



Clinicohematological Study of Different Patterns of Anemia in Infancy and Childhood

F. K. K. Jasima Nilofer¹ and Rajalakshmi V. Mary Lilly^{1*}

¹Department of Pathology, Sree Balaji Medical College and Hospital, Affiliated to Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i20A31347

Editor(s):

(1) Dr. Sawadogo Wamtinga Richard, Ministry of higher education, scientific research and innovation, Burkina Faso.

Reviewers:

(1) Jayasri Vengadapathy, Kasturba Gandhi Nursing college, Sri Balaji Vidyapeeth, India.

(2) Nagham Mahmood Aljamali, Kufa University, Iraq.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/66747>

Received 24 January 2021

Accepted 29 March 2021

Published 03 April 2021

Original Research Article

ABSTRACT

Objectives: Pediatric anemia is one of the major health problems in India and in many parts of the world, as it results in reduced exercise tolerance, slower rate of growth, impaired development and cognition, and delayed wound healing. Anemic children are also at a higher risk of death due to complications associated with malnutrition and infection.

Aim: To evaluate the clinical features and the basic hematological parameters of anemia in infants and children, in the age group of 6 months to 14 years. To study the morphological patterns of different types of anemia on peripheral smear & correlate the corresponding clinical presentation.

Methodology: The study was conducted on 100 patients between the age group of 6 months to 14 years in the pediatric ward of Sree Balaji Medical College & Hospital, Chennai. The hematological analysis was made by using automated analyser (Sysmex KX-21 autoanalyser). The complete haemogram was done from Peripheral smears for each participant. The reticulocyte count was done by the supravital staining technique using Brilliant crystal blue. The experiments were done in triplicates and statistical analysed were performed by using Graphpad Prism (Ver.5).

Results: The present study showed that anemia was more prevalent among male children than female counterparts and pre- school children were severely affected. The commonest presenting

*Corresponding author: E-mail: marylilly.s@bharathuniv.ac.in;

condition was acute gastroenteritis followed by respiratory symptoms. The most common morphological type was microcytic hypochromic anemia and iron deficiency anemia was the most common etiological type.

Conclusion: Pediatric anemia is quite common due to the fact that children are the most vulnerable population for anemia to occur. This compels prompt screening and diagnosis at an early stage through necessary investigations & utilization of available advanced technical modalities in order to initiate timely treatment and management.

Keywords: Complete hemogram; Microcytic hypochromic anemia; Iron deficiency anemia; acute gastroenteritis.

1. INTRODUCTION

Pediatric anemia is one of the major health burdens in India and in major parts of the world, as it results in reduced exercise tolerance, slower rate of growth, impaired development and delayed wound healing [1]. Anemic children are also at a higher risk of death due to complications associated with malnutrition and infection. Prevalence rate of anemia is an essential indicator of the nutritional status within the pediatric population. In the United States, around 18% of the children and in the developing countries about 82% of the children are anemic [2] Because of these factors, the study of the etiopathogenesis of anemia in infancy and childhood has attracted wide attention in the recent years in India [3,4].

In most children, anemia is asymptomatic but has abnormal hemoglobin levels on routine screening. A child with anemia would not always have pallor or all other related symptoms, so acquiring a complete history and elucidating proper physical examination can help in identifying the cause of anemia [2]. The iron stores are easily restored during the first few months of life even when the hemoglobin levels tend to fall. Thus iron deficiency is very rare to induce anemia until the reach of six months. Glucose-6-phosphate dehydrogenase (G6PD) deficiencies occur more commonly in males. Habits Pica or geophagia usually results in iron deficiency. History of recent drug use may suggest G6PD deficiency or aplastic anemia and so does viral illness cause red cell aplasia. Recurrent diarrheal episodes show suspicion of malabsorptive occult blood loss that occurs in inflammatory bowel disease. The physical examination constitutes an important aspect, but is essentially normal in most children with anemia. Findings that suggest chronic anemia include irritability, pallor, glossitis, a systolic cardiac murmur, delayed growth and changes in the nailbed.

Acute anemia presents clinically with jaundice, splenomegaly, tachypnoea, hematuria, tachycardia and even congestive heart failure. Anemia is defined as a reduced hemoglobin concentration as compared to the levels in age-matched controls. In screening situations, when anemia is encountered, the patient should undergo a complete blood count evaluation (CBC). Anemia can be classified into microcytic, normocytic and macrocytic types based on the Mean Corpuscular Volume (MCV) estimation.

Next, anemia work-up includes peripheral smear examination and reticulocyte count measurement. Peripheral smear indicate the etiology of the anemia based on the red cell morphology. Basophilic stippling representing clumped ribosomes is in thalassemia syndromes, iron deficiency anemia and lead poisoning. Howell-Jolly bodies (nuclear fragments) are noted in asplenia, pernicious anemia and severe iron deficiency. The reticulocyte percentage is essential in segregating anemia due to decreased RBC production from a hemolytic anemia (increased RBC destruction). Bone marrow disorders or aplastic anemia show a low reticulocyte count, whereas a hemolytic process or active blood loss represents higher reticulocyte count. Corrected reticulocyte counts more than 1.5 indicates increased RBC production [2,5,6].

If the diagnosis is still not clear after the analysis of the initial laboratory findings, other confirmatory studies may be required. In very low MCV, serum iron level and total iron binding capacity (TIBC) estimation is suggested. In case of suspicion of hemolysis, G6PD assay, hemoglobin electrophoresis, direct Coombs' test, lactate dehydrogenase (LDH), and bilirubin (indirect) estimation may help in arriving at a diagnosis. Anemic children with an elevated MCV, requires vitamin B12 and folate to be estimated in doubtful cases. [7,8,9] Enzymopathies by RBC enzyme panel,

hereditary spherocytosis by osmotic fragility testing, membranopathies by membrane protein studies are other confirmatory tests that can be employed. In certain circumstances, such as a suspected hematologic malignancy, a bone marrow aspiration may be indicated [10, 11,12,9,13].

