ORIGINAL ARTICLE

Aplastic Anemia in Children with Pancytopenia: A Single Center Cross-sectional study from A Tertiary Care Hospital in KPK, Pakistan

SHAFAQ SULTANA, ISMA WAHEED, MUHAMMAD NADEEM QURESHI, UROOJ KHAN

Pak Pediatr J 2026; **50(1):** 28-33

Correspondence to:

Dr. Shafaq Sultana
Assistant Professor, Department of Pediatric Medicine, Children Hospital, Faisalabad

E-mail: shafaqrana07@hotemail.com

Received for publication: Dec. 01, 25
Revised received: Jan. 19, 2026
Revision accepted: March. 29, 2026

How to cite this: Sultana S, Waheed I, Qureshi MN, Khan U

Aplastic Anemia in Children with Pancytopenia: A Single Center Cross-sectional study from A Tertiary Care Hospital in KPK, Pakistan

DOI:
https://doi.org/10.66347/ppj.v50i1.649

ABSTRACT

Objective: To determine the frequency of aplastic anemia in children presenting with pancytopenia.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Pediatrics Department, Ayub Teaching Hospital, Abbottabad from January 2025 to June 2025.

Material and Methods: Ninety-one children from 6 months to 15 years, of either gender fulfilling the inclusion criteria were enrolled using Non-probability consecutive sampling with informed written consent from the parents, after approval from institutional review board. The details of the patients were collected on a predesigned proforma. Data was analysed using SPSS version 20.0.

Results: 91 children were enrolled in the study. Aplastic anemia was found in 12 patients (13.2%), while 79 patients (86.8%) had pancytopenia attributable to other aetiologies. Mean age of the patients was 4.78 ± 2.33 years. Out of 91 patients, 40 (43.9%) were <4 years and 51 (56.0%) were ≥4 years. We found no statistically significant association between age group and aplastic anaemia (p = 0.43). There were 49 males (53.8%) and 42 females (46.2%) in the study. We observed no statistically significant association of gender with aplastic anaemia (p = 0.36).

Conclusion: Aplastic anaemia is an important cause of pancytopenia in children. Children of all ages and both genders had equal risk of aplastic anaemia.

Key Words: *Pancytopenia, Aplastic anemia, Bone marrow.*

INTRODUCTION

Pancytopenia is a disorder involving the simultaneous decline in all three cell lines in blood including red blood cells, white blood cells and platelets, leading to Anemia (Hb<10g/dl), Neutropenia (ANC <1500) and Thrombocytopenia (Platelets <100,000). Patients usually present with clinical features attributed to anemia, thrombocytopenia and rarely leukopenia which in later stages is responsible for downhill course.[1] Anemia has well-known clinical consequences of pallor, malaise, sleepiness, irritability, exercise intolerance and shortness of breath. Children with severe thrombocytopenia develop spontaneous bruising, bleeding, and petechiae. Menstruating females experience menorrhagia heavy and prolonged periods. Leukopenia impairs the

immune system's ability to fight infections causing opportunistic organisms to behave pathologically. Children with severe neutropenia (defined as ANC <500/mm^3) face a high risk of life-threatening bacterial and fungal infections.[2]

The cause of pancytopenia varies from congenital absence of hematopoietic cell lineages in bone marrow to acquired bone marrow failure defects. Congenital syndromes of bone marrow hypoplasia includes disorders like Fanconi syndrome, Bloom's syndrome, dyskeratosis congenita, inborn errors of metabolism/ storage disorders like Organic academia's, lysosomal storage disorders. Acquired bone marrow defects include aplastic anaemia, megaloblastic anaemia due to nutritional or genetic deficiency of vitamin B12 and folic acid and infiltration of bone marrow with abnormal cells and tissues as in malignant transformation and fibrosis like in leukaemia's and myelofibrosis. The other important reason of pancytopenia is excessive destruction of blood cells in the peripheral circulation by hypertrophied and overactive reticuloendothelial system as seen in conditions of hypersplenism (liver cirrhosis, late stages of unmanaged haemolytic anaemias), autoimmune disorders like systemic lupus erythematosus, infections like HIV, Epstein Bar virus infection, Cytomegalovirus infection being common among many causes.[3]

