15% associated with microcytes was considered diagnostic of **IDA**, which was further confirmed by serum ferritin values of

< 12 µgm/dl and reduced iron stores in bone marrow on staining with Perl's stain. **Megaloblastic anaemia** was diagnosed when peripheral smear showed macrocytic anaemia with megaloblastic features, along with a MCV > 100fl, associated with leucopenia, thrombocytopenia and a reduced retic count. Confirmation of the diagnosis was done by demonstration of megaloblastic change in the bone marrow and reduced serum B12 level (<80 pg/ml)

The diagnostic criteria for **hemolytic anaemia** were, peripheral smear with evidence of red cell breakdown in the forms of schistocyte, crenated RBCs, with associated normoblastosis, increased reticulocyte count and predominance of morphological variants like target cells in thalassemia and spherocytes in HS.

Based on the morphology of RBCs, RDW and altered red cell indices, the specific investigations required were undertaken.

The cases which showed marked anisopoikilocytosis with features of microcytic hypochromic anaemia, predominance of target cells

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and a reduced RDW were diagnosed to have thalassemia and were subjected to Hb electrophoresis for confirmation of diagnosis.

The cases which showed predominance of microspherocytes along with reduced MCV and increased reticulocyte count were diagnosed to have HS and were subjected to osmotic fragility test for confirmation.

In the cases of hemolytic anaemia where categorization was not possible by the routine investigations, Hb electrophoresis was used as the gold standard for definitive subtyping.

Statistical software used: SPSS 16 version was used for the analysis of the data.

V. RESULTS

The present study was carried out on 100 anemic pediatric patients in the age group of 6 months to 14 years. These 100 patients were categorised into three age groups namely infants, pre-school and school-going children and their anemic status was analyzed.

In the present study, pre-school children were found to be the most affected thus constituting 48%, followed by 27% of school going children and 25% of infants.

The average age affected was four years and three months with a standard deviation of 8.88.

Out of 100 cases studied, 60 (60%) were males and 40 (40%) were females. The male:female ratio in the present study was found to be 3:2.

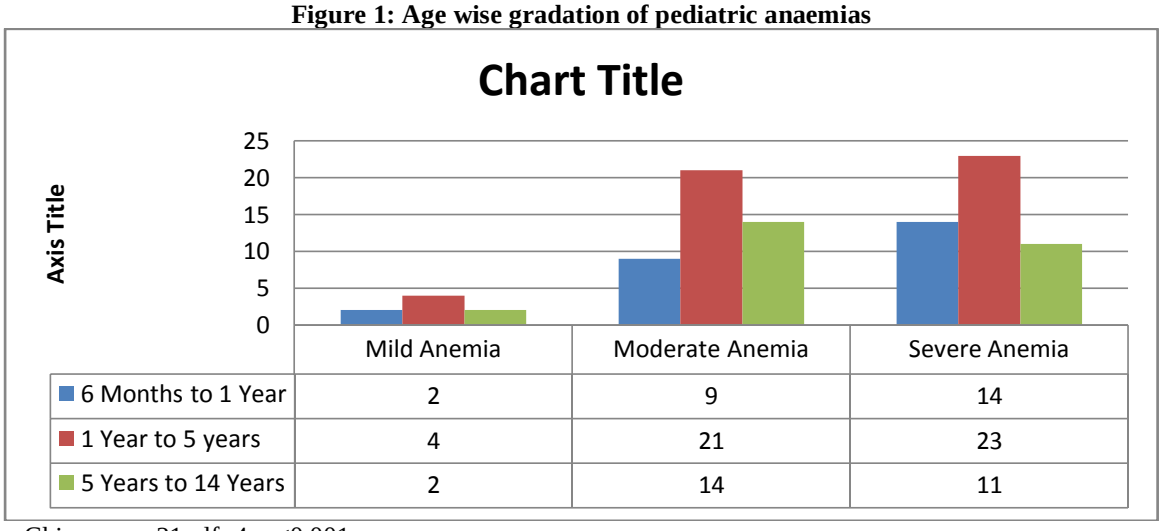
Table 1: Genderwise gradation of pediatric anaemias

Grade of anaemia	Males		Females		Total
	No.	%	No.	%	
Mild (Hb% >10 gm/dl)	5	8.3	3	7.5	8
Moderate (Hb% 7-10 gm/dl)	25	41.7	19	47.5	44
Severe (Hb% < 7 gm/dl)	30	50	18	45	48
Total	60		40		100

Yates Chi-square=0.58; df=2; p=0.97.

In the present study, eight out of 100 children had mild degree of anaemia amongst whom, five were females and three males. Forty-four children were found to have moderate degree of anaemia, amongst whom, 25 were males and 19 females. Severe degree of anaemia was found in 48 children amongst whom, 30 were males and 18 were females. Non-significance was observed between the severity of the anaemia and gender distribution with the Yates Chi-square of 0.58; df=2 and p-value of 0.97.

Figure 1: Age wise gradation of pediatric anaemias



Yates Chi-square=21; df=4; p<0.001

Among infants and pre-school children, severe degree of anaemia was more prevalent. Among school