Anemia most prevalent iron deficiency related health complexity in India. The recent data predicted that approximately 58.6% of children are suffered from anemia. The women population is more prone than men that accounts for 53.2% of non-pregnant and 50.4% of pregnant women were found to be anemic as in 2016 as per the National Family Health Survey (NFHS) [14]. The various patterns of anemia in children are often represented by their underlying etiopathogenetic factors while the investigation of anemia is mainly hematological. For evaluating anemia, a detailed clinical history combined with necessary examination and complete blood counts with peripheral smear examination are the basic steps. In the current study, evaluation of the hematological and the biochemical parameters, if necessary, were done to classify the clinic hematological patterns of anemia and their etiology in children. The prospective of this study was to identify the prevalence, patterns and the various morphological types of pediatric anemia.

2. MATERIALS AND METHODS

The current 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 Sree Balaji Medical College & Hospital, Chennai with anemia and also those who presented with other complaints and were incidentally found to have anemia. 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 October 2017 to August 2019 after getting ethical approval (Ref no. 002/SBMC/IHEC/2018/1049).

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, from which the following parameters were

obtained. 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.

No hemolytic anemia cases were suspected on clinical and peripheral blood examination but one, thereby no further hematological work up including, osmotic fragility or Coomb's test was done, except for the one case warranting hemoglobin electrophoretic analysis. The statistical analysis was performed using Graphpad Prism (Ver.5) and descriptive analysis such as mean and standard deviation and percentage were performed for each parameter separately. Chi-square and independent *t*-test were used for comparison Pearson's correlation tests were performed to examine the relationships between hematological indicators.

3. RESULTS

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

In the current 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.

Among the infants 14 were males and 25 were females. Among the pre-school children, 27 were males and 21 were females. Among the school going children, 19 were males and 8 were females.

In the current study, eight out of 100 children had mild degree of anemia amongst whom; five were females and three males. Forty-four children were found to have moderate degree of anemia, amongst whom, 25 were males and 19 females. Severe degree of anemia was found in 48 children amongst whom, 30 were males and 18 were females.

Non-significance was observed between the severity of the anemia and gender distribution with the Yates Chi-square of 0.58; DF=2 and *p*-value of 0.97.

