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Understanding the Etiologies of Pancytopenia in Pediatric Patients: A Cross-Sectional Study

Inam Ullah[1], Muhammad Sohaib Khan[2], Muhammad Fayaz[3], Sher Alam Khan[4], Nafees Khan[5], Rabia Tabassum[6]

[1]Department of Pediatrics, DHQ Teaching Hospital, Mardan, KP, Pakistan.
[2]Department of Pediatrics, Combined Military Hospital, Abbottabad, KP, Pakistan.
[3]Department of Pediatrics, Abbottabad International Medical Institute, Abbottabad, KP, Pakistan.
[4]Department of Paediatrics, Musharaf Medical Complex, Abbottabad, KP, Pakistan.
[5]Consultant Pediatrician, Health Department Mardan, KP, Pakistan.
[6]Department of Paediatrics, Wateem Medical College, Rawalpindi, Punjab, Pakistan.

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Corresponding Author: Nafees Khan, Consultant Pediatrician, Health Department Mardan, KP, Pakistan.
Email: drnafees637@gmail.com

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ABSTRACT

Introduction: Pancytopenia is not uncommon in children and is termed as a decrease in the production of hemoglobin, platelets and white blood cells resulting in anemia, thrombocytopenia and leucopenia. Wide variety of conditions leads to pancytopenia ranging from benign conditions to malignant diseases that determine the underlying management. **Objective:** To determine the etiology of pancytopenia in the pediatric population. **Methodology:** The current study was conducted at pediatric department of Mardan Medical Complex, Mardan spanning from February 2021 to August 2021. This cross-sectional study includes 131 patients labelled as case of pancytopenia aged 1 to 15 years. Full blood count already done was tracked down and recorded in a pre-designed proforma and a bone marrow examination was done for all patients. Data was analyzed using SPSS 20. **Results:** The mean age was 6.4 years ± 4.1. males were predominant with frequency of 79(60.3%) and females were. 52(39.7%). The predominant symptom was fever with frequency of 86(65.6%) followed by pallor, petechiae/bruises, epistaxis, generalized weakness and bone pains. Aplastic anemia was the prevalent etiology and were reported in 47(35.9) of cases, 24(18.3%) of patients were diagnosed with megaloblastic anemia. No obvious cause was identified in 6(4.6%) of cases. **Conclusion:** Pancytopenia is a not an uncommon entity and delineating the etiological spectrum is crucial in the management and prognosis of patient. Aplastic anemia was the most prevalent cause followed by megaloblastic anemia.

INTRODUCTION

Pancytopenia is a prevalent termed as a decrease in the cell lines of peripheral blood lineages resulting in anemia, thrombocytopenia and leucopenia [1,2]. Pancytopenia can result from ineffective erythropoiesis, cell maturation arrest, peripheral cellular destruction, it's not a disease but a finding on peripheral blood film with a wide variety of etiologies affecting hematopoiesis [3]

The etiology of pancytopenia is multifactorial ranging from benign and malignant disorders, nutritional disorders. The cause of pancytopenia may be congenital such as schwamann diamond syndrome, dyskeratosis congenita, Fanconi anemia, diamond blackfan anemia. Leukemia, lymphoma, hemolytic anemias, megaloblastic anemia and metabolic disorders such as Gaucher, Neiman pick disorders, mucopolysaccharidosis were other notable etiologies [4]. Infectious causes also contribute to the overall burden of pancytopenia with notable causes includes tuberculosis, leishmaniasis, chronic malaria, parvovirus infection and brucellosis. [5]

Nutritional deficiencies particularly Vit B12 and folic acid was recognized as a potential contributor to megaloblastic anemia which is frequently observed among children with pancytopenia. Fortunately, it is one the treatable cause of pancytopenia [6,7]. The findings of bone marrow examination vary considerably, largely depends on the etiology of pancytopenia ranging from a

normal cellular marrow to hypocellular marrow or hypercellular with infiltration of malignant cells. [8]

As majority of the etiologies are treatable so it is imperative to identify the etiology of pancytopenia and treat accordingly. Bone marrow examination is the key to delineate the causes of pancytopenia, however it may not always provide a definitive diagnosis [7,9]. Children with pancytopenia presents with wide range of symptoms, such fever, pallor, fatigue, dyspnea on exertion, petechiae bruises, bleeding gums, hematemesis and melena recurrent infection and oral ulcers etc. [7,10,11]

A study conducted by shams et al. (2020) reported aplastic anemia in approximately 32.5% of the study population followed by megaloblastic anemia reported in 20% of cases, leukemia was reported in 17.5% of cases. [12]

In another study conducted by Rubab et al. (2022) reported aplastic anemia as the commonest cause of pancytopenia and was found in 41.3% of cases followed by acute lymphoblastic leukemia in 21.3% of cases, infectious causes were reported in 14.1% cases, idiopathic thrombocytopenic purpura, megaloblastic anemia, malaria was other notable causes of pancytopenia in the study population [10]

The spectrum of pancytopenia is diversified and it very convincing to identify the etiology as this aligns the management and prognosis. There is limited and conflicting data regarding the various etiologies of pancytopenia, also there has been a significant variability in the etiological spectrum of pancytopenia across different geographical area underscore a localized studies to better understand the causes and their implication for management.