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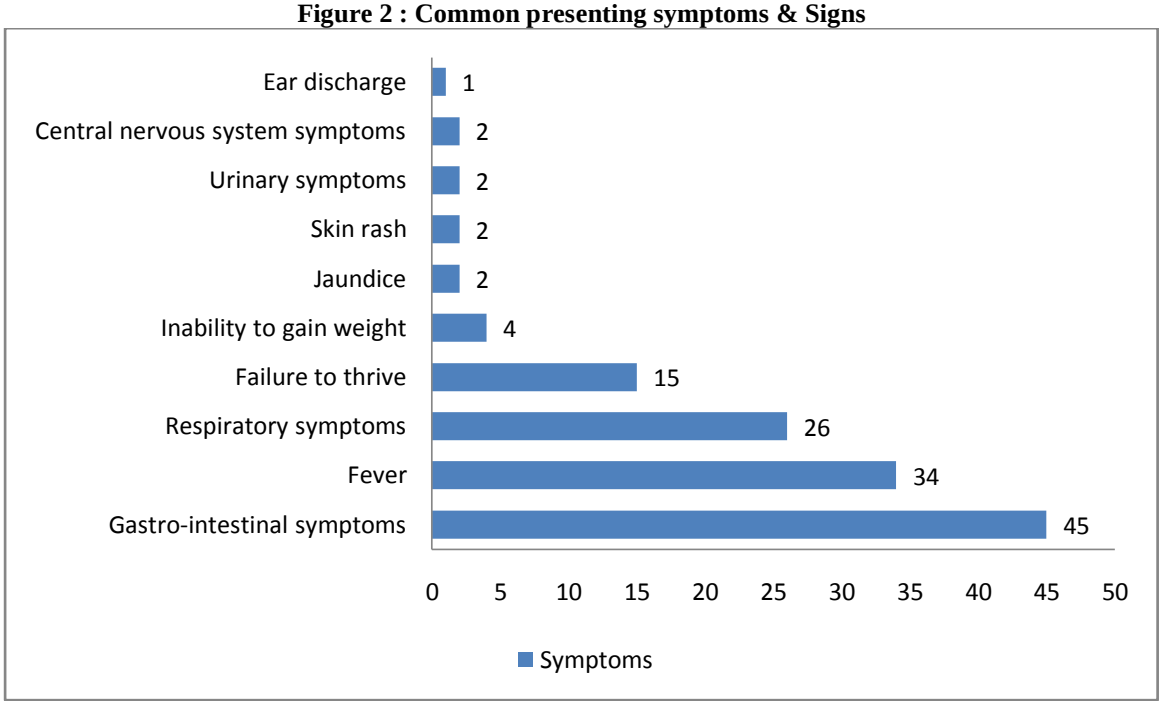
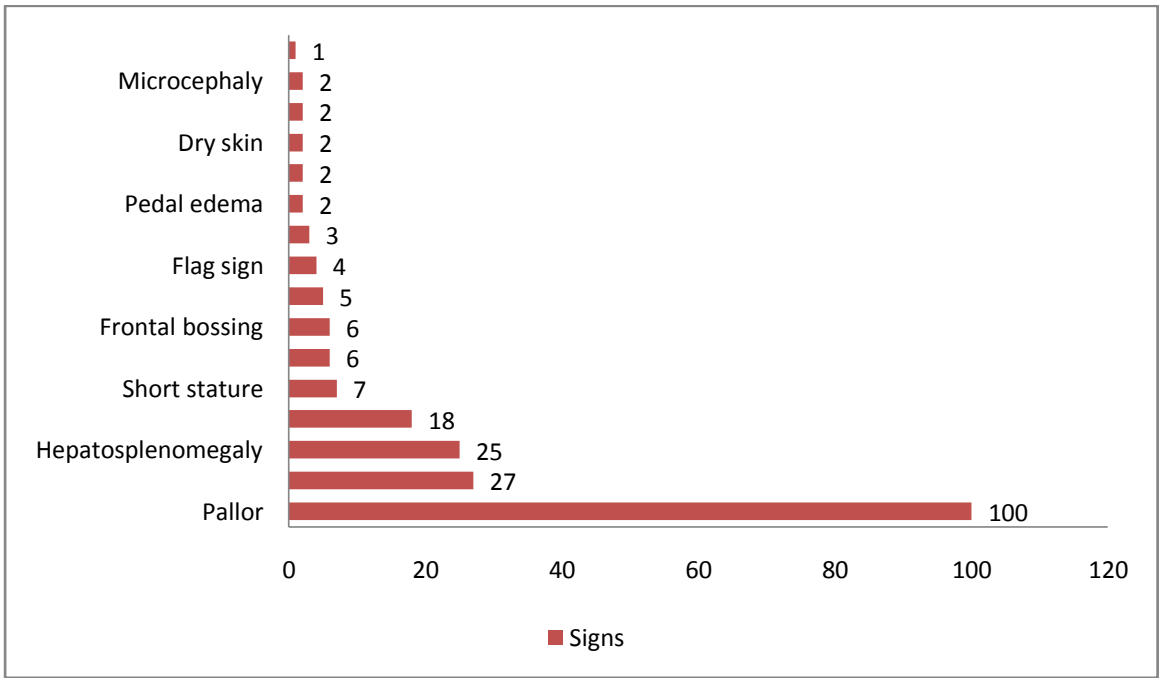
going children, moderate degree of anaemia was more prevalent. This was found statistically significant with the Yates Chi-square value of 21, df=4 and p-value<0.001.

Figure 2 : Common presenting symptoms & Signs





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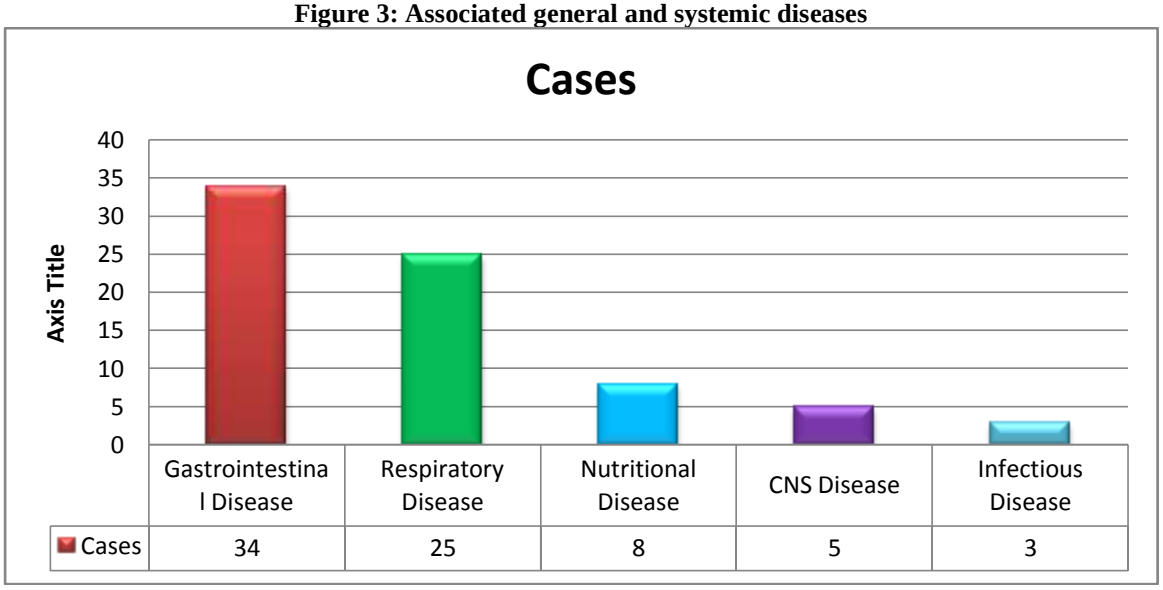
In the present study, the common presenting symptoms were gastrointestinal including vomiting, diarrhoea and pain abdomen followed by fever, respiratory symptoms and failure to thrive. Jaundice, skin rashes, urinary complaints, CNS manifestations, ear discharge and facial puffiness were seen in a few cases.

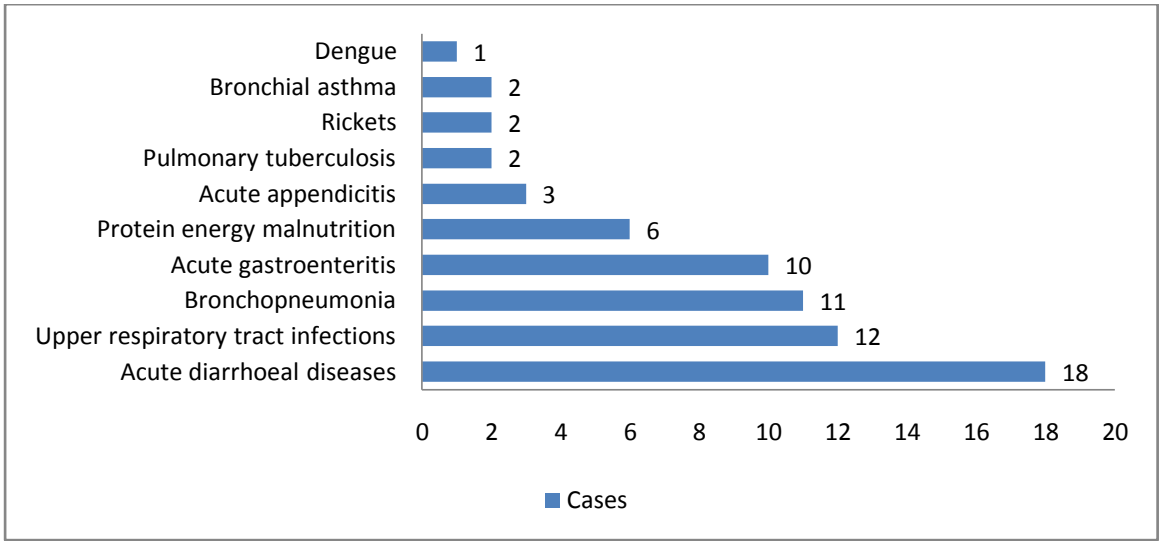
In this study, pallor was found in all the cases. The common signs included signs of dehydration, hepatosplenomegaly, fever, short stature, tachypnoea/ tachycardia and frontal bossing. Flag sign, jaundice, pedal edema, hemiperesis/ hemiplegia, dry skin, muscle wasting, microcephaly and cervical lymphadenopathy were seen in some cases.

