

Clinical, Hematological, and Etiological Profile of Bicytopenia and Pancytopenia in Children: A Prospective Observational Study from a Tertiary Care Center in Southern Rajasthan, India

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Abstract:

Objective: To evaluate the demographic characteristics, clinical presentation, hematological profile, etiological spectrum, and short-term outcomes of children presenting with bicytopenia and pancytopenia at a tertiary care center in Southern Rajasthan.

Methods: This prospective observational study was conducted over 18 months and included children aged 1 month to 18 years with bicytopenia or pancytopenia. Clinical evaluation, complete blood count, peripheral blood smear, relevant biochemical and microbiological investigations, and bone marrow examination when clinically indicated were performed to establish the underlying etiology. Data were analyzed using IBM SPSS Statistics version 26.0, with $p < 0.05$ considered statistically significant.

Results: A total of 46 children were enrolled, comprising 22 (47.8%) with bicytopenia and 24 (52.2%) with pancytopenia. The mean age was 6.5 ± 3.2 years and 29 (63.0%) were males. Fever (93.5%) and pallor (87.0%) were the most common presenting features. Children with pancytopenia had significantly lower hemoglobin (8.65 ± 1.41 vs. 9.75 ± 1.13 g/dL; $p = 0.01$), total leukocyte count ($2,627 \pm 733$ vs. $10,854 \pm 13,781/\text{mm}^3$; $p = 0.01$), and red blood cell count (3.31 ± 0.44 vs. 3.96 ± 0.39 million/ mm^3 ; $p < 0.001$) than those with bicytopenia. Infectious disorders were the predominant etiological category (37.0%), followed by nutritional disorders (19.6%), while vitamin B12 deficiency was the most common individual diagnosis (13.0%). Bone marrow examination was performed in 15 (32.6%) children, with hypercellular marrow being the most frequent finding (33.3%). Blood transfusion was significantly more frequent in pancytopenia than bicytopenia (75.0% vs. 13.6%; $p < 0.001$), and hospital stay was longer (8.6 ± 4.3 vs. 5.9 ± 2.8 days; $p = 0.03$). Mortality occurred exclusively in children with pancytopenia (4/24; 16.7%).

Conclusion: Infectious diseases and nutritional deficiencies were the predominant causes of pediatric bicytopenia and pancytopenia in Southern Rajasthan. Pancytopenia was associated with greater hematological severity, increased transfusion requirements, prolonged hospitalization, and higher mortality. A systematic diagnostic approach incorporating clinical assessment, peripheral blood smear examination, and selective bone marrow evaluation may facilitate early etiological diagnosis and timely management.

Keywords: Bicytopenia; Pancytopenia; Children; Vitamin B12 deficiency; Infectious diseases; Nutritional deficiency; Bone marrow; Pediatric hematology.

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Introduction

Bicytopenia and pancytopenia are important hematological abnormalities encountered in pediatric practice and represent manifestations of various underlying disorders. Bicytopenia is defined as a reduction in any two of the three major peripheral blood cell lineages, whereas pancytopenia refers to a reduction in all three cell lines.⁽¹⁾ These abnormalities may result from impaired bone marrow production, ineffective

hematopoiesis, peripheral destruction, or splenic sequestration. Their causes range from transient, reversible conditions to serious disorders such as hematological malignancies, aplastic anemia, severe infections, and immune-mediated diseases.⁽²⁾

Affected children commonly present with nonspecific features such as fever, pallor, fatigue, recurrent infections, and bleeding manifestations. Hepatosplenomegaly, lymphadenopathy, petechiae,

and bone tenderness may provide useful diagnostic clues.⁽³⁾ A systematic evaluation involving clinical assessment, complete blood count, peripheral blood smear examination, and bone marrow evaluation when indicated is essential for establishing the diagnosis.^(1,3) Early recognition is important because acute leukemia, aplastic anemia, hemophagocytic lymphohistiocytosis, and severe systemic infections may initially present with bicytopenia or pancytopenia.⁽⁴⁾

The etiological spectrum varies across geographical regions owing to differences in nutritional status, endemic infections, socioeconomic conditions, environmental factors, and healthcare accessibility.⁽⁵⁾ Earlier studies from developing countries frequently reported nutritional deficiencies, particularly megaloblastic anemia, as a major cause of pancytopenia.^(6,7) Recent studies, however, indicate increasing contributions from infections, hematological malignancies, aplastic anemia, immune-mediated disorders, and inherited bone marrow failure syndromes.⁽⁸⁾ Regional variations emphasize the need for locally generated data to guide diagnostic evaluation and optimize available resources.⁽⁹⁾