Aplastic anaemia was first described by a pathologist Paul Ehrlich in 1888 based on bone marrow findings on autopsy of a patient. Although it is rare but is a fatal cause of acquired pancytopenia in children after megaloblastic anemia and leukemia's, which requires early diagnosis and prompt management for survival. It is characterized by hypo cellular bone marrow leading to peripheral pancytopenia**,** without abnormal cell infiltrates or fibrosis in the bone marrow.[4] The pathophysiology of aplastic anemia is not well understood in literature but its assumed to involve immune-mediated destruction or suppression of hematopoietic stem cells in the bone marrow. Its aetiology is multifactorial involving viral infections (Parvo B19), drugs, toxins, radiations and autoimmune diseases. There is biphasic peak in age distribution in children with aplastic anemia been common in 2-5 years age group and at adolescent age group. Aplastic anemia is also considered a premalignant condition as in some genetic variants it can transform into acute myeloid leukemia or myelodysplastic syndrome.[5]

The modified Camitta criteria is used to classify aplastic anemia into three categories of non-severe aplastic anemia, severe aplastic anaemia and very severe aplastic anemia based on bone marrow cellularity, an absolute neutrophil count (ANC), platelet count, and reticulocyte count.[6] It is diagnosed through bone marrow biopsy including aspiration and trephine biopsy with supportive investigations like full blood counts, peripheral blood film with reticulocyte count and vitamin B12 and folate levels in serum, flow cytometry and in rare cases chromosomal breakage studies to rule out other potential causes. Early diagnosis and referral to hematologists for proper management including first line therapy with human recombinant antithymocyte globulin (hATG), immunosuppressive therapies with calcineurin inhibitors cyclosporin A or 2nd line treatment with hematopoietic stem cell transplantation is necessary, as it can significantly improve the outcomes in children affected with aplastic anemia. Recent emerging treatments recommended by North American Pediatric Aplastic Anemia Consortium (NAPAAC) includes thrombopoeitin receptor agonists like eltrombopag and romiplastin as promising new modalities with fewer side effects and lasting results.[7]

Most of the literature on aplastic anaemia in children is from the Western world and very limited local and regional data is available on the prevalence of aplastic anemia in pancytopenic children in Pakistan and South Asian region, and this is a common reason for expensive undue workup and delay in diagnosis and management leading to increase in morbidity and mortality of patients and undue burden on the healthcare resources in developing nations.

This study aims to determine the frequency of aplastic anemia in children presenting with pancytopenia at Ayub Teaching Hospital, Abbottabad in Khyber Pakhtunkhwa (KPK) province in Pakistan. These findings will provide evidence to support early diagnostic protocols, help in making local guidelines for diagnosis and management of acquired aplastic anemia in children and to prioritize resource allocation for bone marrow evaluation and possible

transplantation to improve clinical outcomes through timely intervention in a resource limited region of KPK, Pakistan.

Objective: To determine the frequency of aplastic anemia in children presenting with pancytopenia.

Material and methods: This descriptive cross-sectional study was carried out at Pediatrics Department of Ayub Teaching Hospital, Abbottabad from January 2025 to June 2025 with the approval of hospital ethical review committee. (Ref. No.RC-EA-2025/307). Non-probability consecutive sampling technique was used and ninety-one children from ages 6 months to 15 years of either gender with isolated pancytopenia on admission fulfilling the inclusion criteria were enrolled after informed written consent from the parents. Children with hepatosplenomegaly, lymphadenopathy and children with recent blood transfusion in last 6 months were excluded. All required tests including full blood count, peripheral film and reticulocyte count were done in the hospital laboratory. Bone marrow trephine biopsy was done by expert hematologist in pathology department of the hospital. The details of the patients were collected on a predesigned proforma including demographics, complete blood count values and results of trephine bone marrow biopsy specimens with aplastic anemia present or not.