Figure 3: Associated general and systemic diseases



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

Figure 4: Distribution of anaemias based on clinical diagnosis



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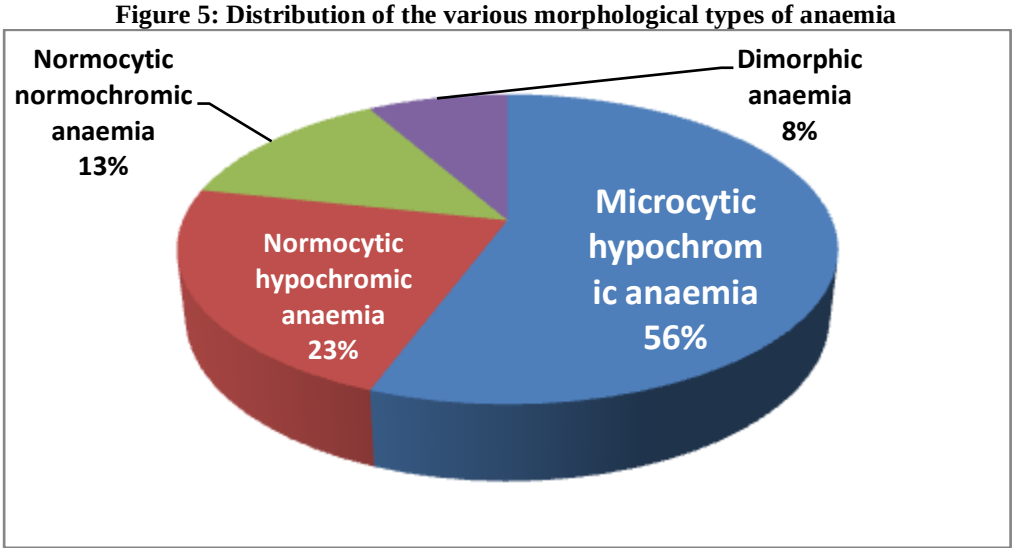
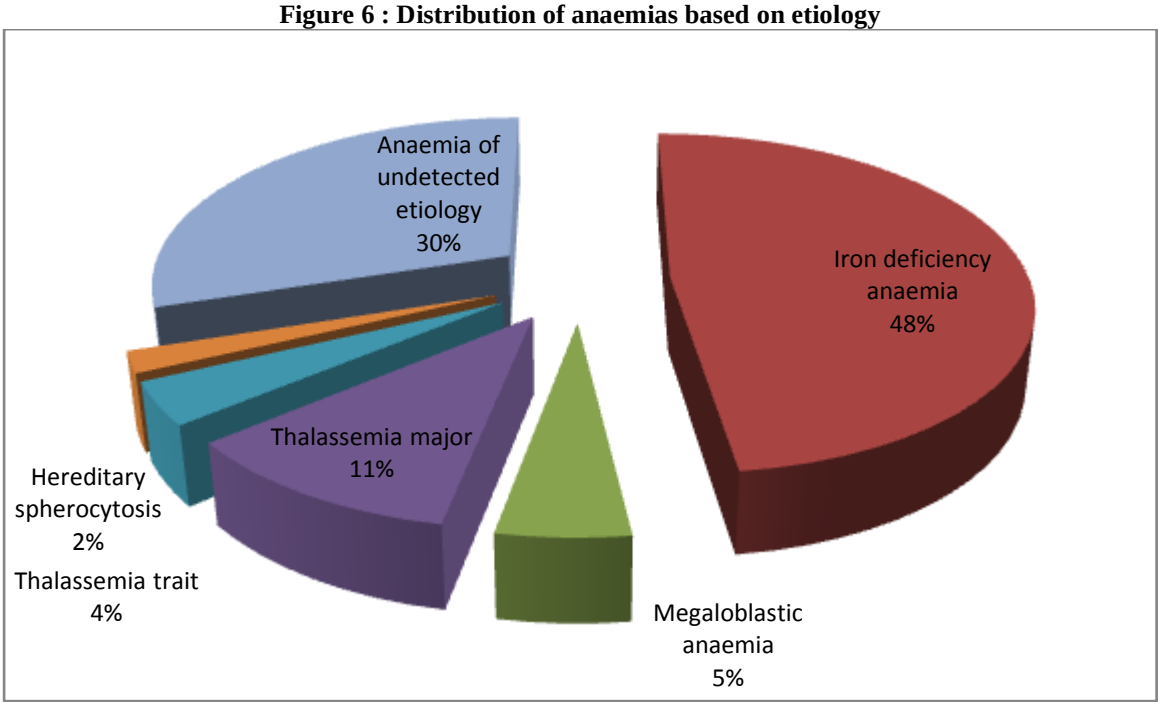
In the present study, acute diarrhoeal diseases followed by upper respiratory tract infections and bronchopneumonia were the common clinical diagnosis associated with anaemia. Rickets, bronchial asthma and dengue were the least common clinical diagnosis.

Figure 5: Distribution of the various morphological types of anaemia



In the present study, the most common morphological type of anaemia was microcytic hypochromic anaemia (54%) followed by normocytic hypochromic anaemia (22%), normocytic normochromic anaemia (13%) and dimorphic anaemia (8%). Macrocytic anaemia (3%) was the least common morphological type.

Figure 6 : Distribution of anaemias based on etiology



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In this study, iron deficiency anaemia (48%) was the most common type followed by Thalassemia major (11%). Megaloblastic anaemia (5%) and Thalassemia trait (4%) with least common type being hereditary spherocytosis (2%).

Table 2: Mean values of Hb% and RDW in IDA and thalassemia trait

	IDA	**Thalassemia trait**
Mean Hb%	5.8 gm%	7.9%
Mean RDW	21.04%	16%

Mean Hb value was found to be more in Thalassemia trait as compared to IDA. Mean value of RDW was found to be increased IDA as compared to Thalassemia trait.

Table 3: Electrophoretic analysis of thalassemia cases

Thalassemia	**HbF**	**HbA_2**	**HbA**
Thalassemia major	91.5	3.2	3.7
	93	2.8	3
	92.5	2	3
	91	2.2	3.5
	93.5	2.4	2.1
	93	2.4	3.2
	94.6	2	3.2
	90.5	3.5	6
	91.1	2.5	4.4
	94.3	1.6	4.1
	92.5	3.9	3.1
Thalassemia trait	35	7.8	57.2
	30	10	60
	32	7.5	55
	33	8.5	52

In the present study, the mean values of **HbF**, **HbA_2** and **HbA** in **Thalassemia major** were **92.5**, **2.59** and **3.61** with standard deviation of 1.3, 0.66 and 1.41 respectively.

Among **Thalassemia trait**, the mean values of **HbF**, **HbA_2** and **HbA** were **31.66**, **8.5** and **56.05** with the standard deviation of 0.88, 1.25 and 3.38 respectively.