Few studies have evaluated bicytopenia and pancytopenia together across the entire pediatric age group, and data from Southern Rajasthan remain limited.⁽¹⁰⁾ Therefore, this study aimed to evaluate the demographic characteristics, clinical presentation, hematological profile, etiological spectrum, and short-term outcomes of children aged 1 month to 18 years presenting with bicytopenia or pancytopenia at a tertiary care teaching hospital in Southern Rajasthan.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of Pediatrics, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India, from June 2024 to December 2025 to evaluate the clinical, hematological, and etiological profiles of children presenting with bicytopenia or pancytopenia. The study was approved by the Institutional Human Research Ethics Committee (HREC), Geetanjali University, Udaipur (IEC Approval No. GU/HREC/EC/2024/2518). Written informed consent was obtained from the parents or legal guardians of all participants before enrolment, and patient confidentiality was maintained throughout the study in accordance with the Declaration of Helsinki.

Study Population: Children aged 1 month to 18 years admitted with bicytopenia or pancytopenia detected on complete blood count before establishment of a definitive diagnosis were included.

Inclusion Criteria

- Age between 1 month and 18 years
- Bicytopenia (reduction in any two blood cell lines) or pancytopenia (reduction in all three blood cell lines)
- Hemoglobin <10 g/dL, total leukocyte count <4,000/mm³ and/or platelet count <100,000/mm³.

Exclusion Criteria: Children with chemotherapy- or radiotherapy-induced cytopenia, recent blood transfusion before evaluation, cytopenia due to acute blood loss, or refusal of consent were excluded.

Sample Size: The minimum sample size was calculated using the single population proportion formula:

$$n = \frac{Z^2 \times pq}{d^2}$$

assuming a prevalence (P) of 3.1%, 95% confidence level (Z = 1.96), and an absolute precision of 5%, yielding a minimum sample size of 46 participants. All eligible children presenting during the study period were enrolled until its completion, resulting in the inclusion of 46 participants.

Data Collection: A detailed clinical history and physical examination were performed for all enrolled children. Baseline investigations included complete blood count with red cell indices, peripheral blood smear examination, and relevant biochemical and microbiological investigations. Bone marrow aspiration and biopsy, serum vitamin B12 and folate levels, autoimmune workup, viral serology, and imaging studies were performed whenever clinically indicated to establish the underlying diagnosis. Bone marrow aspiration was performed in children with persistent unexplained cytopenia, suspected hematological malignancy, aplastic anemia, or marrow failure syndrome.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics (Version 26.0). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Student's *t*-test or Mann–Whitney *U* test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. A *p*-value <0.05 was considered statistically significant.

Bias: Selection bias was minimized by consecutive enrolment of all eligible children, while information bias was reduced through standardized clinical assessment, uniform laboratory evaluation, and predefined diagnostic criteria across all participants.

Results

A total of 46 children fulfilling the predefined Age, sex, and residential distribution were comparable between the bicytopenia and pancytopenia groups, with no statistically significant differences (Table 1).

Vomiting was significantly more frequent in children with pancytopenia. Other clinical features were comparable between the groups (Table 2).

Children with pancytopenia had significantly lower hemoglobin, total leukocyte count, RBC count, and neutrophil percentage, along with a significantly higher lymphocyte percentage. Platelet counts were comparable between the groups (Table 3).

Infectious disorders were the most common cause of bicytopenia (50.0%), whereas pancytopenia showed a broader etiological distribution. Bone marrow failure syndromes and hematological malignancies were observed only in the pancytopenia group. However, none of the etiological categories differed significantly between the two groups (all $p > 0.05$). (Table 4).

Hypercellular marrow was the most frequent finding (33.3%), followed by hypocellular/hypoplastic marrow (26.7%) and severely hypocellular marrow (13.3%). Other findings were observed in one child each (6.7%). (Table 5)

Most children were discharged (84.8%). All four deaths occurred in the pancytopenia group, while all three LAMA cases occurred in the bicytopenia group. Children with pancytopenia had a significantly longer mean hospital stay than those with bicytopenia (8.6 versus 5.9 days; $p = 0.03$). (Table 6)

Severe thrombocytopenia, PICU admission, and requirement for blood transfusion were significantly associated with adverse outcomes. Severe anemia was more frequent among children with adverse outcomes but did not reach statistical significance. Pancytopenia alone was not significantly associated with adverse outcomes (Table 7).