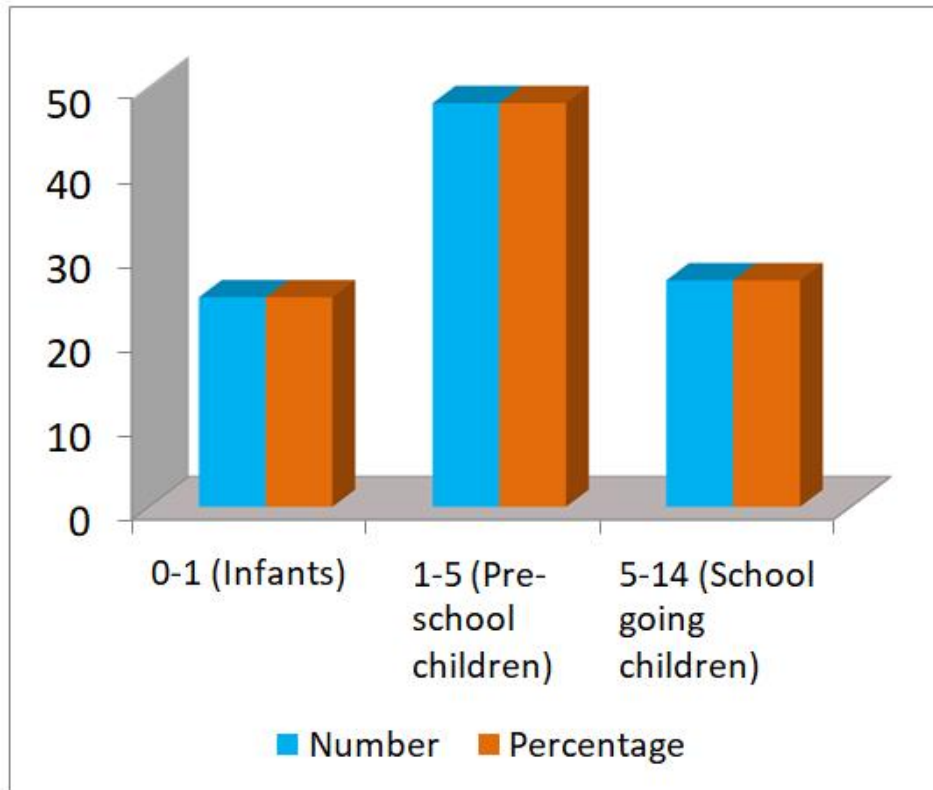


Fig. 1. Age wise distribution of pediatric anemia

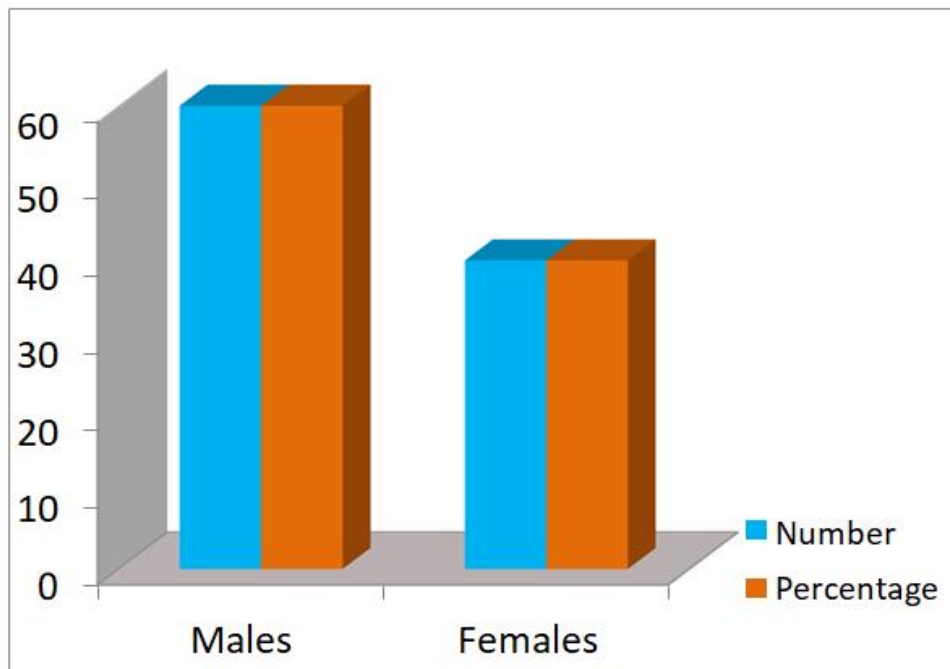


Fig. 2. Gender wise distribution of pediatric anemia

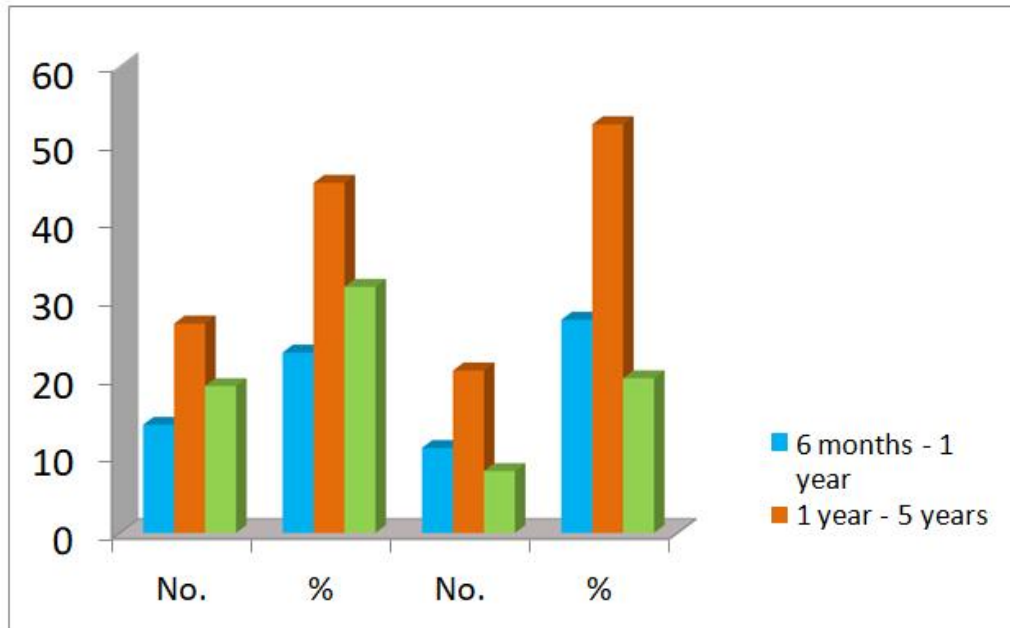


Fig. 3. Gender wise distribution of pediatric anemia in different age groups

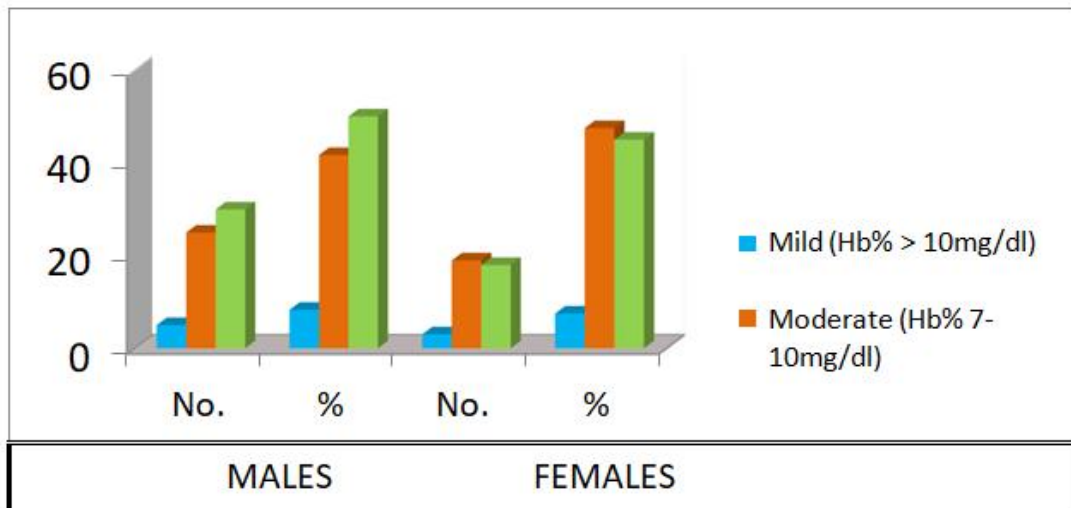


Fig. 4. Gender wise gradation of pediatric anemia

In the current study, among 25 infants, 2 had mild anemia, 9 had moderate anemia and 14 had severe anemia. Out of the 48 pre-school children, 4 had mild anemia, 21 had moderate anemia and 23 had severe anemia. Out of the 27 school going children, 2 had mild anemia, 14 had moderate anemia and 11 had severe anemia. Among infants and pre-school children, severe degree of anemia was more prevalent. Among school going children, moderate degree of anemia was more prevalent. This was found

statistically significant with the Yates Chi-square value of 21, $df = 4$ and p -value < 0.001 .

In the current study, the common presenting symptoms were gastrointestinal including vomiting, diarrhea 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.