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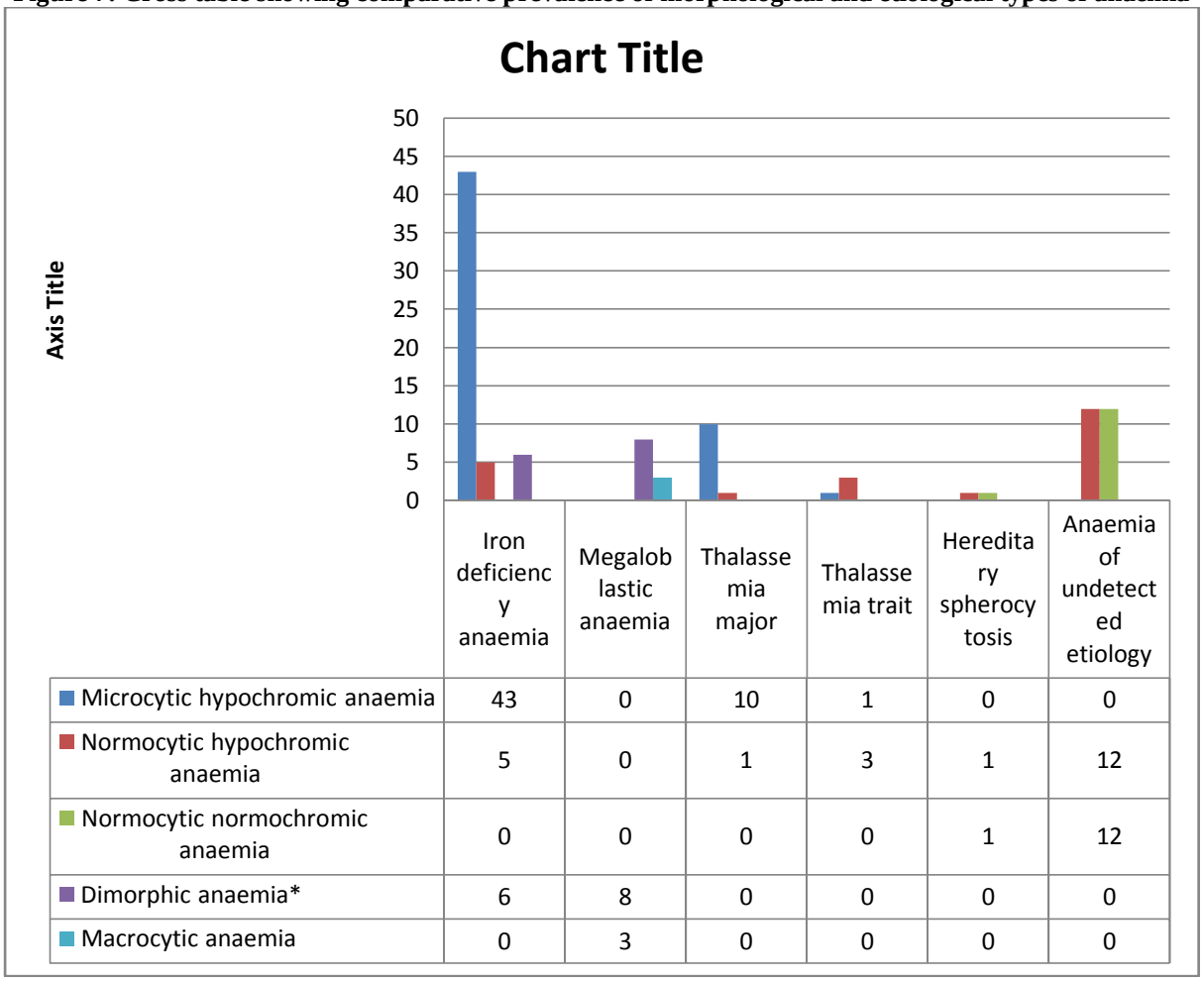
Figure 7: Cross table showing comparative prevalence of morphological and etiological types of anaemia



	Iron deficiency anaemia	Megaloblastic anaemia	Thalassemia major	Thalassemia trait	Hereditary spherocytosis	Anaemia of undetected etiology
Microcytic hypochromic anaemia	43	0	10	1	0	0
Normocytic hypochromic anaemia	5	0	1	3	1	12
Normocytic normochromic anaemia	0	0	0	0	1	12
Dimorphic anaemia*	6	8	0	0	0	0
Macrocytic anaemia	0	3	0	0	0	0

In the present study, it was observed that, among 54 iron deficiency anaemia cases, 43 were microcytic and hypochromic and 11 had varied morphological types, out of which, five were normocytic hypochromic and six were dimorphic. Out of the 11 cases of megaloblastic anaemias, three had macrocytic picture and eight had dimorphic picture. Among the 11 cases of Thalassemia major, ten were microcytic hypochromic and one was normocytic hypochromic. Among the four cases of Thalassemia trait, one was microcytic hypochromic and three were normocytic hypochromic. Among the two cases of hereditary spherocytosis, one had normocytic hypochromic picture and the other had normocytic normochromic picture. The specific etiological factor could be definitively established in 24 cases and these patients were grouped under the category of anaemia of undetected etiology

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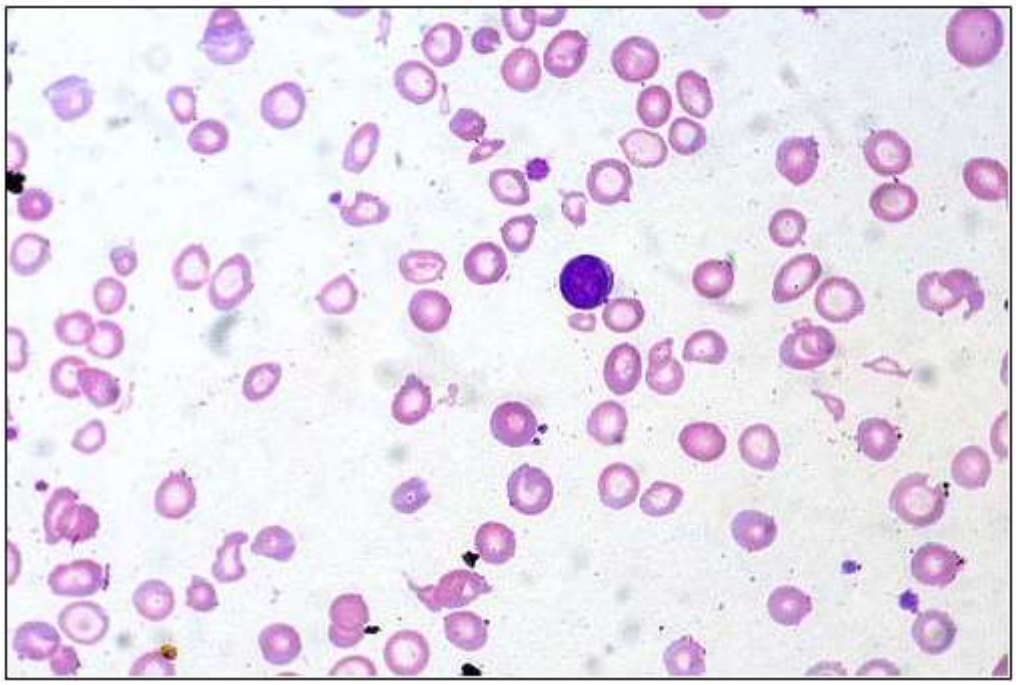

Figure 8: IDA – Peripheral smear showing anisopoikilocytosis & microcytic hypochromic cells, Leishman's stain (X400)