Table 1: Baseline Demographic Characteristics

Variable	Bicytopenia (n = 22)	Pancytopenia (n = 24)	p-value
Mean age (years), mean $\pm$ SD	6.7 $\pm$ 3.4	6.4 $\pm$ 3.1	0.74
Male sex, n (%)	12 (54.5)	17 (70.8)	0.25
Rural residence, n (%)	12 (54.5)	16 (66.7)	0.40

Values are presented as mean $\pm$ SD or n (%), as appropriate.

Table 2: Clinical Presentation

Clinical feature	Bicytopenia (n = 22), n (%)	Pancytopenia (n = 24), n (%)	p-value
Fever	21 (95.5)	22 (91.7)	0.60
Weakness	12 (54.5)	17 (70.8)	0.58
Vomiting	2 (9.1)	12 (50.0)	0.002
Pallor	19 (86.4)	21 (87.5)	0.90
Hepatomegaly	5 (22.7)	10 (41.7)	0.17
Splenomegaly	2 (9.1)	5 (20.8)	0.26

Table 3: Hematological Profile

Hematological parameter	Bicytopenia (n = 22), mean $\pm$ SD	Pancytopenia (n = 24), mean $\pm$ SD	p-value
Hemoglobin (g/dL)	9.75 $\pm$ 1.13	8.65 $\pm$ 1.41	0.01
Total leukocyte count (/mm ³)	10,854 $\pm$ 13,781	2,627 $\pm$ 733	0.01
RBC count (million/mm ³)	3.96 $\pm$ 0.39	3.31 $\pm$ 0.44	<0.001
Neutrophils (%)	47.8 $\pm$ 7.4	41.5 $\pm$ 8.8	0.01
Lymphocytes (%)	43.9 $\pm$ 8.6	50.3 $\pm$ 9.2	0.02
Platelet count (/mm ³)	73,750 $\pm$ 23,893	62,614 $\pm$ 31,525	0.19

SD: standard deviation; RBC: red blood cell; TLC: total leukocyte count. A p-value < 0.05 was considered statistically significant.

Table 4: Distribution of Etiological Diagnosis According to Type of Cytopenia (N = 46)

Etiological Category/Diagnosis	Bicytopenia (n=22)	Pancytopenia (n=24)	p-value
Infectious Disorders	11 (50.0)	6 (25.0)	0.13*
Enteric fever	3	2	
Dengue	3	1	
Sepsis	3	1	
Scrub typhus	1	1	
Malaria	0	1	
Brucellosis	1	0	
Nutritional Disorders	5 (22.7)	4 (16.7)	0.74
Vitamin B12 deficiency	2	4	
Iron deficiency anemia	3	0	
Bone Marrow Failure Syndromes	0 (0.0)	4 (16.7)	0.11*
Aplastic anemia	0	3	
Hypoplastic marrow without a definitive diagnosis	0	1	
Hemolytic Anemias	3 (13.6)	2 (8.3)	0.66
Sickle cell anemia	2	2	
β-thalassemia	1	0	
Hematological Malignancies	0 (0.0)	3 (12.5)	0.23
Acute lymphoblastic leukemia (ALL)	0	3	
Immune-Mediated Disorders	2 (9.1)	2 (8.3)	1.00
Hemophagocytic lymphohistiocytosis (HLH)	0	2	
Immune thrombocytopenic purpura (ITP)	2	0	
Others	1 (4.5)	3 (12.5)	0.61
Hemolytic uremic syndrome (HUS)	1	1	
Hypersplenism	0	1	
Neuroblastoma	0	1	
Total	22 (100)	24 (100)	

Table 5: Bone Marrow Findings Among Children with Cytopenias (N=15)

Bone Marrow Finding	Number (n)	Percentage (%)
Hypercellular Marrow	5	33.3
Hypocellular/Hypoplastic Marrow	4	26.7
Severely Hypocellular	2	13.3
Normocellular Marrow	1	6.7
Blast Cells (Acute Leukemia)	1	6.7
Hemophagocytosis	1	6.7
Mildly Hypercellular	1	6.7
Total	15	100.0

Table 6: Clinical Outcomes and Duration of Hospital Stay Among Children with Bicytopenia and Pancytopenia

