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Evaluation of Hypochromic Microcytic Anemia in Children Presenting in Pediatrics OPD Combined Military Hospital (CMH) Sargodha

Saqib Hussain Korejo, Adeel Arif, Muhammad Zahid*, Mohsin Hussain Nizamani, Muhammad Hussain***, Ashfaq Ahmed******

Departments of Pathology, Combined Military Hospital, Sargodha/National University of Medical Sciences (NUMS) Pakistan, *Department of Pediatrics, Combined Military Hospital, Lahore/National University of Medical Sciences (NUMS) Pakistan, **Department of Pathology, Combined Military Hospital, Bahawalpur/National University of Medical Sciences (NUMS) Pakistan, ***Department of Immunology, Armed Forces Institute of Pathology, Rawalpindi/ National University of Medical Sciences (NUMS) Pakistan, ****Department of Medicine, Combined Military Hospital, Sargodha/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the cause of hypochromic microcytic anemia in children presenting to Pediatric Outpatient Department (OPD).

Study Design: Descriptive cross-sectional.

Place and Duration of Study: Departments of Pathology and Pediatrics, Combined Military Hospital (CMH) Sargodha, from Jan to Jul 2022.

Methodology: All patients having hypochromic microcytic anemia, aged between 6 months to 12 years of age, and fulfilling inclusion and exclusion criteria, were included in the study. Diagnosis and grading of anemia were done according to World Health Organization (WHO) criteria. Detailed clinical history, examination, and a panel of investigations, including hematological indices and parameters, biochemical, and immunological investigations, were done for evaluation.

Results: A total of 359 children with hypochromic microcytic anemia were evaluated. The mean age of children was 2.95±2.40 years with male to female ratio of 1.6:1. In terms of severity, 3(3.03%) children had mild anemia, 38(38.38%) had moderate anemia and 58(58.58%) had severe anemia. Iron deficiency was found in 205(57.10%) children, followed by mixed deficiency in 91(25.30%), β-Thalassemia trait in 42(11.70%), and normal chemical and immunological profile in 21(5.80%) children. One case, each, of hereditary spherocytosis and lymphoblastic leukemia, was diagnosed on the basis of peripheral film.

Conclusion: Nutritional deficiency was the most common etiology of hypochromic microcytic anemia followed by the β-Thalassemia trait; thus, chronic disease should be kept in mind while investigating refractory cases.

Keywords: Anemia, Celiac Disease, Hypochromic microcytic, Iron deficiency, Thalassemia.

How to Cite This Article: *Korejo SH, Arif A, Zahid M, Nizamani MH, Hussain M, Ahmed A. Evaluation of Hypochromic Microcytic Anemia in Children Presenting in Pediatrics OPD Combined Military Hospital (CMH) Sargodha. Pak Armed Forces Med J 2025; 76(Suppl-2): S397-S400. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-2.10140*

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INTRODUCTION

Hypochromic microcytic anemia (HM Anemia) is a frequent morphologic anemia followed by normocytic anemia, hypochromic anemia, normocytic, and macrocytic anemia.[1] Iron deficiency anemia (IDA) and β-Thalassemia trait are the most common disorders presenting with microcytic hypochromic blood picture while other causes can be chronic illnesses, hemoglobinopathies, hemolytic anemias, and lead poisoning.[2] Infants and children diagnosed with IDA require proper iron replacement therapy for neurological growth.[3] The concurrent presence of different anemias masks the typical findings which cause difficulties in reaching accurate diagnosis.[4] After IDA, hemoglobinopathies are common causes of anemia with hypochromic microcytic blood picture. β-thalassemia trait or minor is usually asymptomatic, β-thalassemia intermedia and major are severe forms that are distinguished by their clinical behavior and transfusion dependence. Laboratory findings include HM anemia and normal red cell distribution width (RDW). Proper family and transfusion history, complete blood picture, morphology, hemoglobin electrophoresis, and high performance liquid chromatography are essential for the diagnosis of thalassemia.[5] Sometimes, IDA and vitamin B-12 deficiency co-exist which obscure megaloblastic anemia and present initially with a hypochromic microcytic picture with preexisting iron deficiency anemia or thalassemia.[6] Lactate dehydrogenase enzyme (LDH) can be used as a differentiating marker between megaloblastic anemia and mixed nutritional deficiency anemia as serum LDH levels were high in megaloblastic anemia when compared with mixed deficiency anemia. Direct coombs test Positive autoimmune hemolytic anemia can also present with