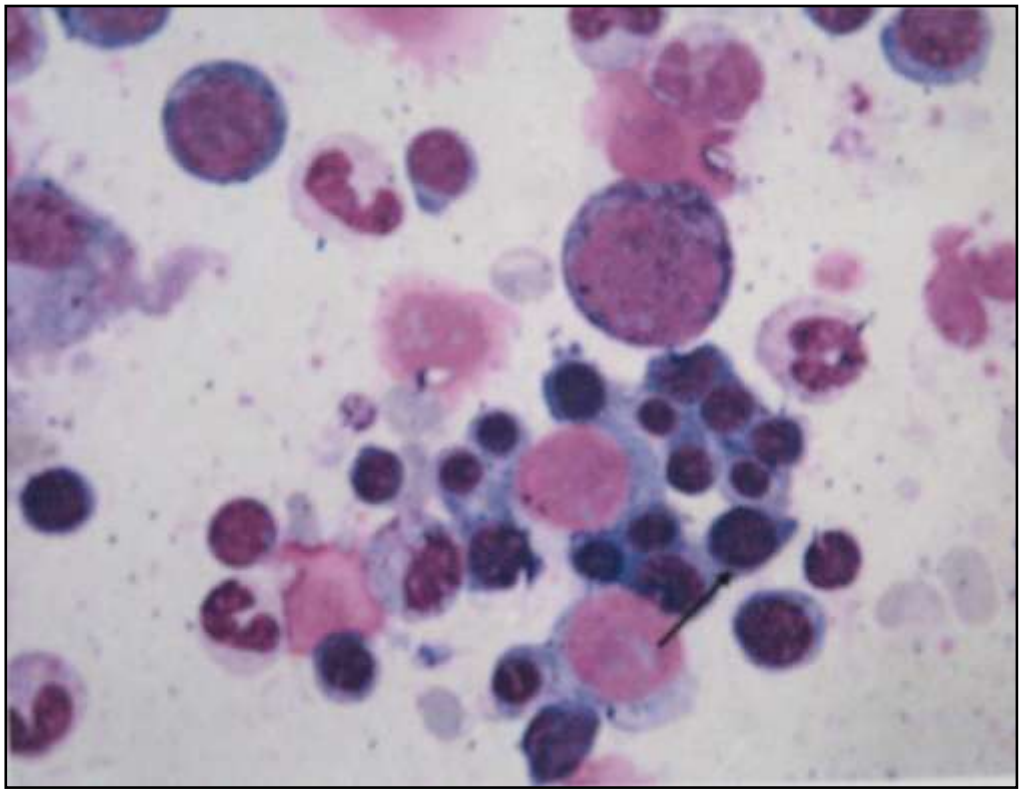

Figure 9: IDA – Bone marrow aspiration smear showing micronormoblasts, Leishman's stain (X1000)

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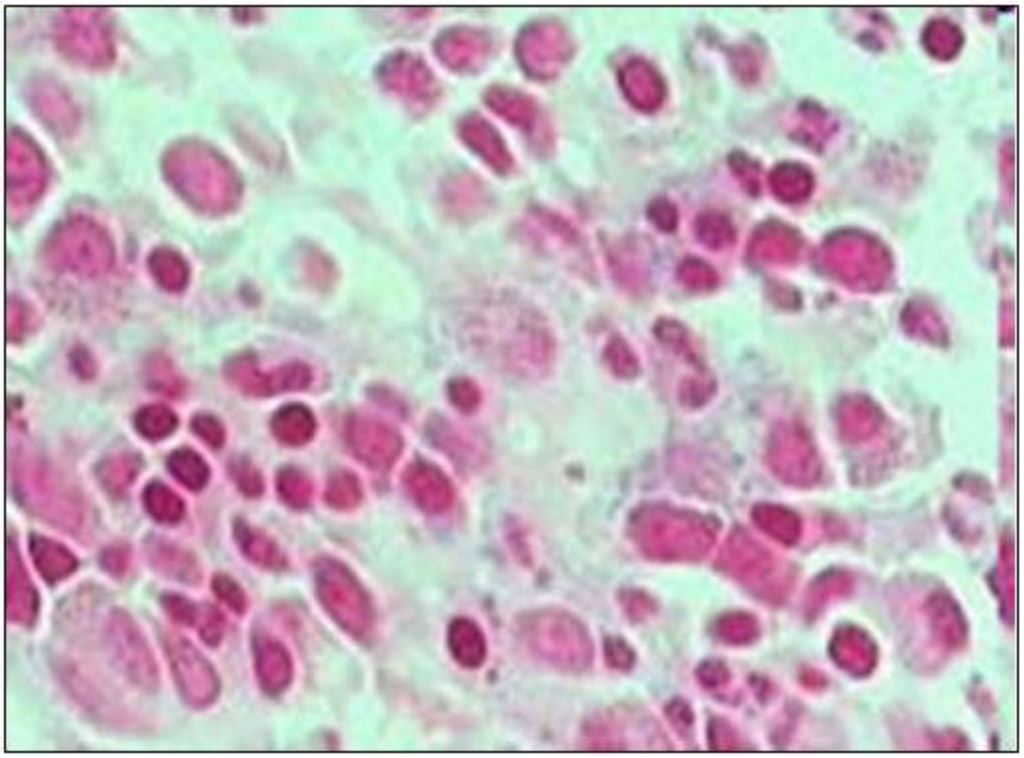

Figure 10: IDA – Bone marrow smear showing absent iron stores on Perl's stain (X1000)

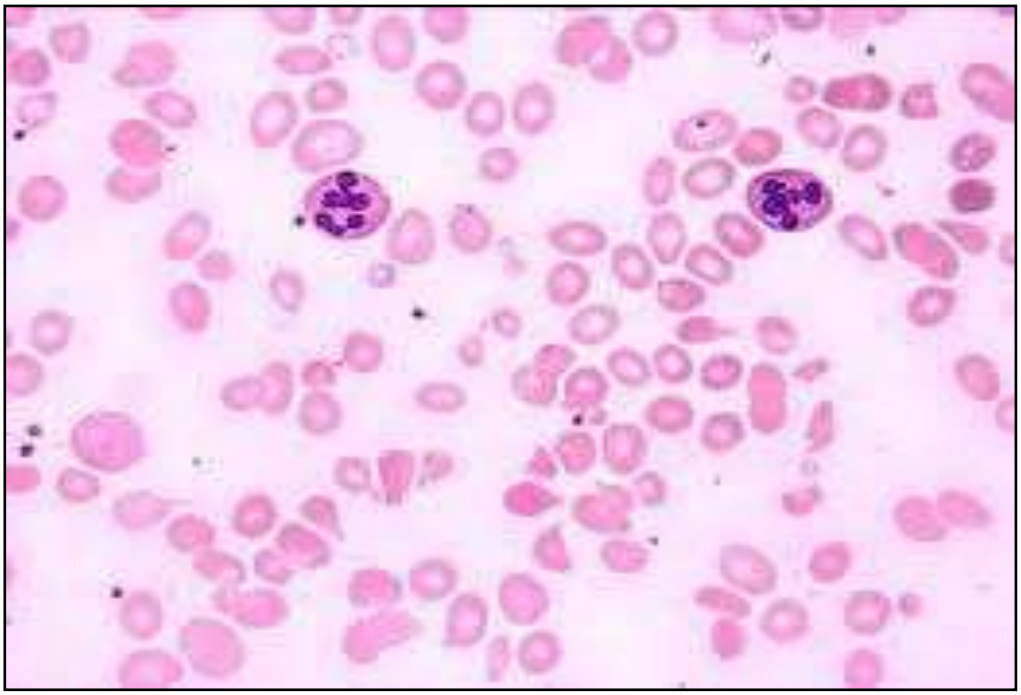

Figure 11: Megaloblastic anaemia – Peripheral smear showing hypersegmented neutrophils and macro-ovalocytes, Leishman's stain (X400)