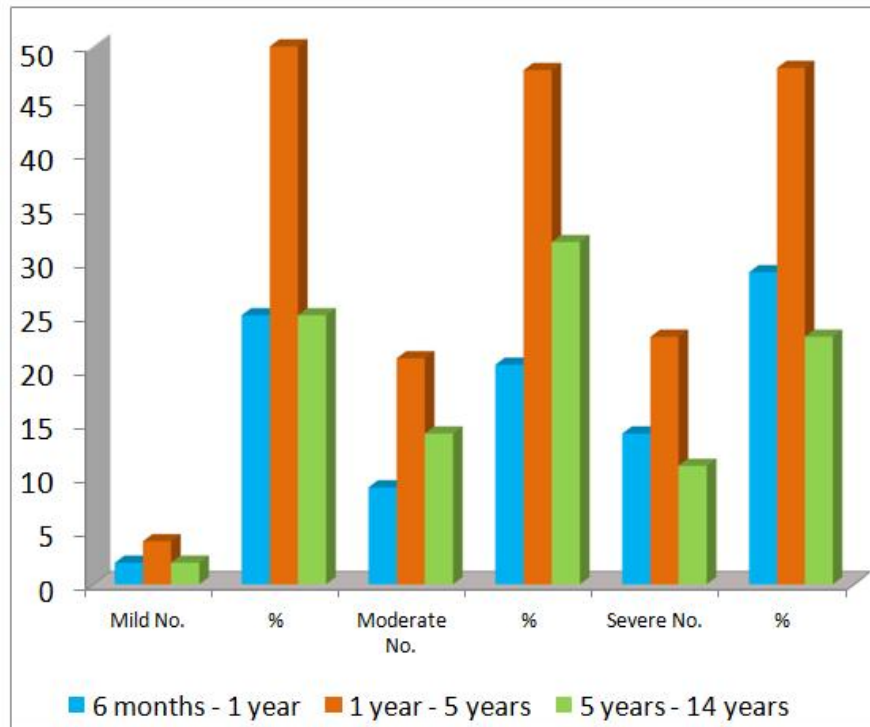


Fig. 5. Age wise gradation of pediatric anemia

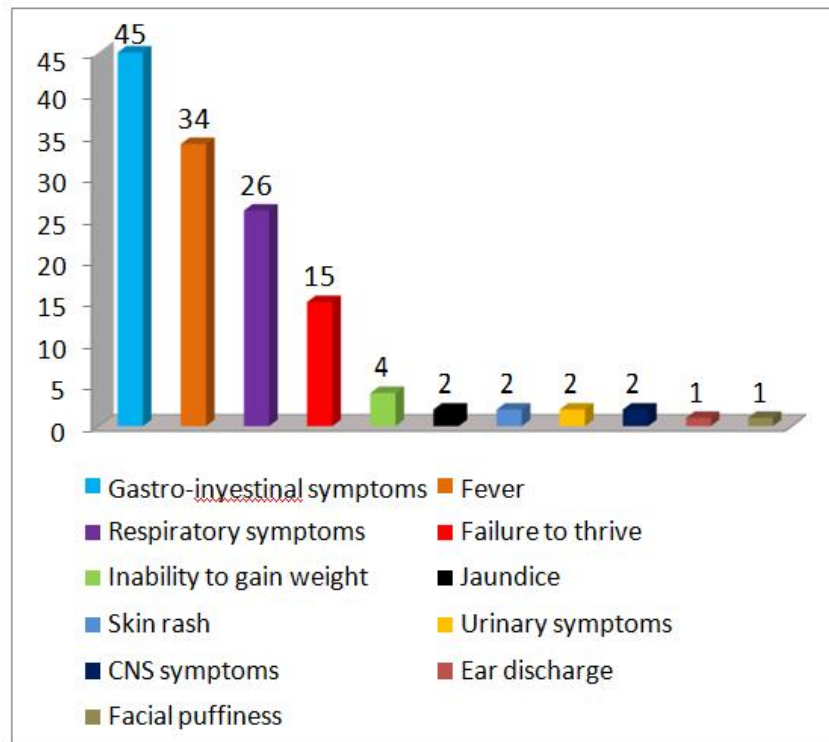


Fig. 6. Common presenting symptoms

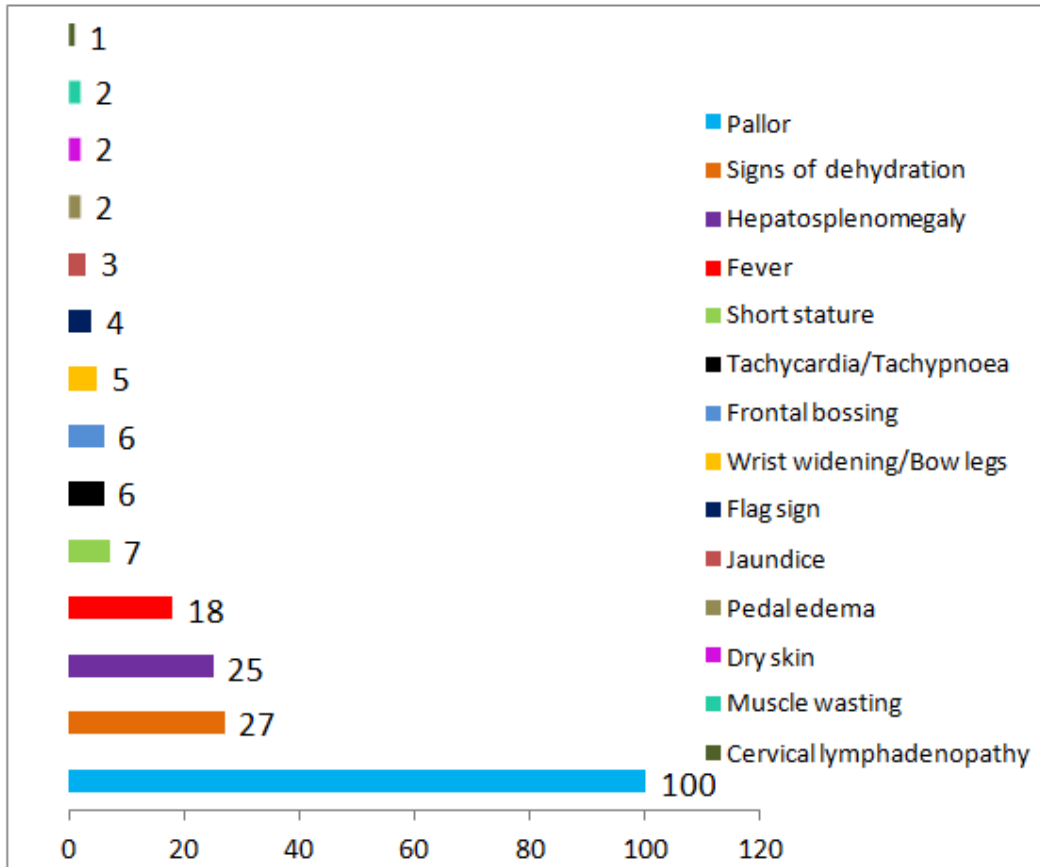


Fig. 7. Common presenting signs

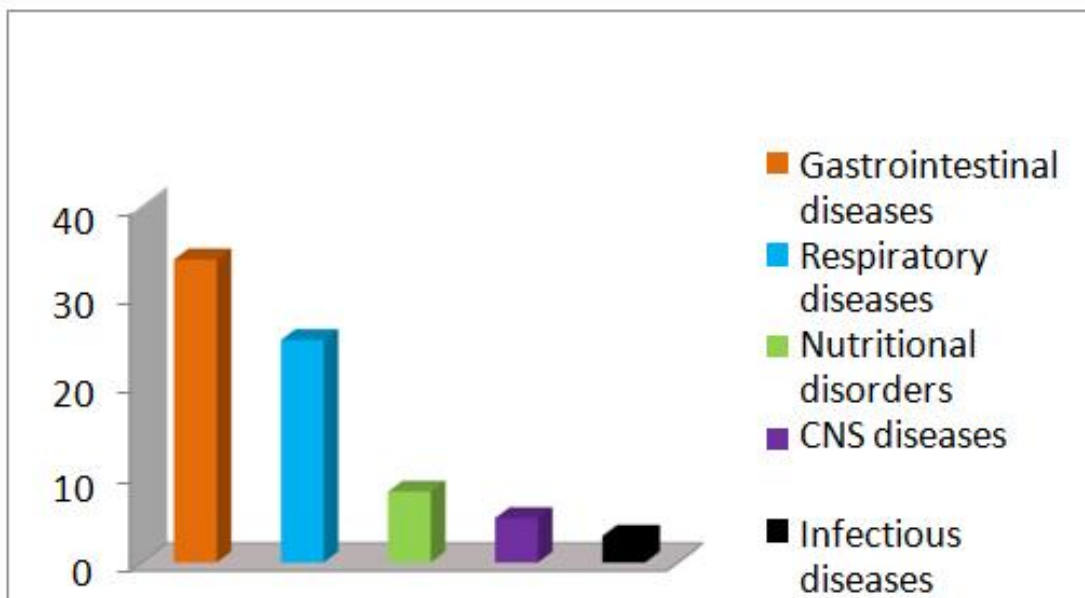


Fig. 8. Associated general and systemic disorders