Correspondence: Dr Saqib Hussain Korejo, Departments of Pathology, Combined Military Hospital, Sargodha Pakistan

Received: 28 Mar 2023; revision received: 27 Jan 2024; accepted: 02 Feb 2024

hypochromic microcytic blood picture.[7] Refractory cases with confirmed IDA along with pallor and delayed growth should be worked up for chronic diseases.[7,8] Rare conditions like acute lymphoblastic leukemia can present in children with simple symptoms of anemia and a detailed workup of the patient is of paramount importance.[9] The rationale of this study was to determine the frequency of different causes of HM Anemia in children presenting to pediatrics OPD.

METHODOLOGY

This descriptive cross-sectional study was conducted in the Departments of Pathology and Pediatrics at Combined Military Hospital (CMH) Sargodha, from January to July 2022. Prior approval of Ethics Board was taken vide Letter Number IERB/ 01/ 2023. A sample size of 270 was calculated using WHO calculator with an anticipated frequency anemia in children of 53%[10] and confidence interval of 90%. A total of 359 samples were collected using non-probability consecutive sampling technique. Newly diagnosed patients, who were cases according to World Health Organization (WHO) recommended ranges, with mean corpuscular volume (MCV) <80 fl and mean corpuscular hemoglobin (MCH) <27 pg were included.[10,11] Informed, written consent was taken from parents of children followed by detailed history and clinical examination. Anemia was diagnosed in children aged 6 months to 5 years with a hemoglobin (Hb) level below 11 g/dl, and in children aged 6 to 12 years with an Hb level below 12 g/dl. Cases were further graded by severity: mild anemia was defined as an Hb greater than 10 g/dl but below the cut-off value for the child's age group, moderate anemia as an Hb between 7 and 10 g/dl, and severe anemia as an Hb at or below 7 g/dl.

Inclusion Criteria: All children having age from 6 months to 12 years, reporting to Pediatrics OPD, having symptoms of anemia and having hypochromic and microcytic picture were included in the study.

Exclusion Criteria: Children suffering from chronic diseases like transfusion-dependent anemias, anemia due to known chronic diseases (tuberculosis, lymphoma, chronic kidney disease, tumors, rheumatoid arthritis, inflammatory bowel disease) and chronic hemolytic disorders such as paroxysmal nocturnal hemoglobinuria were excluded from the study.

Complete blood counts were done using Sysmex XP-100 automated hematology analyzer, and parameters included Hb%, packed cell volume (PCV), red blood cell (RBC) count, RBC indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), total white blood cell (WBC) including differential count and platelet count. Manual peripheral smears and reticulocyte counts were done by a consultant hematologist using Leishman stain and supravital staining with brilliant cresyl blue. Further evaluation was done at reference lab for specialized tests while hemoglobin electrophoresis was done for diagnosis of hemoglobinopathies. Chemical and immunological profiles including serum ferritin, serum Vitamin B-12, folate levels, lactate dehydrogenase (LDH) and direct antiglobulin (DAT) test were also done. Osmotic fragility test and bone marrow aspiration were also done where required. Data was entered in Statistical Package for Social Sciences (SPSS) version 27.00 for statistical analysis. Mean, minimum value, maximum value and standard deviations were computed for continuous variables like age, WBC, Hb, MCV, CMH, RBC, Platelets, RWD. Normality was checked by Shapiro-Wilk Test and Kolmogorov-Smirnov test while total percentage of anemia calculated for all patients.

