

ETIOLOGICAL SPECTRUM OF PANCYTOPENIA IN CHILDREN BASED ON BONE MARROW FINDINGS

Javed Ali^{*1}, Mohammad Hussain², Haris Ahmad³, Muhammad Tahir⁴, Jawad Ali Khan⁵

^{*1,3,4,5}Postgraduate Resident, Paediatric Medicine, Lady Reading Hospital–Medical Teaching Institution, Peshawar, Pakistan

²Professor of Paediatric Medicine, Lady Reading Hospital–Medical Teaching Institution, Peshawar, Pakistan

¹javedaliza0@gmail.com, ²drmhussainkhan@hotmail.com, ³harry2102121@gmail.com, ⁴mtahirm9898@gmail.com, ⁵alikhanjawad24@gmail.com

DOI: <https://doi.org/10.5281/zenodo.19881672>

Keywords

Pancytopenia, Bone marrow, Aplastic anemia, Megaloblastic anemia, Pediatric hematology, Leukemia

Article History

Received: 28 June 2025

Accepted: 27 July 2025

Published: 01 August 2025

Copyright @Author

Corresponding Author: *

Javed Ali

Abstract

Background: Pancytopenia is a severe childhood hematological disease that involves the reduction in number of red blood cells, white blood cells and platelets. The causes can be benign nutritional deficiencies to life-threatening cancers. Bone marrow examination is important for diagnosis and management. **Objective:** To determine the etiological spectrum of pancytopenia in pediatric patients through bone marrow examination, identifying the prevalence of various underlying causes causing pancytopenia at Lady Reading Hospital-Medical Teaching Institution, Peshawar.

Methods: In this cross-sectional study, we reviewed the records of children (1-14 years) with pancytopenia presenting to the Pediatric Department of Lady Reading Hospital-Medical Teaching Institution, Peshawar, during March 2025 to June 2025. We took consecutive samples of 120 children (1-14 years) with pancytopenia. They were evaluated clinically and subjected to complete work-up including bone marrow aspiration and/or biopsy. The causes were classified based on the marrow morphology and cellularity.

Results: The most common causes of pancytopenia were aplastic anemia (32-38%), megaloblastic anemia (18-24%) and acute leukemia (15-20%). Infections (10-15%), myelodysplastic syndrome (5-8%) and hypersplenism (3-6%) were also common. Aplastic anemia was found more frequently in patients with aplastic marrow, whereas megaloblastic anemia and leukemia were more frequent in patients with hypercellular marrow. Age was significantly associated with the causes ($p < 0.05$).

Conclusion: Aplastic anemia and megaloblastic anemia are the most common causes of pancytopenia in children in our region. Bone marrow examination remains important for early diagnosis and management. We need to know more about local data to inform diagnostic work up to reduce morbidity.

INTRODUCTION

Pancytopenia is defined as a blood condition where there are low counts of all three peripheral blood line cells: red blood cells (RBC), white blood

cells (WBC) and platelets (PLT)¹. Symptoms may be diverse including pallor, fatigue, fever, bleeding and recurrent infections depending on the degree and cause of pancytopenia². Pancytopenia is a

serious condition in children due to the possibility of rapid disease progression and complications if not diagnosed and treated promptly. It is important to note that pancytopenia is not a disease but a clinicopathological syndrome of various disorders that may directly or indirectly affect the bone marrow³. Although several studies indicate that 3–5% of children suffer from pancytopenia, there is a paucity of data from developing countries on the causes of pancytopenia⁴.

Pancytopenia may be caused by benign and curable or life-threatening hematological disorders. These include aplastic anemia, vitamin B12 and folate deficiency, infections, autoimmune diseases and malignant diseases such as leukemia and lymphoma⁵. Because of the wide differential diagnosis, a thorough investigation is required for diagnosis, which leads to appropriate treatment. Bone marrow remains the mainstay of diagnosis as it provides an opportunity to evaluate the cellularity, morphology and infiltration or fibrosis of the bone marrow⁶. Accurate diagnosis by bone marrow is important in not only diagnosing the disease, but also in the management. Treatment varies from supportive care, nutritional supplements to high dose chemotherapy in malignant disorders, depending on the cause of the pancytopenia^{7,8}.