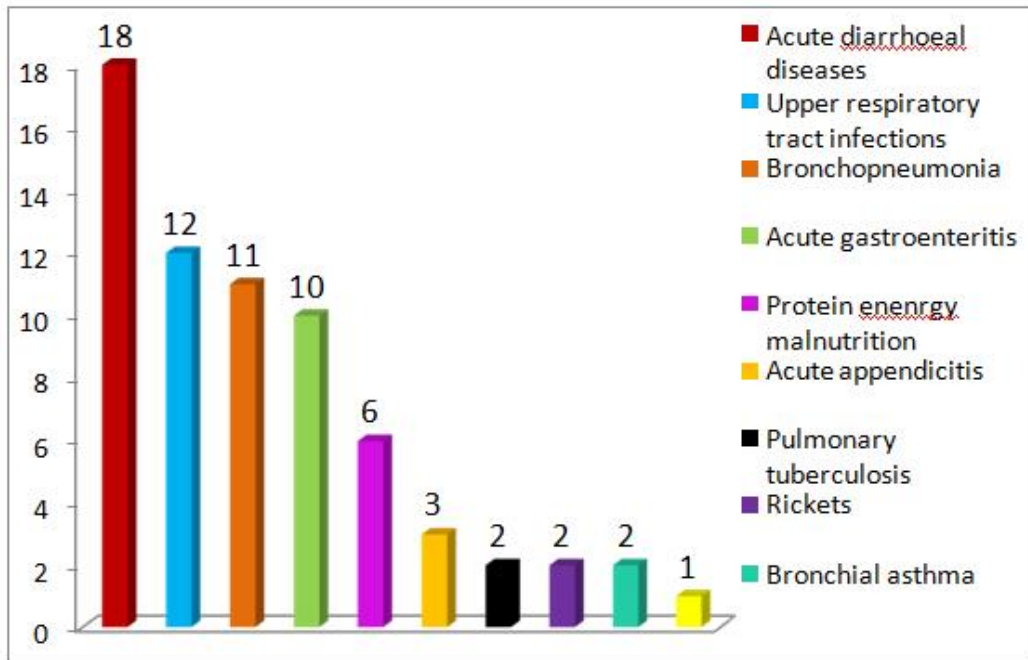


Fig. 9. Distribution of anemia based on clinical diagnosis

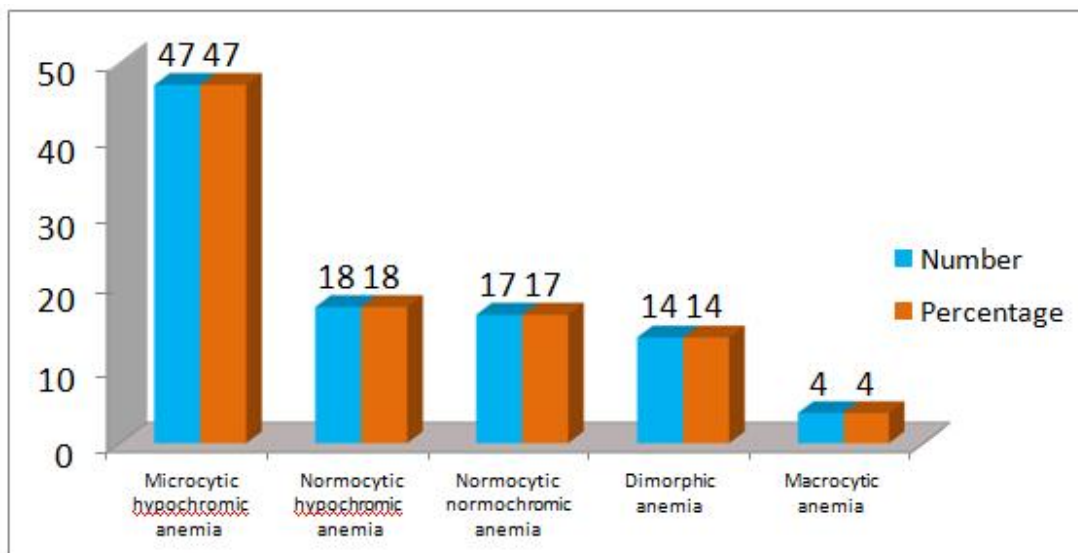


Fig. 10. Distribution of the morphological types of anemia

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, hemiparesis/ hemiplegia, dry skin, muscle wasting, microcephaly and cervical lymphadenopathy were seen in some cases.