RESULTS

A total of 359 children with HM anemia fulfilling inclusion and exclusion criteria were included in the study. Majority of patient population was between the age range of 2 to 5 years with mean age being 2.95±2.40 years, of which 224(62.40%) were male and 135(37.60%) were female, however, age was not normally distribute and male to female ratio was 1.6:1. Severe anemia was noted in 209(58.20%) individuals and was the most commonly occurring while 139(38.70%) patients had moderately severe anemia and 11(3.10%) had mild anemia, as shown in Figure.

Among hypochromic microcytic anemic cases, the most common cause noted in 205(57.10%) cases was iron deficiency followed by mixed deficiency in 91(25.30%) patients while 42(11.70%) patients had β-thalassemia trait and hypochromic microcytic anemia with normal chemical and immunological profile was seen in 21(5.80%) case, however, 21(5.80%) had other diseases, which included celiac disease, which was found with anti-TTG antibodies and hereditary spherocytosis (HS) and acute lymphoblastic leukemia (ALL) on peripheral smear. Both cases were confirmed

by reference lab. A summary of hematological laboratory parameters is shown in Table.

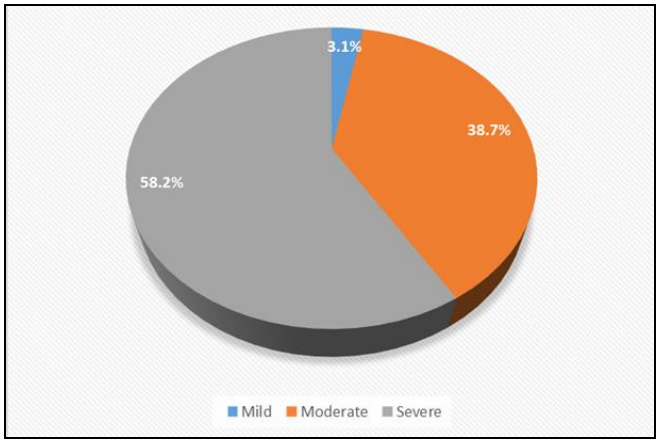

Figure: Distribution of Mild, Moderate and Severe Anemia (n=359)

Table: Summary of Laboratory Parameters (n=359)

	Mean±SD	Maximum	Minimum
WBC	12.10±4.40	24.00	5.50
Hb	7.00±1.50	10.80	4.50
MCV	60.40±9.20	77.00	45.50
MCH	14.70±3.20	23.10	8.80
RBC	4.80±0.73	6.40	3.40
Platelets	412±91.00	676.00	39.00
RDW	41.50±5.20	54.60	32.10

** WBC: Total White Blood Cell, Hb: Hemoglobin, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, RBC: Red Blood Cell, RDW: Red Cell Distribution Width*

DISCUSSION

Hypochromic microcytic anemia is the most common subtype of anemia while iron deficiency anemia and β-thalassemia trait are common causes of hypochromic microcytic anemia.[12] The present study has validated the etiology of HM anemia presenting in Pediatrics OPD as in this present study, the mean age was 2.9±2 years which is slightly higher than the age range of 1.7±0.9 years, noted by another author.[13] The most likely reason is the narrower age range of children included in the study, this being 6 to 59 months, however, in our study, the age range for the inclusion of cases was wider, extending from 6 months to 12 years. Additionally, the sample size of the present study was quite small compared to their study13. In another study, 14 the mean age was 7.5±5 years, which was higher than the mean age found in our study and probable reason for this difference was the wide age range of patients, from 1 month to 18 years, while male to female ratio of both the studies,[13,14] was comparable with the present study. Our study was also comparable with another study, where 2% cases had mild anemia, 40% had moderate anemia and 58 % had severe anemia.[15] In our study, the most common cause of anemia was iron deficiency anemia followed by mixed deficiency anemia and β-Thalassemia trait, which is comparable with other studies,[16-18] found in literature. Nutritional deficiency may present as iron deficiency, vitamin B12 deficiency, and/or folate deficiency, and while peripheral blood smear is always considered an important diagnostic tool for the evaluation of anemia, it not only aids in identification of the type of nutritional deficiency but also helps in screening important disorders like leukemia, microangiopathic hemolytic anemias, and chronic malaria, and early intervention in such cases found on peripheral smear drastically improves clinical outcomes of the patients.[17-19] In the present study, we were also able to identify one case of acute lymphoblastic leukemia and one case of hereditary spherocytosis on the peripheral film which was found to be comparable on literature search with previously conducted studies,[19,20] were the authors were also able to find similar percentage of such cases on the peripheral film. As IDA often presents as the only presenting sign of chronic diseases such as celiac disease and other malabsorption syndromes, patients who are not responding to treatment should be screened for these chronic diseases and early specific treatment should be given to these children to prevent them from developing neurological deficits.[21,22]