Data was analysed using SPSS version 20.0. Quantitative variables like age is presented as mean and standard deviation (SD). Categorical variable like gender and presence or absence of aplastic anemia are presented as frequency tables and percentages. Data was stratified for age and gender of the patients. Post-stratification Chi square test was applied with 95% confidence interval and 8% absolute precision.

RESULTS

Total 91 children with pancytopenia were included in this study. The mean age was 4.78 ± 2.33 years. There were 40 (43.9%) children of age <4 years while 51 (56.0%) had age ≥4 years. There was slight gender predilection for males, being 49 (53.8%) males and 42 (46.1%) females **table 1.**

TABLE 1: Demographic distribution of patients.

Variables		Percentage/ Mean SD	Total
Age in years		4.78±2.33	
	<4years	40(43.9%)	91
	≥4years	51(56.0%)	
Gender	Male	49(53.8%)	91
	Female	42(46.1%)	

In this study, 12 (13.1%) children had aplastic anaemia while 79 (86.3%) had pancytopenia related to other causes **table 2.**

TABLE 2: Frequency of aplastic anaemia in pancytopenic patients

Cause of pancytopenia	Frequency	Percentage
Aplastic Anemia	12	13.19
Others	79	86.81
Total	**91**	**100.0**

Data was stratified for age and gender of the patients. In children aged <4 years 4 (33.3%) had aplastic anemia and in children aged ≥4 years 8 (66.66%) had aplastic anemia. The difference between both age strata was insignificant (p= 0.43).

Regarding gender stratification of children. 7(58.3%) males had aplastic anemia and 5 (41.6%) females had aplastic anemia. The difference between both gender strata was insignificant (p= 0.36) **table 3.**

TABLE 3: Data stratification of aplastic anemia patients with respect to age and gender

Variables		Frequency (n)	Percentage	Total	p-value
Age in years	<4 years	4	33.3		
	≥4 years	8	66.6	12	0.43
Gender	Male	7	58.3	12	
	Female	5	41.6		0.36

DISCUSSION

Aplastic anemia is one of the many important causes of pancytopenia in pediatric age group along with megaloblastic anemia and leukaemia's leading to long term morbidity and mortality if not

managed early in children. The survival rate of aplastic anemia depends upon its cause and severity. Overall all pediatric age group 5 years survival of moderate aplastic anemia is 50-55%. Survival depends upon cause, type of aplastic anemia, severity of disease, age of patient and timely diagnosis before development of complications.[8] But contrary to other etiologies of pancytopenia many of causes of acquired aplastic anemia are preventable including viral and protozoal infections, drugs, radiations, toxins, chemotherapy. Acquired aplastic anemia can be treated with recent modalities of immunosuppression and bone marrow transplantation provided the child is timely diagnosed before developing complications (myelodysplasia or acute myeloid leukemia). The geographical distribution of the aplastic anemia shows considerable variation, with an incidence of approximately 2–3 cases per million population per year in European countries. In contrast, Asian countries exhibit nearly twice the burden of pediatric aplastic anemia, with incidence rates estimated to be 2–3 times higher than those observed across the Americas, Europe, and Africa combined.[9]

Aplastic anemia shows a bimodal age distribution among children, with incidence peaks occurring at 2–5 years and again during adolescence. Age at presentation is a critical prognostic factor in aplastic anemia. The mean age at presentation in our study population was 4.7 years with variation of 2.3 years, which is similar with findings from several domestic and South Asian studies, including those by Khalid *et al.* in Pakistan (mean age: 6.7 years) and Karun *et al.* in India (1–6 years; 43.9% of cases).[10,11] In contrast, Das *et al.* from Bangladesh reported a higher mean age of 7 years in Bangladeshi population which is consistent with studies from Karachi, Pakistan by Fatima *et al.* (8 years) and by Yousaf *et al.* (9 years) in an Egyptian study.[12-14] Notably, none of the studies reviewed reported a significant burden of aplastic anemia among infants below one year of age.