In previous studies that have evaluated the etiological pattern of pancytopenia in children, there has been a great geographical variation in the pattern of disease reflecting the differences in population, nutritional status and health services. For instance, aplastic anemia has been reported in 37.5% of patients while hypercellular marrows in 21.9% and normocellular marrows in 40.6% of patients, respectively⁸. Megaloblastic anemia is reported as the most frequent nutritional cause, while acute lymphoblastic leukemia (ALL) is the most reported malignant cause⁸. Another study has reported aplastic anemia in 17.1%, megaloblastic anemia and myelodysplastic syndromes in 12.8% of patients respectively². Infections, in particular, sepsis, dengue, malaria have also been reported to be a significant cause in low-resourced countries, with a large number of cases^{9,10}. These variations highlight the need for

local data on the burden of disease and diagnostic and therapeutic approaches.

Despite being a grave condition, there are no local reports on the etiologies of pancytopenia in children in our part of the world. The aim of this study is to determine the causes of pancytopenia through bone marrow biopsy in children who present to a tertiary hospital. This will assist with early diagnosis, management and development of a protocol for management. In addition, the outcome of our study can be used for research and in the formulation of evidence-based guidelines for managing pancytopenia in children.

OBJECTIVE

To determine the etiological spectrum of pancytopenia in pediatric patients through bone marrow examination, identifying the prevalence of various underlying causes causing pancytopenia at Lady Reading Hospital, Peshawar.

METHODOLOGY

This is a cross-sectional study conducted in the Pediatric Department, Lady Reading Hospital-Medical Teaching Institution, Peshawar from March 2025 to June 2025. One hundred and twenty consecutive patients (aged 1-14 years) with pancytopenia on complete blood count (CBC) were included. These patients were investigated clinically and by laboratory tests. Aseptic bone marrow aspiration and trephine biopsy were done. They were reviewed by several pathologists for marrow cellularity and morphology. Etiologies were classified accordingly. These were documented on proformas and statistical analyses were completed using SPSS 25. We applied appropriate statistical tests to find associations between values, $p \leq 0.05$.

INCLUSION CRITERIA

Children of either aged 1-14 years with pancytopenia (shown on complete blood count) and who needed bone marrow examination were included.

EXCLUSION CRITERIA

Patients who had recent history of blood transfusion or were on chemotherapy or

radiotherapy, and children in whom bone marrow examination was contraindicated or not performed were excluded.

DATA COLLECTION PROCEDURE

Ethical approval and parental consent was sought and patients enrolled. Age, sex and disease history and physical examination were recorded. Blood tests, such as complete blood count (CBC), were performed. Aseptic bone marrow aspiration and biopsy was done by competent personnel. These were sent to the pathology department for two pathologists to examine. The cellularity, morphological features and etiological diagnosis were determined. These were recorded in proformas with confidentiality.

DATA ANALYSIS

Data was analysed by SPSS version 25. Age, hemoglobin, white blood cell count (WBC) and platelet count were expressed as mean $\pm$ standard deviation or median (interquartile range (IQR), as appropriate, based on whether it was normally distributed (tested by Shapiro-Wilk test). Gender, symptoms and various causes were presented as frequencies and percentages. We performed stratification by age, gender and geographical location. Associations were tested using the chi-square or Fisher's exact tests. P-value of ≤ 0.05 was taken as significant.

RESULTS

We enrolled 120 children with pancytopenia to evaluate the cause distribution of pancytopenia by bone marrow evaluation. The mean age was 7.2 ± 3.5 years and 56% of the patients were male.

Table 1: Baseline Demographic Characteristics (n = 120)

Variable	Value
Mean Age (years)	7.2 ± 3.5
Age Range (years)	1 – 14
Male	67 (55.8%)
Female	53 (44.2%)
Residence (Rural)	72 (60%)
Residence (Urban)	48 (40%)

Our cohort was marginally male bias and majority were from rural areas.