LIMITATIONS OF STUDY

While serum ferritin levels are used for the evaluation of decreased iron levels in the blood in conjunction with hypochromic microcytic RBC's morphology, ferritin is an acute phase reactant protein, which has a diagnostic value in case of low levels, however, it has less reliability in the case of normal and high levels. In cases where IDA is suspected despite ferritin being normal, Perl's stain is used to demonstrate iron reserves, morphologically, on bone marrow aspirate (BMA) but as BMA is an invasive procedure and in the majority of cases it is not justified to subject pediatric patients to this, thus, we did not perform this test and were limited to testing serum only.

CONCLUSION

Iron deficiency anemia is the most common cause of hypochromic microcytic anemia and peripheral blood smear is an important diagnostic tool which provides essential information about underlying diseases, warranting early intervention and improved outcome. As one of the major areas for improvement in primary health care is prevention and early diagnosis of anemia, due to its association with

delay in psychomotor development among school going children.

ACKNOWLEDGEMENT

None.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SHK & AA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MZ & MHN: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

MH & AA: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Lilly RV, Nilofer FK. Clinicohematological study of different patterns of anemia in infancy and childhood. J Pharm Res Int 2021; 33(20A): 44–55. https://doi.org/10.9734/jpri/2021/v33i20A31347
2. Kafle R, Bastola A, Samdurkar AP, Gautam N, Poudel A, Shah A. Haematological profile in microcytic hypochromic anaemia in children. J Univ Coll Med Sci 2021; 9(02): 3–7. https://doi.org/10.3126/jucms.v9i02.41941
3. Matysiak M. Anemia in children: a pediatrician's view. Acta Haematol Pol 2021; 52(4): 402–405. https://doi.org/10.5603/AHP.2021.0075
4. Busaleh F, Alasmakh OA, Almohammedsaleh F, Almutairi MF, Al Najjar JS, Alabdulatif A. Microcytic anemia hiding vitamin B12 deficiency anemia. Cureus 2021; 13(12): e20741. https://doi.org/10.7759/cureus.20741
5. Sharma DC, Arya A, Kishor P, Woike P, Bindal J. Overview on thalassemias: a review article. Medico Res Chron 2017; 4(03): 325–337.
6. Busaleh F, Alasmakh OA, Almohammedsaleh F, Almutairi MF, Al Najjar JS, Alabdulatif A et al. Microcytic anemia hiding vitamin B12 deficiency anemia. Cureus 2021; 13(12): e20741. https://doi.org/10.7759/cureus.20741
7. Brage ET, Santos MF, Mejorada RL, Domínguez RG, Hernández AO, Martín AA, et al. Autoimmune haemolytic anaemia due to cold antibodies in a renal cancer patient. Case Rep Oncol 2022; 15: 507–513. https://doi.org/10.1159/000524592
8. Talarico V, Giancotti L, Mazza GA, Miniero R, Bertini M. Iron deficiency anemia in celiac disease. Nutrients 2021; 13(5): 1695. https://doi.org/10.3390/nu13051695