Gender is also considered an important epidemiological factor in development and prognosis of paediatric aplastic anemia with several studies showing either equal distribution or female predominance especially in adolescent age group possibly related to autoimmune predisposition, hormonal factors and environmental exposures. Patil *et al*. in their study on Indian cohort showed females being more affected with aplastic anemia than males(1:0.7).[15] However, in our study we found slight male predominance (1.1:1) which is very much aligned with results from many local Pakistani studies done by Rasool *et al.* Fatima *et al.* (61.4%), and Khalid *et al*. (1.2:1) in different cities of Pakistan and also with studies in neighbouring country India by Mishra *et al.* (1:0.8).[16,17,13,10] Vaht *et al*. in Sweden and Yosaf *et al.* in Egypt showed no variation in gender distribution being make and females equally affected.[18,14]

Among all the ninety-one children presenting with pancytopenia in our study acquired aplastic anemia was identified in 13.1% of patients, making it a relatively uncommon yet clinically significant and potentially manageable cause of pancytopenia. Comparable frequencies have been documented in several domestic and regional studies, including those by Kaleem *et al.* in Peshawar, Kankane *et al.* (14%), and Piekarska *et al.* in India.[19-21] However, a number of studies from Pakistan and neighbouring countries India and Iran have reported a substantially higher prevalence of pediatric aplastic anemia, including studies done by Inamullah *et al*. (35.9%), Jan *et al* (28. 3%), Aziz *et al.* (31.90%) and Khalid *et al.* (33.6%) in Pakistan,[22,23,10] and Dasgupta *et al.* (33.50%) in India and Jalaeikhoo *et al.* (29.50%) in Iran.[24,25] All these studies report nearly twice the disease burden observed in our patients. This variation may be attributed to difference in sample size, environmental exposures, or diagnostic criteria employed across different populations.

Limitations: This was a single centre based study with a small sample size. More multicentre collaborative studies should be done on this issue.

Suggestions: Large scale multi-centred collaborative studies with large sample size involving population from different areas of Pakistan should be conducted to exactly estimate the burden of disease in Pakistani population and also to delineate the most common causes of aplastic anemia so that we can make policies and funds could be arranged and allocated for proper management and care of these children.

CONCLUSION

Hence we concluded that aplastic anemia is a rare yet serious cause of pancytopenia in children in Pakistan and by its timely diagnosis and management many lives can be saved and quality of life of children suffering from this disease can be improved and burden on healthcare resources can be decreased with proper policy making and allocation of budget for diagnosis and management of aplastic anaemia and training the medical staff for diagnostic and transplantation services. This will enable us to divert these resources to be utilized for other important yet ignored issues especially in resource limited countries like Pakistan.

Acknowledgements: We acknowledge hospital administration and hematology and pathology staff for providing free-of-cost laboratory facilities for the patients enrolled in the study. We are also thankful to patients and parents for there co-operation and support which made this study possible.

Source of funding: None
Conflict of interest: None

Authors' affiliation

Dr. Shafaq Sultana
Assistant Professor, Department of Pediatric Medicine, Children Hospital, Faisalabad

Dr. Isma Waheed,
Medical Officer,
Department of Pediatrics, DHQ Hospital, Abbottabad

Dr. Muhammad Nadeem Qureshi,
Senior Medical Fellow,
Department of Endocrinology, Manchester Foundation Trust, UK