OBJECTIVE

Understanding and identifying the etiologies of pancytopenia in children.

METHODOLOGY

It was a descriptive cross-sectional study conducted at pediatric department, Mardan Medical Complex Mardan from February 2021 to august 2021. A Sample size of 131 was determined, considering 95% confidence interval and 7% margin of error and anticipated frequency pancytopenia at 21.2 % [13] using OpenEpi calculator for sample size estimation. Patient was enrolled using a non-probability consecutive method. Parents were informed about the nature and purpose of study and written informed consent was obtained. Ethical approval was sought from hospital ethical committee (No. 218/BKMC, Dated: 05/01/2021)

The inclusion criteria were children aged 1 to 15 years of both genders, diagnosed with pancytopenia. The exclusion criteria were: blood transfusion in the past 6 months, children diagnosed with hematological malignancies such as leukemia and lymphoma, patients with aplastic anemia and chronic ITP. Pancytopenia was characterized by hemoglobin < 10g/dl, ANC < 1.5 $\times 10^9$, and a platelet count of $<100\times10^9$.

From all the children, the full blood count which had already been conducted was tracked and recorded. From all patient's bone marrow aspirates were obtained from posterior iliac spine and in the presence of hypoplastic bone marrow a trephine biopsy was obtained. The examination was done in hematology section under supervision of hematologist under rigorous aseptic conditions and sent to hospital laboratory.

All the above-mentioned information including name, age, sex, fever, petechiae, bruises, pallor, epistaxis, melena, hematemesis, child developmental milestones, vaccination status and family history of hematological disorders were collected. The exclusion criteria were strictly enforced to control confounders and reduce bias in results. The etiology of pancytopenia in children was determined. All the collected data was analyzed in SPSS version 23. Numerical values were presented in the form of Mean $\pm$ SD whereas the categorical variables were presented by frequency/percentage. The data was further stratified with age, gender, socioeconomic status, to see the effect modification. Chi square test was applied post stratification, significance was obtained at $P<0.05$.

RESULTS

The study group consists of 131 patients. The Mean age was 6.4 years ± 4.1. Male were predominant with frequency of 79(60.3%) whereas females was 52(39.7). Majority of the patients were in group 1(1 to 5 years) with a frequency of 70(53.4%), regarding the socioeconomic status majority falls in the satisfactory group with frequency of 72(55%) whereas the remaining 59(45%) have poor socioeconomic status. (Table 1)

Table 1

Sociodemographics

Age Groups	Frequency	Percent
1 to 5 years	70	53.4
6 to 10 years	31	23.7
11 to 15 years	30	22.9
Total	131	100.0
Gender Distribution	**Frequency**	**Percentages**
Male	79	60.3%
Female	52	39.7
Total	131	100.0
Socioeconomic Status	**Frequency**	**Percentages**
Satisfactory	72	55.0
Poor	59	45.0
Total	131	100.0

The predominant symptom experienced by patients was fever with frequency of 86(65.6%) followed by pallor, petechiae/bruises, epistaxis, generalized weakness and bone pains. (Table 2)

Table 2
Signs and Symptoms of Children Presenting with Pancytopenia

Symptoms	Frequency	Percentage
Fever	86	65.6
Pallor	73	55.7
Petechiae/bruises	35	26.7
Epistaxis	19	14.5
Generalized weakness	8	6.1
Bone pains	9	6.9
Hematuria	9	6.9
Hematemesis	10	7.6
Others	8	6.1
Total	131	100.0

Notably on assessing the etiological factors, the most prevalent etiology was aplastic anemia and were reported in 47(35.9) of cases, followed by megaloblastic anemia reported in 24(18.3%) of cases. Leukemia was reported in 20(15.3%) of cases whereas lymphoma was reported in 13(9.9%) of cases. Bone marrow examination was inconclusive in 6(4.6%) of cases. Myelodysplastic syndrome was reported in 8(6.1%) of the cases. Gaucher disease was diagnosed in 9(6.9%) of cases and leishmaniasis was reported in 4(3.1%) of cases.

Table 3
Etiological Spectrum of Pancytopenia (N =131)

Etiology	Frequency	Percent
Aplastic anemia	47	35.9
Megaloblastic anemia	24	18.3
Leukemia	20	15.3
Lymphoma	13	9.9
Myelodysplastic syndrome	8	6.1
Gaucher disease	9	6.9
Leishmaniasis	4	3.1
No obvious cause	6	4.6

Majority of patients with Aplastic anemia fell within the age group of 1 to 5 years, similar trend was observed for megaloblastic anemia. Proportion of leukemia was fairly distributed among age group (1 to 5 years) and (11 to 15 years). (Table 4)