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

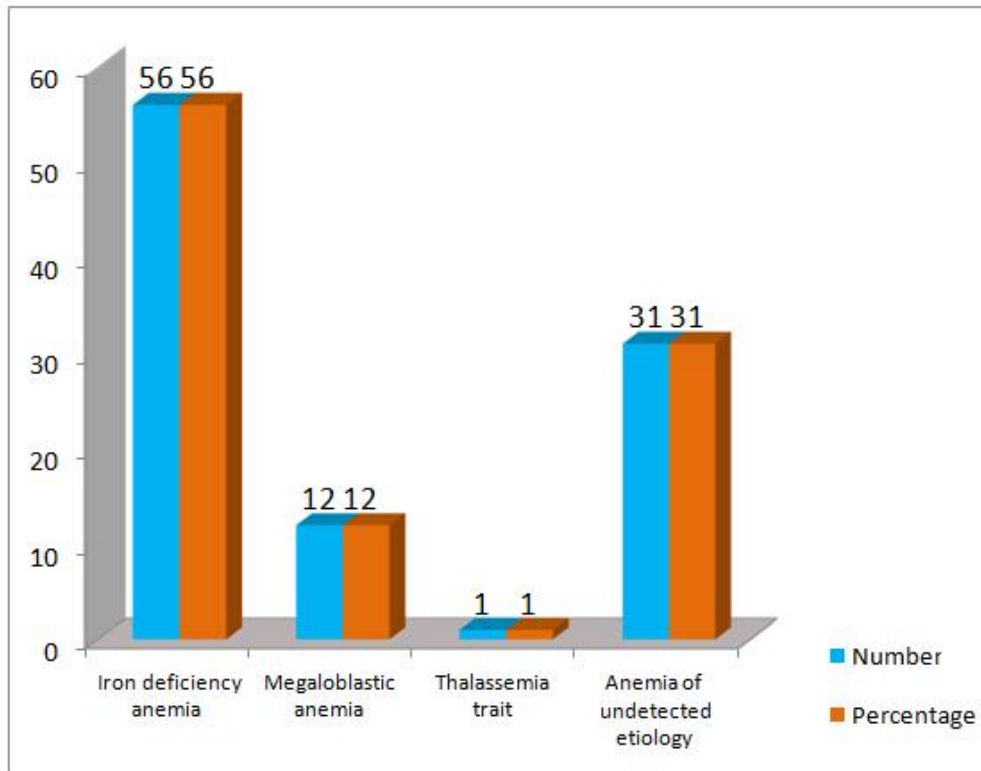


Fig. 11. Distribution of anemia based on etiology

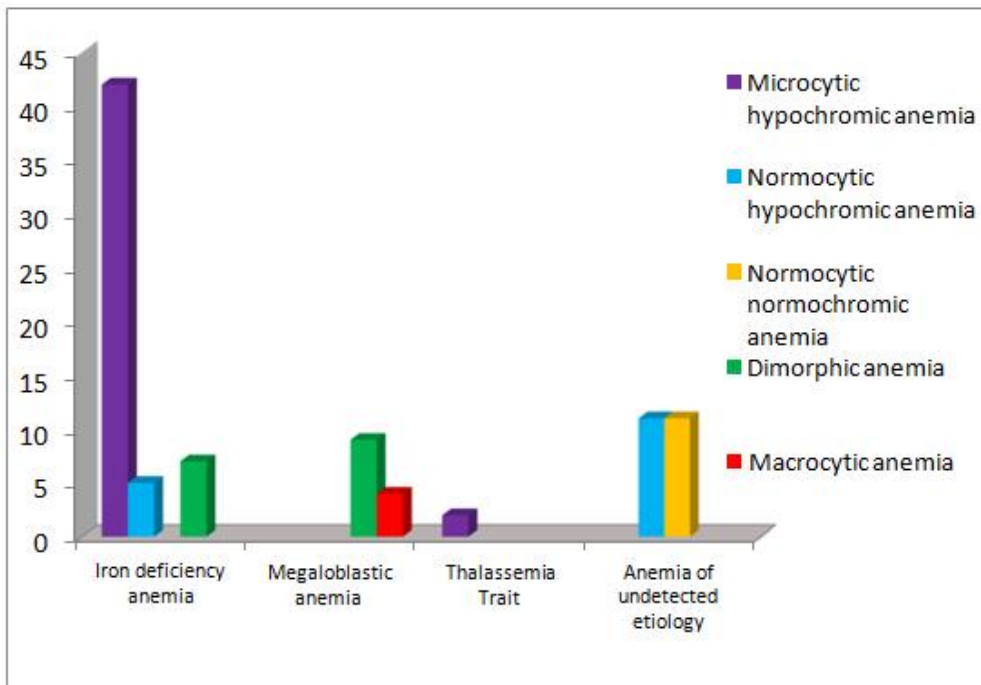


Fig. 12. Cross table showing comparative prevalence of morphological and etiological types of anemia