Dr. Urooj Khan
4th year student,
Ayub Medical College, Abbottabad

REFERENCES

1. Sharma A, Rajeshwari K, Kumar D. Clinicoetiological profile of children with bicytopenia and pancytopenia. Pediatric Hematology Oncology Journal. 2023 Mar 1;8(1):34-8. https://doi.org/10.1016/j.phoj.2023.01.006
2. Goronkova OV, Pavlova AV, Raykina EV. Aplastic anemia in children: the current concept of differential diagnosis. Pediatric Hematology/Oncology and Immunopathology. 2024 Jul 23;23(2):208-20. https://doi.org/10.24287/1726-1708-2024-23-2-208-220
3. Onishi Y. Aplastic anemia: history and recent developments in diagnosis and treatment. International journal of hematology. 2024 Mar;119(3):217-9. https://doi.org/10.1007/s12185-024-03715-1
4. Salimova TY, Goronkova OV, Protsvetkina AV, Maschan AA, Novichkova GA. Epidemiology of acquired aplastic anemia in children in the Russian Federation. Pediatric Hematology/Oncology and Immunopathology. 2024 Dec 13;23(4):14-22. https://doi.org/10.24287/1726-1708-2024-23-4-14-22
5. Yoshida N. Recent advances in the diagnosis and treatment of pediatric acquired aplastic anemia. International journal of hematology. 2024 Mar;119(3):240-7.
6. Solimando AG, Palumbo C, Pragnell MV, Bittrich M, Argentiero A, Krebs M. Aplastic anemia as a roadmap for bone marrow failure: an overview and a clinical workflow. International journal of molecular sciences. 2022 Oct 4;23(19):11765. https://doi.org/10.3390/ijms231911765
7. DeZern AE, Churpek JE. Approach to the diagnosis of aplastic anemia. Blood Advances. 2021 Jun 22;5(12):2660-71. https://doi.org/10.1182/bloodadvances.2021004345
8. Forester CM, Sartain SE, Guo D, Harris MH, Weinberg OK, Fleming MD, London WB, Williams DA, Hofmann I. Pediatric aplastic anemia and refractory cytopenia: A retrospective analysis assessing outcomes and histomorphologic predictors. Am J Hematol. 2015 Apr;90(4):320-6. https://doi.org/10.1002/ajh.23937
9. Guarina A, Farruggia P, Mariani E, Saracco P, Barone A, Onofrillo D, Cesaro S, Angarano R, Barberi W, Bonanomi S, Corti P, Crescenzi B, Dell'Orso G, De Matteo A, Giagnuolo G, Iori AP, Ladogana S, Lucarelli A, Lupia M, Martire B, Mastrodicasa E, Massaccesi E, Arcuri L, Giarratana MC, Menna G, Miano M, Notarangelo LD, Palazzi G, Palmisani E, Pestarino S, Pierri F, Pillon M, Ramenghi U, Russo G, Saettini F, Timeus F, Verzegnassi F, Zecca M, Fioredda F, Dufour C. Diagnosis and management of acquired aplastic anemia in childhood. Guidelines from the Marrow Failure Study Group of the Pediatric Haemato-Oncology Italian Association (AIEOP). Blood Cells Mol Dis. 2024 Sep;108:102860. https://doi.org/10.1016/j.bcmd.2024.102860