Table 4
Etiology of Pancytopenia in Terms of Age Groups of Patients

Age Groups	ETIOLOGY OF PANCYTOPENIA								Total
	Aplastic Anemia	Megaloblastic Anemia	Leukemia	Lymphoma	Myelodysplastic Syndrome	Gaucher Disease	Leishmaniasis	No Obvious Cause	
1 to 5 years	28	12	10	7	4	7	2	0	70
6 to 10 years	12	8	0	6	3	2	0	0	31
11 to 15 years	7	4	10	0	1	0	2	6	30
Total	47	24	20	13	8	9	4	6	131

A significant proportion of patients with aplastic anemia were males, however a fair distribution was observed among gender for megaloblastic anemia. In contrast leukemia was diagnosed largely in female patients. (Table 5)

Table 5
Gender-Based Distribution of Pancytopenia Etiologies

GENDER	ETIOLOGY OF PANCYTOPENIA								Total
	Aplastic Anemia	Megaloblastic Anemia	Leukemia	Lymphoma	Myelodysplastic Syndrome	Gaucher Disease	Leishmaniasis	No Obvious Cause	
Male	34	12	9	11	3	5	2	3	79
Female	13	12	11	2	5	4	2	3	52
Total	47	24	20	13	8	9	4	6	131

In regards to socioeconomic status, aplastic anemia was reported in patients with a satisfactory socioeconomic status, whereas leukemia and lymphoma were diagnosed in the majority with poor socioeconomic status. (Table 6)

Table 6
Distribution of Pancytopenia Etiologies Across Socioeconomic

SOCIOECONOMIC STATUS	ETIOLOGY OF PANCYTOPENIA								Total
	Aplastic Anemia	Megaloblastic Anemia	Leukemia	Lymphoma	Myelodysplastic Syndrome	Gaucher Disease	Leishmaniasis	No Obvious Cause	
Satisfactory	33	12	6	3	6	5	4	3	72
Poor	14	12	14	10	2	4	0	3	59
Total	47	24	20	13	8	9	4	6	131

DISCUSSION

Pancytopenia is a serious hematological issue that warrants urgent attention because it poses the patient at greater risk of complications characterized by decreased in all the three cell lines resulting in anemia, thrombocytopenia and leukopenia.

Bone marrow examination is an important tool to investigate a case of pancytopenia and to determine the cause of pancytopenia. It's a common diagnostic procedure carried out at pediatric departments for both hematological and non-hematological disorders.

In our current research the mean age reported was 6.4 ± 4.1 years with predominant male gender comprising (60.3%) whereas females were (39.7%). A study conducted by Sarbay et al [14] to determine the etiology of pancytopenia in children reported the mean age of patients was 4.9 years old, with male predominance comprising 56.2% of the study population. These finding are consistent with our study results.

Fever was the predominant symptom experienced by 65.6% of the study population. In a study by Zubair et al. (2022) found fever as the major manifestation in patients with pancytopenia, reported by 71.9% of the total cases [15]. Zeeshan R et al. (2019) also reported fever as the predominant symptom in children with pancytopenia.[16] In contrast pallor was the most frequent finding reported in 100% of cases by Maru L et al (2022) followed by fever in 88% of cases [17].

In current study the most prevalent etiology was Aplastic anemia and was reported in 35.9% of cases. A study conducted by Patil et al. (2023) to identify the etiology of pancytopenia in children reported Aplastic anemia in 37.5% of the study cases, this is similar to our findings [18]. A similar study conducted by Alim et al. (2021) reported 37% cases of pancytopenia was diagnosed with Aplastic anemia, which is consistent with our findings [7]. similarly, Zubair et al. (2022) reported Aplastic Anemia in 37.50% of cases as the commonest etiology of pancytopenia, these findings are consistent with our study [15]. However, Maru et al. reported a contrasting result showing aplastic anemia in 7.1% of cases [17]. A study conducted by Panda et al. (2023) reported acute lymphoblastic leukemia as the commonest etiological factor in 58.5% of cases [19]. Bahal N et al (2021) reported megaloblastic anemia as the most prevalent etiological factor and was found in 28.8% of cases followed by acute leukemia in 24.7% of cases [20].

In current study after Aplastic anemia, majority of patients were diagnosed with megaloblastic anemia and reported in 18.3 of cases. Same observations were reported by Zubair et al (2022) which reported megaloblastic anemia in 21.85% of cases [15]. Leukemia was observed in 15.3% of cases in our study followed by lymphoma, Maru l et al reported leukemia in 21.4% of cases [17].

Understanding and diagnosing the etiology of pancytopenia is imperative because majority of the causes can be treated with a favorable prognosis. As there is a significant variability in the etiology of pancytopenia among demographic and geographical area, future studies could help in delineating geographical and population specific variation in the causes of pancytopenia. Further studies could be done to study the progression of pancytopenia cases, it will help in understanding the progression of disease, response to treatment.

CONCLUSION

Pancytopenia is a not an uncommon condition in pediatric population. There is long list of etiologies ranging from nutritional deficiencies, benign conditions to malignant diseases and in major proportion of cases it is treatable, understanding the etiology of pancytopenia in children is crucial for the management of patient.

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