	Variable	Total (N=46)	Bicytopenia (n=22)	Pancytopenia (n=24)	p-value
Clinical outcome, n (%)	Discharged	39 (84.8)	19 (86.4)	20 (83.3)	—
	Death	4 (8.7)	0 (0.0)	4 (16.7)	0.04*
	LAMA	3 (6.5)	3 (13.6)	0 (0.0)	—
Duration of hospital stay (days)	Mean ± SD	7.3 ± 3.9	5.9 ± 2.8	8.6 ± 4.3	0.03
	Median	6	5	8	—
	Range	2–21	2–14	3–21	—

SD: standard deviation; LAMA: left against medical advice. p-values are retained as supplied; the statistical test underlying the mortality p-value () should be verified.*

Table 7: Univariable Analysis of Factors Associated with Adverse Clinical Outcome

Variable	Discharged (n = 39), n (%)	Adverse Outcome* (n = 7), n (%)	p-value†
Pancytopenia	20 (51.3)	4 (57.1)	1.000
Severe anemia (Hb <7 g/dL)	12 (30.8)	5 (71.4)	0.083
Severe thrombocytopenia (<20,000/mm ³)	10 (25.6)	5 (71.4)	0.029
PICU admission	12 (30.8)	6 (85.7)	0.010
Blood transfusion required	13 (33.3)	6 (85.7)	0.015

Discussion

The present prospective observational study evaluated 46 children with cytopenias, including 22 (47.8%) with bicytopenia and 24 (52.2%) with pancytopenia. The groups were comparable in their demographic characteristics, but differed in hematological parameters and management requirements. Infectious disorders predominated, while bone marrow failure syndromes and hematological malignancies occurred exclusively among children with pancytopenia. However, none of the etiological categories differed significantly between groups. These findings highlight the diverse causes of childhood cytopenias and the importance of identifying the underlying disorder rather than relying on the number of affected cell lines alone.

Demographic characteristics: The mean age was comparable between children with bicytopenia and pancytopenia (6.7 ± 3.4 versus 6.4 ± 3.1 years; $p=0.74$). Males constituted 54.5% and 70.8% of the respective groups, without a significant difference ($p=0.25$). Male predominance was also reported by Wadhwa et al.⁽¹¹⁾, Venkat et al.⁽⁹⁾ and Sharif et al.⁽¹²⁾. Nevertheless, hospital-based observations cannot establish biological susceptibility, as referral patterns and healthcare utilization may influence sex distribution.

Rural residence was more frequent in pancytopenia than bicytopenia (66.7% versus 54.5%), although the difference was not significant ($p=0.40$). This distribution may reflect the institution's catchment population. The study does not establish rural residence as a risk factor for cytopenia because it did not include a comparison group without cytopenia.

Clinical presentation: Fever and pallor were the predominant clinical features in both groups. Fever occurred in 95.5% of children with bicytopenia and 91.7% with pancytopenia, while pallor was observed in 86.4% and 87.5%, respectively. Similar clinical patterns were described by Thappa et al.⁽¹³⁾, Wadhwa et al.⁽¹¹⁾ and Venkat et al.⁽⁹⁾. The high frequency of fever is consistent with the substantial proportion of infectious etiologies, although fever may also accompany malignant and inflammatory disorders.

Vomiting was significantly more frequent in pancytopenia (50.0% versus 9.1%; $p=0.002$). However, its relationship with individual diagnoses was not evaluated, and a specific explanation cannot

be established from these results. Weakness, hepatomegaly and splenomegaly were also more frequent in pancytopenia, but the differences were not significant. Organomegaly has similarly been reported by Venkat et al.⁽⁹⁾ and Padhi et al.⁽¹⁴⁾. These findings provide useful clinical clues but cannot independently distinguish the two cytopenic groups.

Hematological profile: Children with pancytopenia had significantly lower hemoglobin levels than those with bicytopenia (8.65 ± 1.41 versus 9.75 ± 1.13 g/dL; $p=0.01$). RBC counts were also significantly lower (3.31 ± 0.44 versus 3.96 ± 0.39 million/mm³; $p<0.001$), indicating more pronounced anemia in the pancytopenia group.

The mean total leukocyte count was significantly lower in pancytopenia ($2,627 \pm 733$ versus $10,854 \pm 13,781$ /mm³; $p=0.01$). This difference partly reflects the definition of pancytopenia, which requires reduction of all three blood cell lines. The wide variation in leukocyte counts among children with bicytopenia suggests a heterogeneous distribution and warrants caution when interpreting the mean.