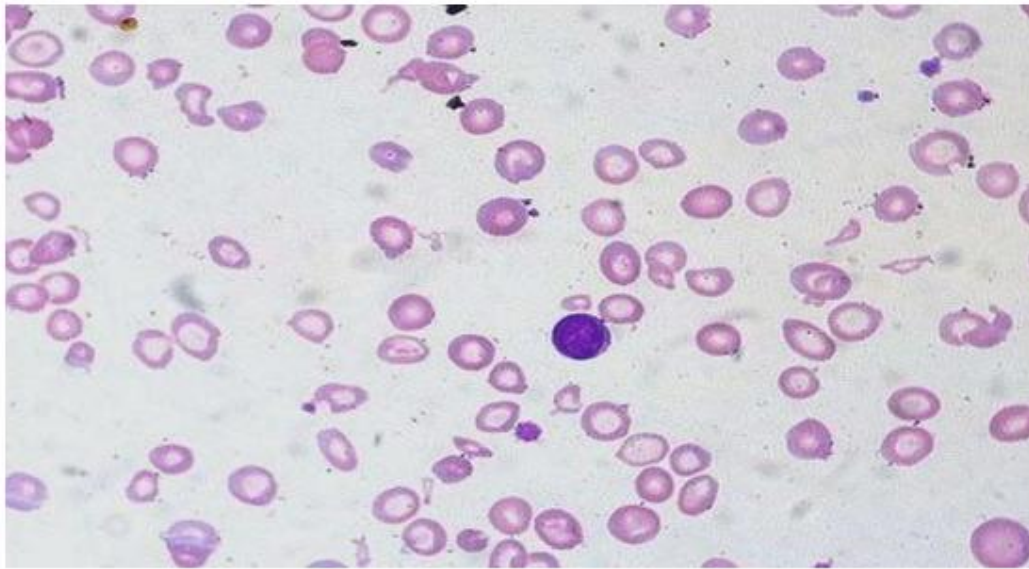
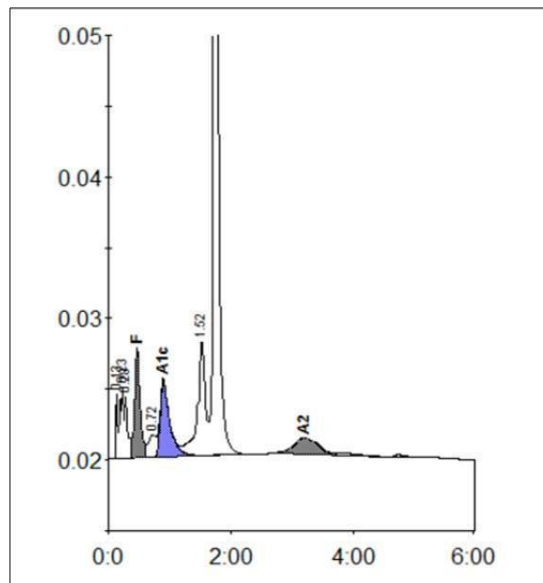


Fig. 13. IDA – Peripheral smear showing anisopoikilocytosis & microcytic hypochromic cells, Leishman's stain (X400)



Concentration:	%
F	4.8
A1c	8.0
A2	3.6

Fig. 14. Thalassemia minor – Hb electrophoresis graph showing increased HbA and HbF

In the current study, acute diarrheal diseases followed by respiratory tract infections and bronchopneumonia were the common clinical diagnosis associated with anemia. Rickets, bronchial asthma and dengue were the least common clinical diagnosis.

In the current study, the most frequent morphologic type of anemia was microcytic

hypochromic anemia (47%) followed by normocytic hypochromic anemia (18%), normocytic normochromic anemia (17%) and dimorphic anemia (14%). Macrocytic anemia (4%) was the least common morphological type. In this study, iron deficiency anemia (56%) was the most common type followed by anemia of undetected etiology (31%). Megaloblastic anemia (12%) with least common type being

Thalassemia minor (1%). In the single case of Thalassemia minor, the value of HbF, HbA2 and HbA1c were 4.8, 3.6 and 8.0 respectively.

Out of the 12 cases of megaloblastic anemia, four had macrocytic picture and eight had dimorphic picture. The specific etiological factor could not be definitively established in 31 cases and these patients were grouped under the category of anemia of undetected etiology and one was being a thalassemia minor case.

4. DISCUSSION

Pediatric anemia is a crucial universal problem [7]. It is a critical issue which has to be addressed on a priority basis especially in the developing countries. Nutritional anemia is a recognized public health problem worldwide. Anemia is the most common nutritional problem in India, affecting more than half of the total population, particularly the children and the pregnant women [15,16,17]. Given the detrimental effects of iron deficiency anemia, its prevention in childhood is an important public health issue [6,2]. Patients with hemoglobinopathies are commonly encountered in hematology. Of these, the commonest disorder in our country is thalassemia [18,19,20,21].

The clinic hematological patterns, the morphologic and the etiologic types of anemia as analyzed in the current study of 100 pediatric anemia cases were compared with the other similar studies. In the current study, microcytic hypochromic anemia (47%) was the most common type followed by normocytic hypochromic anemia (18%), normocytic normochromic anemia (17%), dimorphic anemia (14%) and macrocytic anemia (4%). This finding is in concurrence with the study by Kapur et al., wherein microcytic hypochromic anemia (43.2%) was found to be the most common followed by normocytic hypochromic anemia (28%), normocytic normochromic anemia (17%), dimorphic anemia (10%) and macrocytic anemia (2.7%).

