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Etiology of Anemia in Hospitalized Children in Combined Military Hospital

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Author`s Contribution

[1]Conception, data acquisition, drafting the manuscript, approval of the final version to be Published, [2]Data acquisition, data analysis, critical review, [3]drafting the manuscript, Study design, [4] data interpretation, [5]drafting the manuscript,

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ABSTRACT

Objectives: To determine the frequency of different etiologies for anaemia in anaemic children reporting to Combined Military Hospital, Abbottabad.

Methodology: This descriptive cross-sectional study was conducted at Department of Paediatrics, Combined Military Hospital, Abbottabad, Jan 2022 to May 2024. A total of 181 children with ages between two and twelve years with haemoglobin <11.0g/dL were studied. Patients who received a blood transfusion, surgery or trauma within the past three months, or who did not complete workup to determine etiological cause for anaemia were lost to follow-up, or had received treatment prior to presentation for anaemia were excluded. Blood and other samples (where required) were collected from each child and analyzed in the hospital laboratory. Ancillary tests such as haemoglobin electrophoresis, stool/urine examination, bone marrow aspiration and trephine sampling and endoscopic examinations were performed as, and when, needed.

Results: The median age of the children was 6.00 (5.00) years, with 102 (56.4%) cases being male. Dietary iron deficiency anaemia was seen in 89 (49.2%) cases. Malabsorption-associated mixed deficiency, dietary mixed deficiency and isolated vitamin B12 deficiency occurred in 24 (13.3%), 17 (9.4%), and 16 (8.8%) cases, respectively. Other causes included β-thalassemia trait, IDA secondary to worm infestation, isolated folic acid deficiency and IDA secondary to menorrhagia which were seen in 10 (5.5%), 9 (5.0%), 8 (4.4%) and 5 (2.8%) cases, respectively.

Conclusion: Iron deficiency anaemia is the most common cause of deficiency in children in Abbottabad.

Keywords: Anaemia, Etiology, Paediatric Patients.

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Introduction

Anaemia is a pervasive global health issue, particularly afflicting children in low- and middle-income countries.[1] It is defined as a reduction in red blood cells or hemoglobin concentration and results in the compromise of the oxygen transport system in the body, leading to innumerable health problems.[2] Among paediatric populations, anaemia is associated with cognitive deficits, stunted growth, and increased morbidity and mortality rates.[3] In Pakistan, the prevalence of anaemia remains alarmingly high, especially among hospitalized children, necessitating a comprehensive understanding of its etiology to devise effective interventions.[4]

The etiology of anemia is multifactorial, often reflecting a complex interplay of nutritional deficiencies, infectious diseases, genetic disorders, and chronic illnesses.[5] Iron deficiency, primarily due to inadequate dietary intake or poor absorption, is globally recognized as the leading cause of anemia in children, and Pakistan appears to be no exception.[6] Additionally, deficiencies in other micronutrients such as folate and vitamin B12 further exacerbate the condition.[7] Infectious diseases, including malaria, helminth infections, and chronic inflammatory conditions, significantly contribute to anaemia by disrupting red blood cell production and increasing haemolysis.[8] Genetic disorders like thalassemia and sickle cell disease, which can exist concurrently, prevalent in certain regions of Pakistan, also play a crucial role in the etiology of anaemia.[9,10]

This study focuses on the etiology of anemia in hospitalized children at a tertiary care center in Abbottabad, which is a city situated in the Hazara region of Khyber Pakhtunkhwa and presents unique epidemiological characteristics due to its diverse population and socioeconomic spectrum. Investigating the causes of anemia within this context provides valuable insights that can inform targeted healthcare strategies and policy formulation. Specifically, this article aims to delineate the specific causes of anemia in

hospitalized children, employing a systematic approach to identify and analyze contributing factors. Understanding these etiological factors is imperative for developing tailored treatment protocols and preventive measures that can effectively address anemia in this vulnerable population. Furthermore, this study underscores the importance of multidisciplinary approaches in tackling anemia, integrating nutritional support, infection control, genetic counseling, and comprehensive healthcare services. The findings from CMH Abbottabad are anticipated to have broader implications, contributing to the global body of knowledge on paediatric anemia and enhancing healthcare practices in similar settings. Ultimately, this research endeavors to improve clinical outcomes and quality of life for children suffering from anemia, paving the way for healthier futures in Pakistan and beyond.