Neutrophil percentage was significantly lower, whereas lymphocyte percentage was higher, in pancytopenia. A higher lymphocyte percentage does not necessarily indicate absolute lymphocytosis, particularly in the presence of leukopenia. Platelet counts were lower in pancytopenia, but the difference was not significant ($p=0.19$). Thus, platelet reduction alone did not distinguish the groups, and clinically important thrombocytopenia may accompany either presentation.

Etiological spectrum: Infectious disorders were the leading etiological category, affecting 50.0% of children with bicytopenia and 25.0% with pancytopenia. However, this difference was not statistically significant ($p=0.13$). Enteric fever, dengue and sepsis were the principal infectious diagnoses. The importance of infections is consistent with observations by Kumar et al.⁽⁸⁾, Anand et al.⁽¹⁵⁾ and Venkat et al.⁽⁹⁾. Regional differences in infectious causes, including the prominence of scrub typhus reported by Katoch et al.⁽¹⁶⁾, emphasize the relevance of local epidemiology during investigation.

Nutritional disorders occurred in 22.7% of bicytopenia and 16.7% of pancytopenia cases ($p=0.74$). Vitamin B12 deficiency was more frequent in pancytopenia, whereas iron deficiency anemia occurred only in

bicytopenia. Bhati et al.⁽¹⁷⁾, Maru et al.⁽¹⁸⁾ and Thappa et al.⁽¹³⁾ also identified nutritional disorders as important etiologies. These findings support considering treatable micronutrient deficiencies during the evaluation of unexplained cytopenias.

Bone marrow failure syndromes and acute lymphoblastic leukemia occurred exclusively in pancytopenia, affecting 16.7% and 12.5% of that group, respectively. Neither association reached statistical significance. Wadhwa et al.⁽¹¹⁾ similarly identified aplastic anemia among children with pancytopenia but also reported leukemia in bicytopenia, demonstrating that malignancy cannot be excluded on the basis of the cytopenic pattern. Hemolytic, immune-mediated and miscellaneous disorders further illustrate the heterogeneous etiological spectrum.

Bone marrow findings: Bone marrow examination was performed in 15 children. Hypercellular marrow was the most frequent finding (33.3%), followed by hypocellular/hypoplastic marrow (26.7%) and severely hypocellular marrow (13.3%). Normocellular marrow, blast cells, hemophagocytosis and mildly hypercellular marrow were each observed in one child.

These findings demonstrate the range of marrow abnormalities encountered in childhood cytopenias. Wadhwa et al.⁽¹¹⁾ likewise emphasized the diagnostic contribution of marrow examination. However, cellularity alone does not establish etiology, and hemophagocytosis alone does not confirm HLH. Findings require correlation with clinical and laboratory evidence. As only selected children underwent examination, these proportions cannot be generalized to the entire cohort.

Management and outcomes: Transfusion requirements were significantly higher in pancytopenia than bicytopenia (75.0% versus 13.6%; $p < 0.001$). Hospitalization was also longer (8.6 ± 4.3 versus 5.9 ± 2.8 days; $p = 0.03$), indicating greater inpatient resource requirements.

Overall, 84.8% were discharged, 8.7% died and 6.5% left against medical advice. All four deaths occurred in pancytopenia. Although Table 7 reports a significant mortality difference, the small number of deaths warrants cautious interpretation and confirmation of the statistical test. Pancytopenia was not associated with the composite adverse outcome of death or LAMA, partly reflecting the inclusion of three LAMA cases from the bicytopenia group.

Severe thrombocytopenia, PICU admission and transfusion requirement were significantly associated with adverse outcomes, whereas severe anemia was not ($p = 0.083$). These are univariable associations, not independent predictors; PICU admission and transfusion may primarily reflect illness severity. The small sample, limited adverse events and combination of death with LAMA restrict interpretation.

Nevertheless, the findings support careful etiological assessment and closer monitoring of children with severe hematological abnormalities.

Conclusion

Infectious diseases and nutritional deficiencies were the predominant etiological categories among children with bicytopenia and pancytopenia in this study. Pancytopenia was associated with more severe hematological abnormalities, greater transfusion requirements, and longer hospital stay than bicytopenia. Early systematic evaluation with complete blood count, peripheral blood smear examination, and selective bone marrow assessment can facilitate timely etiological diagnosis and improve patient management.

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