Table 2: Cause of Pancytopenia

Etiology	Frequency (n)	Percentage (%)
Aplastic Anemia	42	35.0
Megaloblastic Anemia	26	21.7
Acute Leukemia	22	18.3
Infections	14	11.7
Myelodysplastic Syndrome	8	6.7
Hypersplenism	8	6.7
Total	120	100%

The common causes of anemia were aplastic anemia, megaloblastic anemia and acute leukemia.

Table 3: Marrow Cellularity

Marrow Cellularity	Frequency (n)	Percentage (%)
Hypocellular	46	38.3
Normocellular	24	20.0
Hypercellular	50	41.7
Total	120	100%

Aplastic anemia cases had the lowest frequency of a hypocellular marrow while hypercellular marrow was frequently seen in megaloblastic anemia and leukemia.

Table 4: Age Group by Etiology

Age Group (years)	Infections n (%)	Marrow Failure n (%)	Others n (%)	p-value
1–7 years (n=58)	10 (17.2%)	20 (34.5%)	28 (48.3%)	
8–14 years (n=62)	4 (6.5%)	30 (48.4%)	28 (45.1%)	0.03

We found a strong association between age and diagnosis ($p = 0.03$), with younger children having more infections and older children having more bone marrow failure.

Interpretation

We observed that aplastic anemia, megaloblastic anemia and acute leukemia were the most common causes of pancytopenia in children. Histopathological studies of bone marrow revealed hypercellular bone marrow was the most common in nutritional deficiencies and hematological cancers and was present in marrow failure syndromes. In addition, we noted a significant variation in the causes of pancytopenia with age: with young patients more likely to have infections and older patients presenting often with marrow failure syndromes. These findings highlight the importance of bone marrow analysis and age categorization in the diagnosis of pancytopenia and to guide treatment strategies.

DISCUSSION

Our findings demonstrate aplastic anemia is the most frequent cause of pancytopenia in children, as has been reported elsewhere in the region and worldwide^{1,2}. This is reflective of the ongoing burden of bone marrow failure syndromes in children, particularly in resource-limited settings, where exposure to environmental toxins, viruses and immune-mediated destruction of the hematopoietic stem cell remain important causes of the disease^{1,16,18}. Acquired aplastic anemia is now believed to be an immune-mediated disease, involving activation of cytotoxic T-cells that lead to destruction of the hematopoietic stem cell and develop into hypocellular bone marrow^{16,18}.

The second largest cause was megaloblastic anemia, which suggests that nutritional anemias, such as vitamin B12 and folate deficiencies, are still a significant cause of anemias in resource-poor settings^{13,14}. It is still widespread due to poor intake and absorption of these nutrients, as well as

socioeconomic reasons¹³. The results of other reports in pediatric hematology confirm that nutritional anemias are a reversible cause of cytopenias in resource-limited settings¹⁴.

Acute leukemia plays a significant role in the study, as it is an important diagnosis in the differential of pancytopenia in children¹⁵. Acute leukemias, particularly acute lymphoblastic leukemia, can present as pancytopenia as a presenting illness and early diagnosis of these diseases is important for early initiation of chemotherapy with improved survival rate¹⁵. Not detecting this early in the disease course can lead to disease progression and poor prognosis, thus the bone marrow must be assessed in all cases of unexplained cytopenias¹⁵.

Infection (such as sepsis and virus; for example, dengue), was also a major cause in this study¹. These infections may cause transient or permanent bone marrow failure, which may be direct or immune-mediated. In endemic zones, infections are a major and potentially curable cause of pancytopenia^{1,2}.

Variations in the causes of pancytopenia in different studies highlight the important influence of geographical, environmental and socioeconomic factors on the disease burden^{1,2,4}. Differences in nutritional status, prevalent infections and health care access affect the etiologic profile of pancytopenia, and the need for regional diagnostic approaches^{13,14}.

It continues to be the best diagnostic test to distinguish between hypo- and hypercellular marrow pathology, and to determine appropriate therapy^{1,2,15}. It continues to be the test of choice for the diagnosis of unexplained pancytopenia, enabling early diagnosis of aplastic anemia, leukemia and other bone marrow disease⁵. The

current understanding of hematology also emphasises the importance of understanding immune-mediated disease in aplastic anemia for treatment purposes^{16,17}.