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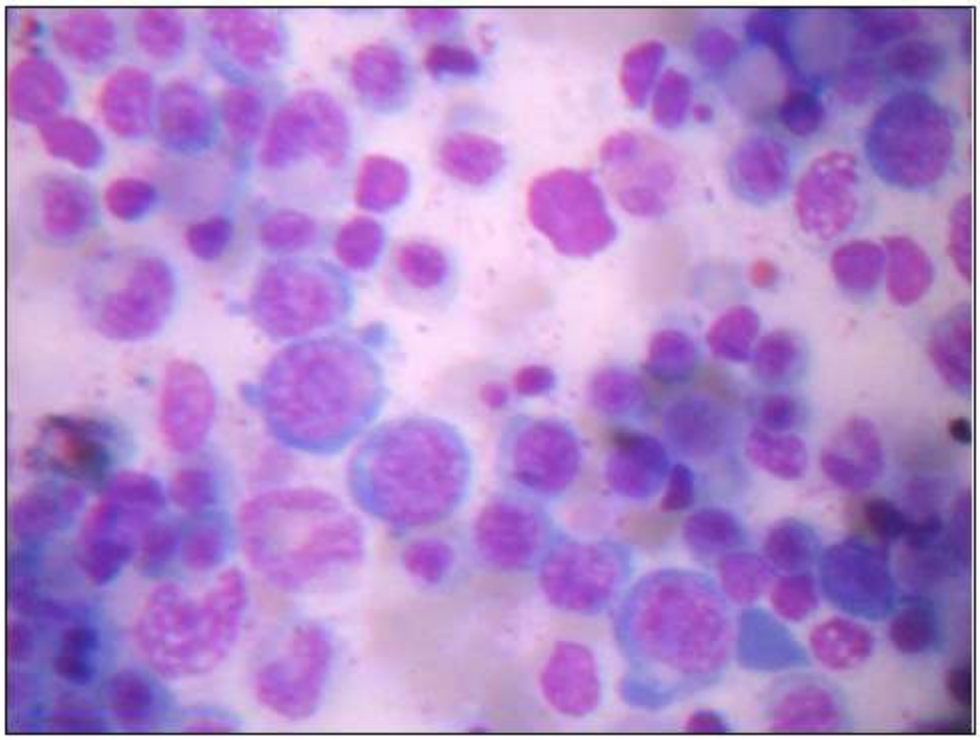

Figure 12: Megaloblastic anaemia – Bone marrow smear showing megaloblasts with sieve-like chromatin, Leishman's stain (X1000)

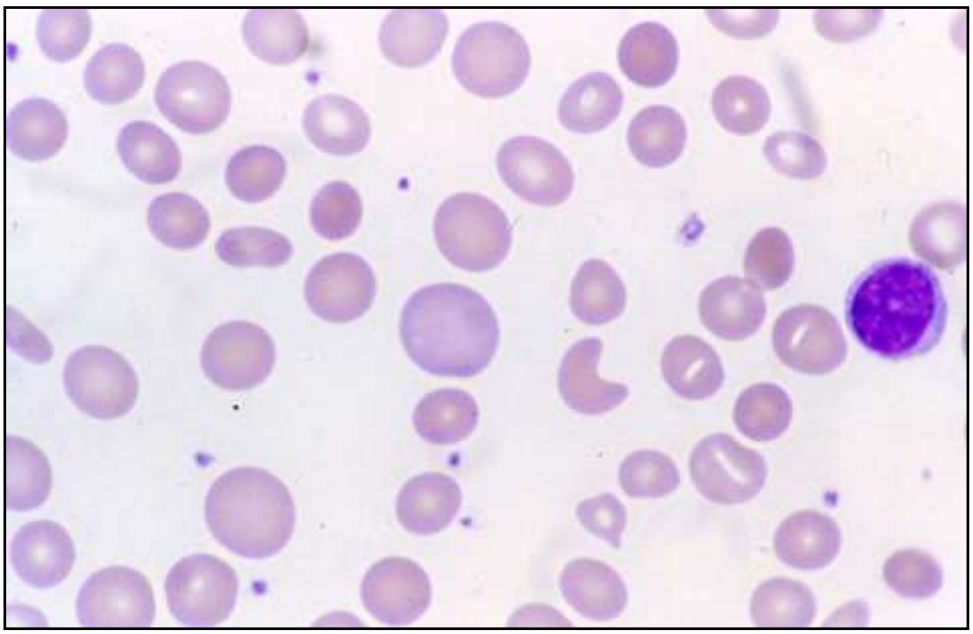

Figure 13: Dimorphic anaemia – Peripheral smear showing macrocytes and microcytic hypochromic cells, Leishman's stain (X1000)

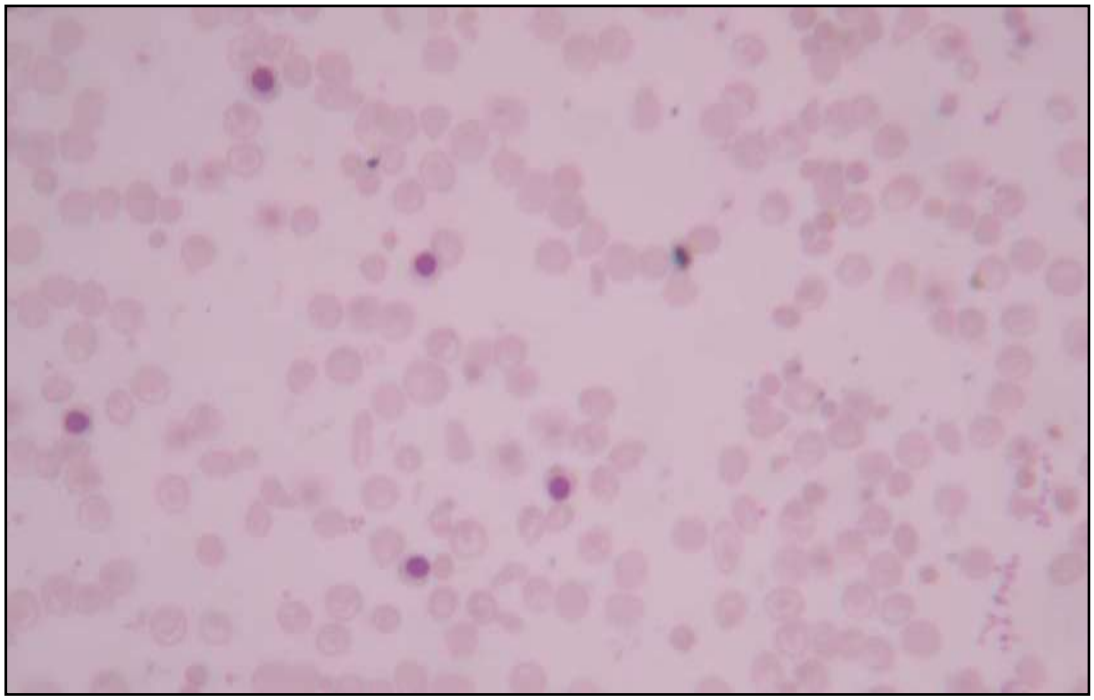

Figure 14: Hemolytic anaemia – Peripheral smear showing nucleated RBCs and polychromatophils, Leishman's stain (X400)