9. Ng C, Alessandri A, Bowen AC, Ramachandran S. Acute lymphoblastic leukaemia presenting with bone marrow necrosis. Ann Hematol Oncol 2018; 5(1): 1186.
10. Habib MA, Black K, Soofi SB, Hussain I, Bhatti Z, Bhutta ZA, et al. Prevalence and predictors of iron deficiency anemia in children under five years of age in Pakistan, a secondary analysis of national nutrition survey data 2011–2012. PLoS One 2016; 11(5): e0155051. https://doi.org/10.1371/journal.pone.0155051
11. Simbauranga RH, Kamugisha E, Hokororo A, Kidenya BR, Makani J. Prevalence and factors associated with severe anaemia amongst under-five children hospitalized at Bugando Medical Centre, Mwanza, Tanzania. BMC Hematol 2015; 15(1): 8. https://doi.org/10.1186/s12878-015-0033-5
12. Janjale A, Pande S, Sonawane R, Ahire N, Sonawane S. A study of severe anemia in children in a tertiary care institute. MVP J Med Sci 2018; 5(1): 33–8. https://doi.org/10.18203/2349-3291.ijcp20230079
13. Sivakami A, Seth B. Pediatric anemia – profile in the Indian subcontinent. J Pediatr Assoc India 2020; 9(3): 91–6. https://doi.org/10.4103/jpai.jpai_12_20
14. Tan SE, Ishak NN, Yusoff NM. Prevalence of anaemia in children treated in Kepala Batas, Penang. Malays J Paediatr Child Health 2020; 26(2): 35–50. https://doi.org/10.51407/MJPCH.V26I2.110
15. Ba ID, Abou Ba AS, Dieng YJ, Ly ID, Diouf S, Ndiaye O et al. Anemia among children aged 6–59 months at the Institute of Social Pediatric (ISP) in Dakar suburban area. J Pediatr Perinatol Child Health 2021; 5(3): 158–63. https://doi.org/10.26502/jppch.74050074
16. Kahouli S, Masrar A, Hessissen L, Kababri M, Kili A, El Khorassani M et al. Blood smear and diagnosis of anaemia in children: experience of the hematology laboratory of the Avicenna Hospital in Rabat with review of the literature. Eur J Clin Biomed Sci 2020; 6(3): 43–8. https://doi.org/10.11648/j.ejcbs.20200603.13
17. Kafle R, Bastola A, Samdurkar AP, Gautam N, Poudel A, Shah A et al. Haematological profile in microcytic hypochromic anaemia in children. J Univ Coll Med Sci 2021; 9(02): 3–7. https://doi.org/10.3126/jucms.v9i02.41941
18. Marken P, Bharat V, Chawla S, Singhal P. Clinicohaematological and biochemical profile of anemia in pediatric age group. Int J Res Rev 2020; 7(1): 335–341.
19. Chatterjee D, More SA, Joshi SR. Evaluation of pediatric anemia in rural population of Maharashtra, India. J Appl Hematol 2022; 13(1): 9–14. https://doi.org/10.4103/joah.joah_50_21
20. Duyuran Ö, Acıpayam C, Akkeçeci NS, İpek S, Duyuran R. Etiology of anemia in children aged between 6 months and 18 years. J Surg Med 2019; 3(5): 402–5. https://doi.org/10.28982/josam.568900
21. Banjare B, Das A, Bhardwaj AK, Gautam J, Bhargava P. Distribution of anaemia and leukemia in an urban cohort. J Med Sci Clin Res 2020; 8(1): 27–32. https://doi.org/10.18535/jmscr/v8i1.27
22. Liao L, Xu Y, Wei H, Qiu Y, Chen W, Huang J, et al. Blood cell parameters for screening and diagnosis of hereditary spherocytosis. J Clin Lab Anal 2019; 33(4): e22844. https://doi.org/10.1002/jcla.22844