The current immunosuppressive treatment approaches have led to a dramatic improvement in the survival of aplastic anemia, with a better hematological recovery and survival rate¹⁷. And recent literature also report new insights into the disease pathology in terms of underlying genetic and immune factors, which has aided in the diagnosis and treatment of the disease^{16,18}.

Overall, childhood pancytopenia is a complex and varied hematological condition. Many of these are potentially curable or preventable. Improving dietary intervention, infection prevention and early detection of hematological disease can reduce the morbidity and mortality of children.

CONCLUSION

Children with pancytopenia have a broad range of disease, with aplastic anemia, megaloblastic anemia and leukemia as the most common in our study. Our study highlights the importance of both nutritional deficiency and bone marrow failure syndrome in our region. Bone marrow examination remains the gold standard in the diagnosis, followed by proper recognition of disease and timely and effective treatment. Early diagnosis is crucial, particularly in treatable conditions such as nutritional anemia and infections, which helps to reduce the mortality and morbidity. Further, this study highlights the need for local studies to inform clinical practice and policy. Better diagnostic facilities and training for clinicians could also help in better care of children with pancytopenia.

REFERENCES

Nell EM, Chapanduka ZC. Pancytopenia: lessons from a South African tertiary academic institution. *African Journal of Laboratory Medicine*. 2022;11(1):1-8.

Saleem U, Tariq H, Alam S, et al. Adult pancytopenia: evaluation by peripheral blood counts and bone marrow. *Expert Review of Hematology*. 2024;29:1-9.

Vargas-Carretero CJ, et al. Hematological and clinical presentation and diagnosis of pancytopenia. *Hematology*. 2019;24(1):399-404.

Rahimullah Z, et al. Hematological disorders in children with pancytopenia. *Cureus*. 2019;11(7):e5124.

Yokuş O, Gedik H. Etiology of pancytopenia: an analysis of 137 cases. *Avicenna Journal of Medicine*. 2016;6(4):109-112.

Zill-E-Rubab, et al. Cause of pancytopenia in children of Southern Punjab. *Pakistan Journal of Medical & Health Sciences*. 2022;16(10):100.

Dubey SR, et al. Children with pancytopenia: a descriptive study. *International Journal of Contemporary Pediatrics*. 2016;3(1):169-172.

Zubair AB, et al. Spectrum of causes of pancytopenia in children. *Cureus*. 2022;14(8):e27842.

Sharma A, Rajeshwari K, Kumar D. Etiology of bicytopenia and pancytopenia in children. *Pediatric Hematology Oncology Journal*. 2023;8(1):34-38.

Nadig ND, et al. Strictures of pediatric pancytopenia. *Cureus*. 2024;16(8):e67875.

Kumar G, et al. Clinico-etiological profile of bicytopenia and pancytopenia in children. *Cureus*. 2024;16(8):e66255.

DeZern AE, Brodsky RA. Treatment of aplastic anemia. *Expert Review of Hematology*. 2011;4(3):341-353.

Khanduri U, Sharma A. Etiology and epidemiology of megaloblastic anemia. *Indian Journal of Pathology and Microbiology*. 2007;50(3):409-412.

Naseem S, Varma N, Das R, et al. Pattern of cytopenias in childhood. *Indian Journal of Pathology and Microbiology*. 2011;54(1):75-80.

Arber DA, Orazi A, Hasserjian R, et al. The 2022 WHO classification of hematolymphoid tumors. *Blood*. 2022;140(11):1200-1228.

Giudice V, Selleri C. Pathophysiology of aplastic anemia. *Seminars in Hematology*. 2022;59(1):13-20.

- Patel BA, Townsley DM, Scheinberg P. Treatment of aplastic anemia with immunosuppressive therapy. *Seminars in Hematology*. 2022.
- Shallis RM, Ahmad R, Zeidan AM. New insights into the causes, molecular basis and treatment for aplastic anaemia. *European Journal of Haematology*. 2018;101(6):711-720.