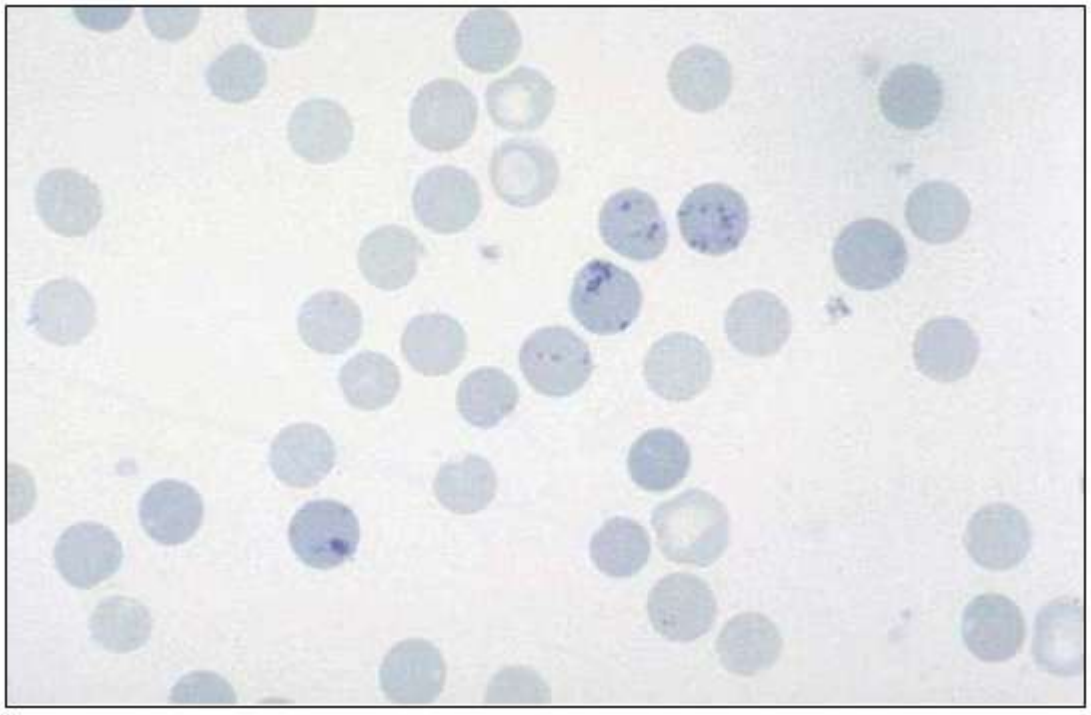

Figure 15: Hemolytic anaemia – Supravital stain showing increased reticulocytes (X1000)

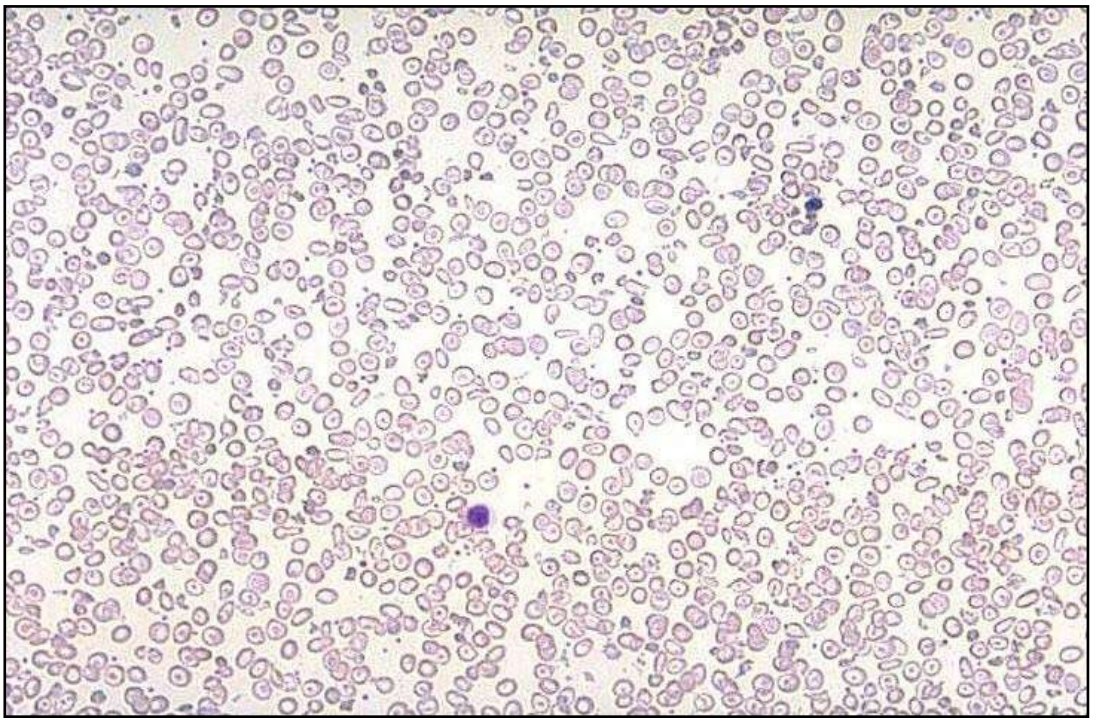

Figure 16: Thalassemia major – Peripheral smear showing MHA with target cells, Leishman's stain (X100)

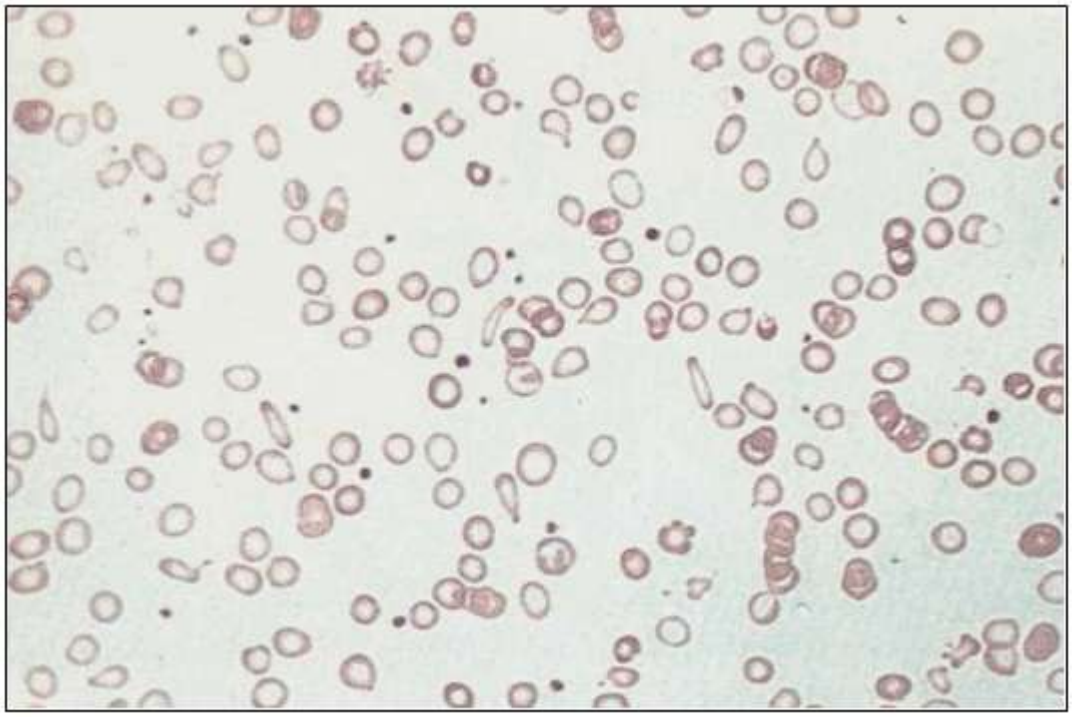

Figure 17: Thalassemia minor – Peripheral smear showing microcytic hypochromic cells