Methodology

This descriptive cross-sectional study was conducted from Jan 2022 to May 2024 in the Department of Paediatrics, Combined Miitary Hospital, Abbottabad on 181 patients diagnosed as suffering from anaemia. Informed consent was obtained from all participants. The study strictly adhered to the Declaration of Helsinki and followed the ethical guidelines of our institution. The confidentiality of all participants was maintained throughout the study. Patients were selected through consecutive, non-probability sampling. The WHO sample size calculator was used to calculate the sample size keeping a confidence level (1-α) of 95%, absolute precision (d) required of 0.05, and an anticipated population proportion of 13.6%,[11] which was the frequency of prevalence of iron deficiency as a cause of anaemia in children, from Kundu et al.[11]

Inclusion Criteria: All paediatric patients aged between 2 and 12 years diagnosed as suffering from anaemia, which was defined as a haemoglobin (Hb) level less than 11.0 g/dL,[12] were included for study.

Exclusion Criteria: Those children who had received a blood transfusion, those who have undergone surgery or received trauma, within the past three months were excluded. Children who were not permanent residents of Abbottabad or those whose parents or guardians did not provide consent, or did not complete workup to determine etiological cause for anaemia/were lost to follow-up, or had received treatment prior to presentation for anaemia were also excluded.

Demographic data and detailed clinical histories were documented for all participants, followed by relevant clinical examinations. Blood samples were collected from each child and analyzed in the hospital laboratory. Samples included complete blood counts (CBC), peripheral smear examinations, reticulocyte count, serum ferritin, serum iron, and total iron binding capacity (TIBC), as well as vitamin B12, and folate levels. Additional testing was based on requirement as per patient's clinical condition and included tests for renal function (urea, creatinine, sodium, potassium), liver function (bilirubin, alanine transaminase, alkaline phosphatase), Hb electrophoresis, stool examination for blood and parasites, urine examination as well as, when indicated, bone marrow aspiration and trephine sampling. Patients also underwent endoscopic examination if malabsorption or gastrointestinal loss was suspected. Anaemia was graded based on severity as mild (Hb 10.0 to 11.0 g/dL), moderate (Hb 8.0 to 9.9 g/dL) or severe (<8.0 g/dL). Patients with MCV <80 fL were classified in as microcytic, 80 to 96 fL were normocytic, while >96 were labeled macrocytic.

Data was analyzed using Statistical Package for the Social Sciences (Version 27, IBM Corp; Armonk, USA). Mean and standard deviation/median and interquartile range were calculated for quantitative variables, whichever was appropriate, specifically for patient age, Hb level, and mean corpuscular volume (MCV). Qualitative variables like gender, severity of anaemia, and etiology of anaemia were recorded in terms of frequency and percentage. Patients were grouped according to gender, size of RBC corpuscle and severity of anaemia. Qualitative data was compared between groups using the Chi Square test/Fischer Exact test, while quantitative variables were compared using the independent samples t test/Mann-Whitney U test/Kruskal Wallis test. Normality was assessed using the Shapiro-Wilk test. A p value of ≤0.05 was considered significant.

Results

Our study sample was based on 181 anaemic children. The median age of the children upon study enrollment was 6.00 (5.00) years, with 102 (56.4%) cases being male. The study sample had a median Hb level of 9.2 (IQR: 2.3) g/dL. A total of 61 (33.7%) patients had mild anaemia, 76 (42.0%) had moderate anaemia, while the remaining 44 (24.3%) had severe anaemia. Our patients had a median MCV of 82.00 (IQR: 24.00) fL. A total of 75 (41.4%) patients had microcytic anaemia, 69 (38.1%)

had normocytic anaemia, while the remaining 37 (20.4%) had macrocytic anaemia. Dietary iron deficiency anaemia (IDA) was the most common cause of anaemia seen in our study, accounting for 89 (49.2%) cases.

Malabsorption-associated mixed deficiency, dietary mixed deficiency and isolated vitamin B12 deficiency were the next most common causes, accounting for 24 (13.3%), 17 (9.4%), and 16 (8.8%) cases, respectively. Other infrequent causes included β-thalassemia trait, IDA secondary to worm infestation, isolated folic acid deficiency and IDA secondary to menorrhagia which were seen in 10 (5.5%), 9 (5.0%), 8 (4.4%) and 5 (2.8%) cases, respectively. Rare causes included β-thalassemia major of which there were 2 (1.1%), while 1 (0.6%) patient had a marrow infiltrative disorder. Table-I shows the different patient characters and study results distributed according to gender. The only difference seen between genders was the frequency of IDA secondary to blood loss which was more common in females due to menorrhagia, (p=0.015).

Table II shows the different patient characteristics/study outcomes distributed according to severity of anaemia. None of the parameters were statistically significantly different across the groups.