It was observed in the current study that, thalassemia minor couldn't be differentiated from IDA on a peripheral smear. RDW helped in distinguishing the two conditions. It was found to be increased in IDA (mean RDW =21.04) and decreased in thalassemia minor (RDW =16). Hb electrophoresis and demonstration of HbF, helped in the confirmation of diagnosis in the case. Similar observations were noted in the

studies done by Madan et al. [22] Swarup [23] and Mussarat Niazi et al. [18,22,24].

Thalassemia and other hemoglobinopathies impose financial as well as emotional stress on the patients and their families alike, besides the draining valuable resources of our country. Hence, screening for these diseases is mandatory. Use of prenatal diagnostics and early detection of these disorders would ensure tremendous benefits and alleviation of suffering.

5. CONCLUSION

In the current study, the preschool children are found to be the most affected. Hence, it is recommended that, this age group is compulsorily screened for anemia. A uniform definition of screening criteria and an effective system to respond to abnormalities is the need of the hour. The current study was taken up, keeping this need in view.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee (Ref no. 002/SBMC/IHEC/2018/1049).

ACKNOWLEDGEMENTS

The encouragement and support from Bharath University, Chennai is gratefully acknowledged. For provided the laboratory facilities to carry out the research work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Jain S, Chopra V, Agar SK, Bhatnagar M, Singh KV. Anemia in early childhood. Indian Journal of Pediatrics. 2000; 67(1):19-21.
2. Irwin JJ, Kirchner JT. Anemia in children. American Family Physician. 2001;64(8): 1379-86.

3. Saraya AK, Singla PN, Ramachandra K, Ghar OP. Nutritional macrocytic anemia of infancy and childhood. *The American Journal of Nutrition*. 1970;23(11):1284-378.
4. DeGruehy CG. The red cell: Basic aspects of anemia. 5th Ed. In: de Grueby's Practical Hematology in Medical Practice, Franklin Firkun, Colin Chessman, David Pennington, Brian Rush, eds. Great Britain: Blackwell Science Ltd. 1989;17-36.
5. Sharada Sindu, Khanta Kumari, Manjulaa Uppal. Prevalence of anemia in school children of Haryana. *Indian Journal of Medical Science*. 2002;56(5):218-21.
6. Sunil Ghomber, Bhawarna Nishi Madhan, Avtaar Lal, Kusum Kela. Prevalence and etiology of nutritional anemia among school going children of slums. *Indian Journal Med Res*. 2003;118:167-71.
7. Milher DJ, Dunn PV, Berg B, Abdoni SF. A hematological survey of school children in the United Arab Emirates. *Saudi Medical Journal*. 2003;24(6):609-13.
8. Brugnara C, Oski FA, Nathan DG. Diagnostic approach to the anemic patient. 12.7th Ed. In: Natan and Oski's hematology of childhood, David G Nathan, Stuart Horkin, David Ginsburg, Thomas A Look, David Fisher, eds. Philadelphia: Elsevier. 2008;456.
10. Demaeyer EM, Dollaman P, Gurney JM, Hallberg L, Sood SK. Preventing and controlling iron deficiency anemia through primary health care. Geneva: World Health Organization. 1989;26-36.
11. George NK, Suresh Kumar N, Lal JJ, Sreedevi R. Anemia and nutritional status of pre-school children in Kerala. *Indian Journal of Pediatrics*. 2000;67(8):575.
12. DeMaeyer E, Adiels-Tegman M. The prevalence of anemia worldwide. *World Health Stat*. 1985;38:302-16.
13. Robbins Cotran. Red blood cell and bleeding disorders. 8th Ed. In: *Pathologic Basis of Diseases*, Vinay Kumar, Abul K Abbas, Nelson Fausto, Jon C Aster, eds. Philadelphia: Elsevier. 2010;640.
14. Available:<http://rchiips.org/nfhs/index.shtml>
15. Brotanck LM, Gosz J, Weittman M, Flores G. Iron deficiency in children in United States; Risk factors and ethnic disparities. *Pediatrics*. 2007;120(3):568-75.
16. Swarup M. Clinical and hematologic profile of thalassemia and hemoglobinopathics in India. *Ind Ped*. 1983;20:701-13.
17. Susan GT, Benjamin JT. The incidence, treatment and follow-up of iron deficiency anemia in a tertiary care pediatric department. *Clinic Ped*. 2005;333:7.
18. Hydrasys, Operator's Manual, Sebia Cheryl Burns MS. Automation in hematology. 2nd ed. Chapter 41. In: *Clinical laboratory hematology*, McKenzie SB, ed. New Jersey: Pearson Education. 2004;815-7.
19. Using clinical signs to diagnose anemia in African children. *Bulletin of World Health Organization*. 1995;73(4):477-82.
20. Agarwal BR. Nutritional anemia. *Pediatrics on Call*. Chen AWU, Respirance L, Birnstein H. Screening for iron deficiency. *Ped in Review*. 2002;23(5):171-7.
21. Stellinga-Boelen AAM, Storm H, Neigerman PA, Bijelvel CMA. Iron deficiency among children of Asylum seekers in the Netherlands. *Journal of Pediatric Gastro Enterology and Nutrition*. 2007;45(5):591-5.
22. Madan N, Sikka M, Sharma S, Kera K. Comparison of hematological status of two common causes of microcytosis. *Ind J Hematology Blood Transfusion*. 1998;16(2):43-6.
23. Swarup M. Clinical and hematological profile of thalassemia and hemoglobinopathies in India. *Ind Ped*. 1983;20:701-13.
24. Claude Owen Black. Distinguishing thalassemia trait and iron deficiency by direct inspection. *American Journal of Pathology*. 2009;131:444-5.

© 2021 Nilofer and Lilly; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/66747>