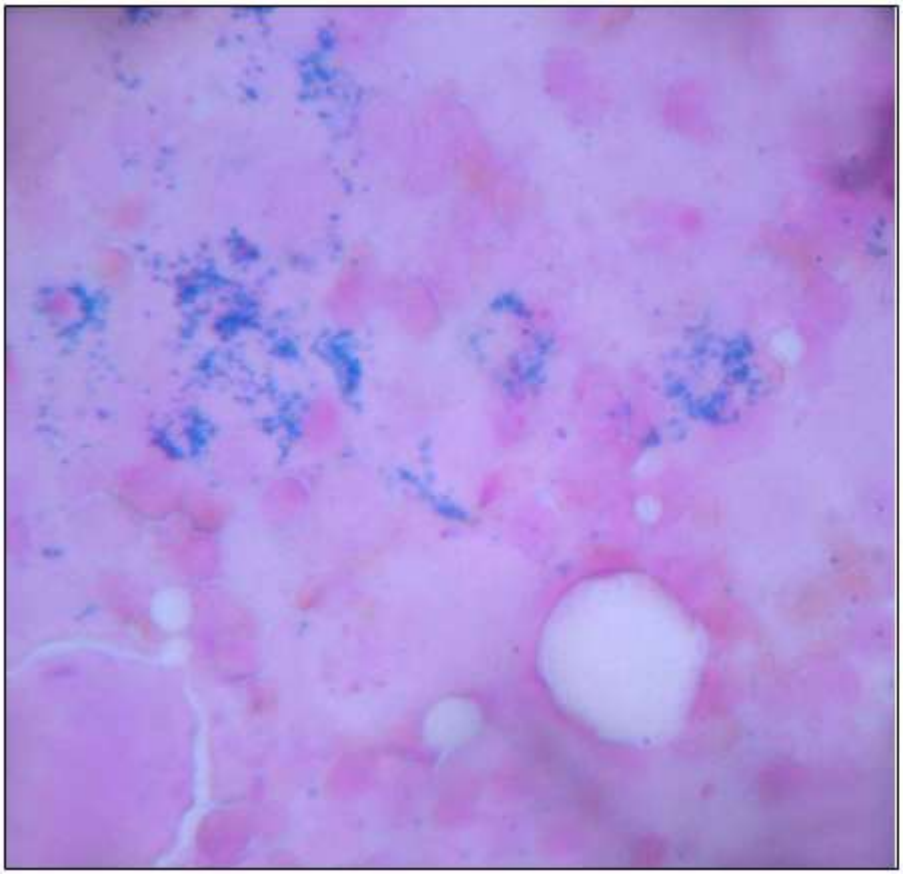

Figure 18: Thalassemia minor – Bone marrow smear showing normal iron stores on Perl's stain (X1000)

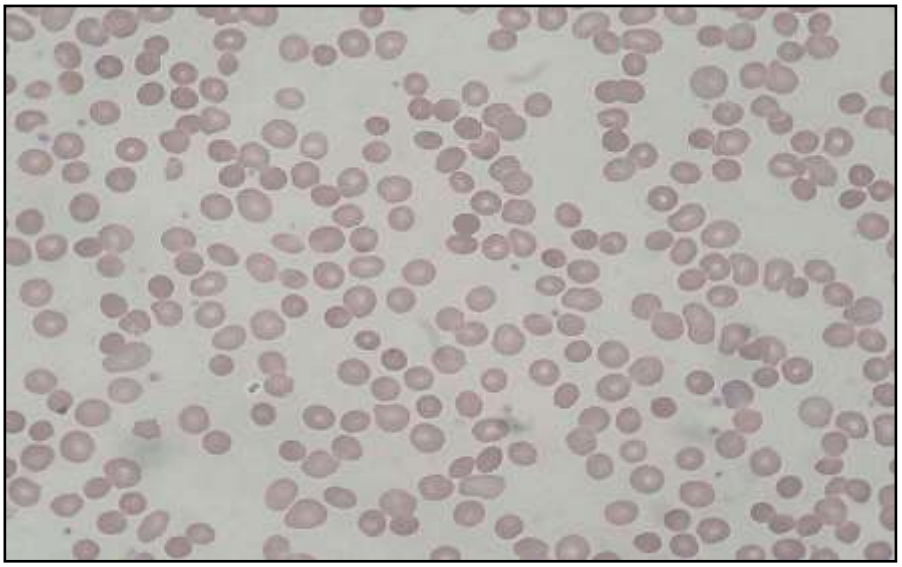

Figure 19: Hereditary spherocytosis – Peripheral smear showing Microspherocytes, Leishman's stain (X400)

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VI. DISCUSSION

Pediatric anaemia is an important universal problem.[4] It is a critical issue which needs to be addressed on a priority basis especially in the developing countries.[6] Nutritional anaemia is a recognized public health problem worldwide.[5] In India, anaemia is the most common nutritional problem affecting more than half of the total population, particularly the children and the pregnant women.[7]

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.[8]

Given the detrimental long term effects and high prevalence of iron deficiency, its prevention in early childhood is an important public health issue.[9]

Patients with hemoglobinopathy syndromes are commonly encountered in hematology clinics. Of these, the commonest disorder in India is thalassemia.[10]

The clinicopathological patterns, the morphological and the etiological types of anaemia as analyzed in the present study of 100 pediatric anaemia cases were compared with the other similar studies.

In the present study, more males were found to be anemic as compared to females(3:2). A similar gender distribution was noted in the study by Gomber et al.(1.2:1). Whereas, in a study conducted by Kapur et al. there was no difference in the gender distribution.[11]

In the present study, preschool children were maximally affected which is in concurrence with the study by Stellinga-Boelan et al.[12] Whereas, in a study by Sharada et al. the school going children were maximally affected(75%) and in a study by Susan et al[13]. infants were maximally affected(64%).

In the present study, severe degree of anaemia was found in the maximum number of cases(48%), whereas, in a study by S. Jain et al., moderate degree of anaemia(49.8%) was the most prevalent type.

The probable factors contributing to the prevalence of severe anaemia in the present study may be attributed to the low socioeconomic status, illiteracy and ignorance of the parents because of which most of the children would have developed severe degree of anaemia at the time of presentation. Besides this, the present study was undertaken in the tertiary care hospital where patients were brought in only after the initial screening and a significant lapse of time.

Table 4: Comparative study of morphological variations in pediatric anaemias

Morphological variations	**Present study**	**Kapur et al.**[71]
Microcytic hypochromic anaemia	54%	43.2%
Normocytic hypochromic anaemia	22%	17%
Normocytic normochromic anaemia	13%	27%
Dimorphic anaemia	8%	10%
Macrocytic anaemia	3%	2.7%

The peripheral smear findings in the thalassemia major cases in the present study included anisopoikilocytosis, increased number of polychromatophilic RBCs and normoblasts. An increased reticulocyte count was also seen. Hb electrophoresis showed an increase in HbF. These findings are in concurrence with the study by Swarup et al.[14]

In the present study, the mean Hb values in IDA and thalassemia trait were 5.8gm/dl and

7.9gm/dl respectively, revealing that, the Hb value in thalassemia trait is
higher as compared to IDA, in which, Hb values are usually lower. This observation is similar to that in the study by Madan et al.[15]

It was observed in the present study that, thalassemia trait could not be differentiated from IDA on peripheral smear examination. RDW was helpful in distinguishing between the two conditions. It was found to be increased in IDA (mean RDW=21.04) and decreased in thalassemia trait (mean RDW=16). Hb electrophoresis and demonstration of HbF, helped in the confirmation of diagnosis in these cases. Similar observations were noted in the studies done by George et al.,[16] Claude Owen Black et al.[17] and Mussarat Niazi et al.[18]

VII. CONCLUSION

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. 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.

Children being the most vulnerable group for nutritional deficiencies, require early screening for anaemias and associated illnesses. Initial screening and subsequent diagnostic tests enable early diagnosis and appropriate management. Utilisation of technologic advances is beneficial in arriving at a definite diagnosis. The basal blood parameters are mandatory before initiating treatment in pediatric anaemia cases.

Thalassemias and other hemoglobinopathies impose financial, emotional and psychological stress on the patients and their families besides draining valuable resources of the country. Hence, screening for these diseases is mandatory. Use of prenatal diagnostic techniques and early detection of these disorders would ensure tremendous benefits and alleviation of suffering.

In the present study, the preschool children were found to be the most affected. Hence, it is recommended that, this age group is compulsorily screened for anaemia.

A uniform definition of screening criteria and an effective system to respond to abnormalities is the need of the hour. The present study was undertaken, keeping this need in view.

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