Table I. Patient characteristics/study outcomes according to gender. (n=181)

Variable	Male (n=102)	Female (n=79)	p-value
Age (years)	6.00 (IQR: 5.00)	5.00 (IQR: 4.00)	0.035
Hb level (g/dL)	9.00 (IQR: 2.40)	9.40 (IQR: 2.20)	0.960
Anaemia severity			
Mild	35 (34.3%)	26 (32.9%)	0.967
Moderate	42 (41.2%)	34 (43.0%)	
Severity	25 (24.5%)	19 (24.1%)	
MCV (fL)	83.50 (IQR: 25.00)	81.00 (IQR: 21.0)	0.333
Anaemia based on corpuscular size			
Microcytic	38 (37.3%)	37 (46.8%)	0.415
Normocytic	41 (40.2%)	28 (35.4%)	
Macrocytic	23 (22.5%)	14 (21.5%)	
Etiology of anaemia			
Dietary IDA	52 (51.0%)	37 (46.8%)	0.580
IDA secondary to menorrhagia	-	5 (6.3%)	0.015
IDA secondary to worm infestation	4 (3.9%)	5 (6.3%)	0.507
Vitamin B12 deficiency	10 (9.8%)	6 (7.6%)	0.682
Folic acid deficiency	5 (4.9%)	3 (3.8%)	1.000
Dietary mixed deficiency	10 (9.8%)	7 (8.9%)	0.829
Malabsorption-associated mixed deficiency	15 (14.7%)	9 (11.4%)	0.514
β-thalassemia major	1 (1.0%)	1 (1.3%)	0.855
β-thalassemia trait	5 (4.9%)	5 (6.3%)	0.677
Marrow infiltrative disorder	-	1 (1.3%)	0.436

Table-II. Patient characteristics/study outcomes according to severity of anaemia (n=181)

Variable	Mild (n=61)	Moderate (n=76)	Severe (n=44)	*p*-value
Age (years)	6.00 (IQR: 5.00)	5.00 (IQR: 5.00)	6.00 (IQR: 5.00)	0.242
MCV (fL)	82.00 (IQR: 28.00)	81.00 (IQR: 26.00)	84.00 (IQR: 14.00)	0.661
Anaemia based on corpuscular size				
Microcytic	26 (42.6%)	36 (47.4%)	13 (29.5%)	0.235
Normocytic	21 (34.4%)	25 (32.9%)	23 (52.3%)	
Macrocytic	14 (23.0%)	15 (19.7%)	8 (18.2%)	
Etiology of anaemia				
Dietary IDA	29 (47.5%)	36 (47.4%)	24 (54.5%)	0.715
IDA secondary to menorrhagia	-	3 (3.9%)	2 (4.5%)	0.298
IDA secondary to worm infestation	4 (6.6%)	3 (3.9%)	2 (4.5%)	0.834
Vitamin B12 deficiency	5 (8.2%)	7 (9.2%)	4 (9.1%)	0.981
Folic acid deficiency	3 (4.9%)	4 (5.3%)	1 (2.3%)	0.809
Dietary mixed deficiency	7 (11.5%)	7 (9.2%)	3 (6.8%)	0.728
Malabsorption-associated mixed deficiency	8 (13.1%)	10 (13.2%)	6 (13.6%)	0.996
β-thalassemia major	-	1 (1.3%)	1 (2.3%)	0.716
β-thalassemia trait	5 (8.2%)	5 (6.6%)	-	0.169
Marrow infiltrative disorder	-	-	1 (2.3%)	0.246

Table III. Patient characteristics/study outcomes according to RBC size. (n=181)

Variable	Micro- (n=75)	Normo- (n=69)	Macro- (n=37)	*p*-value
Age (years)	6.00 (IQR: 4.00)	6.00 (IQR: 5.00)	6.00 (IQR: 6.00)	0.951
Etiology of anaemia				
Dietary IDA	43 (57.3%)	45 (65.2%)	1 (2.7%)	<0.001
IDA secondary to menorrhagia	5 (6.7%)	-	-	0.024
IDA secondary to worm infestation	5 (6.7%)	4 (5.8%)	-	0.316
Vitamin B12 deficiency	-	-	16 (43.2%)	<0.001
Folic acid deficiency	-	-	8 (21.6%)	<0.001
Dietary mixed deficiency	5 (6.7%)	7 (10.1%)	5 (13.6%)	0.487
Malabsorption-associated mixed deficiency	5 (6.7%)	12 (17.4%)	7 (18.9%)	0.087
β-thalassemia major	2 (2.6%)	-	-	0.353
β-thalassemia trait	10 (13.3%)	-	-	<0.001
Marrow infiltrative disorder	-	1 (1.5%)	-	0.585

Table III shows the different patient characteristics/study outcomes distributed according to RBC size. As expected microcytosis was common in patients with dietary IDA (p<0.001), IDA secondary to blood loss (p=0.024) and with β-thalassemia trait (p<0.001). While macrocytic anaemia was more common with vitamin B12 deficiency (p<0.001) and folate deficiency (p<0.001).