10. Khalid H, Saleem MU, Raza AB, Mahmud M, Sultan AN, Jamil MS. Frequency of Aplastic Anemia in Children (1-15 years) with New-Onset Pancytopenia. Annals of Punjab Medical College. 2023 Sep 30;17(3):320-3. https://doi.org/10.29054/apmc/2023.1416
11. Karun thaPPa S, MaSilaMani D, PraSanna S. Aetiological profiles of pancytopenia in children between 2 months to 12 years of age-A retrospective study from a tertiary care centre, Chennai, India. Tuberculosis (TB). 2022 Feb 1;1:1-09.
12. DAS M, SAHA A, GIRI A. Clinico-aetiological and Demographic Profile of Pancytopenia among Children in a Tertiary Care Hospital of Northern Part of West Bengal-A Cross-sectional Study. Journal of Clinical & Diagnostic Research. 2022 Mar 1;16(3). **10.7860/JCDR/2022/51595.16135**
13. Fatima N, Ashfaq M, Hussain W, Raza M, Anwar A. Clinical spectrum, laboratory profile and outcome of aplastic anemia in children presenting at tertiary care hospital. The Professional Medical Journal. 2025 Nov 2;32(11):1543-9. https://doi.org/10.29309/TPMJ/2025.32.11.9917
14. Youssef M.A.M., Ahmed E.S., Kamal D.T., Elsayh K.I., Abdelfattah M.A., Mahran H.H., Embaby M.M. Clinical signs and treatment of New-onset Bone marrow failure associated SARS-CoV-2 infection in Children: a single institution prospective cohort study. Mediterr J Hematol Infect Dis 2024, 16(1): e2024034, DOI: http://dx.doi.org/10.4084/MJHID.2024.034
15. Patil GR, Hatti S, Kumar BN, Sandeep H, Nagaraj N. Clinico-etiological profile of children presenting with pancytopenia in a tertiary care centre of North Karnataka region: A prospective observational study. Int J Life Sci Biotechnol Pharma Res. 2023;12:1907-11.
16. Rasool I, Minhas AM, Fatima M, Umar S, Imran A, Malik NA. Frequency of causes of pancytopenia in bone marrow samples of patients. Pakistan Journal of Pathology. 2023 Jun 27;34(2):51-5. https://doi.org/10.55629/pakjpathol.v34i2.742
17. MISHRA D, KOHLI A, YADAV RB, CHANDRA S. Pancytopenia in Indian children: a clinico-hematological analysis. Asian Journal of Paediatric Practice. 2021 Apr;2(2).
18. Vaht K, Göransson M, Carlson K, Isaksson C, Lenhoff S, Sandstedt A, Uggla B, Winiarski J, Ljungman P, Brune M, Andersson PO. Incidence and outcome of acquired aplastic anemia: real-world data from patients diagnosed in Sweden from 2000-2011. Haematologica. 2017 Oct;102(10):1683-1690. Doi:10.3324/haematol.2017.169862
19. Kaleem Z, Rehman A, Rafique MA, Altaf A. Aplastic Anemia in Patients with New-Onset Pancytopenia. Pakistan Journal of Medical & Health Sciences. 2022 Jun 10;16(04):977-.
20. Kankane A, Kumar V, Pandey N, Chaurasia OS. Clinical and etiopathological profile of pancytopenia in children (1-18 years): A study from tertiary care center of Bundelkhand region, central India.
21. Piekarska A, Pawelec K, Szmigielska-Kapłon A, Ussowicz M. The state of the art in the treatment of severe aplastic anemia: immunotherapy and hematopoietic cell transplantation in children and adults. Frontiers in immunology. 2024 Apr 5;15:1378432.
22. Ullah I, Khan MS, Fayaz M, Khan SA, Khan N, Tabassum R. Understanding the Etiologies of Pancytopenia in Pediatric Patients: A Cross-Sectional Study. Indus Journal of Bioscience Research. 2025 Jan 10;3(1):185-9.
23. Jan AZ, Zahid B, Ahmad S, Gul Z. Pancytopenia in children: A 6-year spectrum of patients admitted to Pediatric Department of Rehman Medical Institute, Peshawar. Pak J Med Sci 2013;29(5):1153-1157. doi:http://dx.doi.org/10.12669/pjms.295.3865
24. Dasgupta A, Padma SK, Sajitha K, Shetty J. Etiological evaluation of pancytopenia in a tertiary care hospital. Ann Pathol Lab Med 2016;3(5):441-50.
25. Jalaeikhoo H, Azimzadeh P, Narimani A. Acute myeloid leukemia as the main cause of pancytopenia in Iranian popul. Iran J Pathol 2017;12(3):265-71.

Author's Contribution

SS: Concept, manuscript writing, Discussion writing, Data analysis, final drafting
IW: Data collection, manuscript writing, review
MNQ: Data collection, manuscript review
UK: Data collection

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.