Discussion

The study aimed to identify the etiological factors contributing to anaemia in children presenting at CMH Abbottabad. The demographic profile of our sample revealed a predominance of male patients (56.4%). This is in keeping with previous data on the subject such as from Habib et al, who noted that anaemia was more common in male Pakistani children, possibly due to a higher prevalence of IDA in this population.[13] Zeleke et al also reported a higher frequency of anaemia in male children and postulated that this higher incidence might be secondary to an increase in frequency of parasitic infestation and less intake of fibre-rich foods by male children.[14] However, it is pertinent to note here that our study did not show a statistically significant difference between males and females with regards to IDA or parasite infestation, which would indicate that there may be other factors at play and, as such, this aspect of our study requires further investigation before concrete facts can be proposed.

The anaemia spectrum in our cohort was wide-ranging, with 42.0% exhibiting moderate anaemia, followed by 33.7% with mild anaemia, and 24.3% with severe anaemia. This distribution aligns with trends in developing countries indicating a substantial burden of moderate anaemia among pediatric populations in low- and middle-income countries. *Studies such as* Ncogo et al have reported that the burden of moderate anaemia accounted for nearly three-quarters of their study sample of paediatric patients with anaemia.[15] However, this is not a universal fact and other studies such as Li et al and Kebede et al have reported that mild anaemia is more common.[16,17] This difference in our studies can be accounted for by two reasons: 1) different studies have varying definitions of what constitutes mild, moderate and severe anaemia, and 2) some variation across diverse populations is something to be expected.

The current study showed that microcytic anaemia was most prevalent, a finding consistent with other studies from similar settings where nutritional deficiencies are common, especially in developing countries. Notably, dietary IDA emerged as the leading cause in our study, underscoring the critical role of iron deficiency in paediatric anaemia in our region. This high prevalence of IDA can be attributed to poor dietary intake and socioeconomic factors affecting access to iron-rich foods. Studies from other parts of the world are in agreement the results of our study in that microcytic anaemia has been repeatedly reported as the most common cause of anaemia with IDA being the most common underlying etiological factor in children, mostly secondary to dietary deficiency, with another important cause being β-thalassemia.[18-20]

Malabsorption-associated mixed deficiency, was also significant contributor to the occurrence of anaemia in children in the present study. These findings highlight the multifactorial nature of anaemia in children, where dietary insufficiencies and gastrointestinal malabsorption are pivotal factors. Studies such as Stahl et al have reported that incidence of malabsorption syndromes such as celiac disease vary across different populations and that the disease is not uncommon in children, and may account for a significant burden of anaemia.[21] In fact, King et al reported in their study that the incidence of celiac disease was the highest among adult females and in children, with a gradually increasing prevalence in the latter population.[22] The etiology of anaemia secondary to

celiac disease is multifactorial and, while iron deficiency is the most common cause associated with it, it may occur due to deficiencies of multiple nutrients including vitamin B12 and folic acid.

Lastly, the observed cases of β-thalassemia trait (5.5%) emphasizes the need for genetic screening and counseling in endemic areas in Pakistan. This incidence is largely in keeping with other studies conducted on the subject in our country which have reported a β-thalassemia trait carrier of between 5% and 8% in other populations within the country.[23,24]

Study limitations: Firstly, the sample size, while adequate for preliminary analysis, limits the generalizability of our findings to broader populations. Additionally, our study was conducted in a single military hospital setting, which may not reflect the wider community or other healthcare settings. Furthermore, the study did not account for seasonal variations in anaemia prevalence, which could affect the interpretation of dietary and infectious causes of anaemia. Moreover, our patients did not include a large number of children who had received previous treatment for anaemia, such as blood transfusions, which will have resulted in some degree of confounding within the frequencies of the different disease, particularly for β-thalassemia major. Lastly, we studied patients two years or older, which meant that patients with genetic disorders such as β-thalassemia major, who are usually diagnosed earlier, may have been under-represented.

Conclusion

The predominant cause of anaemia in children presenting to CMH Abbottabad was dietary iron deficiency, underscoring the need for public health interventions focused on improving nutritional intake among children. The study highlights the multifactorial etiology of anaemia, with significant contributions from vitamin deficiencies and genetic factors such as β-thalassemia trait. Addressing these varied causes requires a comprehensive approach, including dietary education, supplementation programs, and genetic counseling. Future studies should aim for larger, multicentre samples to validate these findings and explore the impact of targeted interventions on reducing the burden of paediatric anaemia.

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