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Original Research Article

Clinico-etiological profile and outcomes of bicytopenia and pancytopenia in children at a tertiary care hospital

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ABSTRACT

Background: Bicytopenia and pancytopenia in children are haematological manifestations indicating underlying bone marrow dysfunction, peripheral destruction or systemic disease. The etiological spectrum in developing countries varies with nutritional deficiencies and infections playing a predominant role. There is limited data describing the clinicoetiological profile of bicytopenia and pancytopenia in children in recent times.
Methods: This is a cross-sectional observational study conducted at a teaching hospital, over a period of 18 months. A total of 110 children aged 1 month to 12 years (68 with pancytopenia, 42 with bicytopenia) were enrolled after obtaining informed consent. Basic patient information and clinical findings along with relevant investigations including complete blood count, peripheral smear, bone marrow examination and relevant biochemical and serological tests were done. Data was obtained on a predesigned proforma and analyzed using descriptive statistics.
Results: There was a male predominance (54.5%) with the majority (49%) in the 6–12-year age group. Fever (88.18%) was the most common presentation. The leading causes of cytopenia were infections 48 (43.6%) followed by nutritional deficiencies 43(39%). Other less common causes were primary haematological disorders that included acute leukaemia 11(10 %), thalassemia with hypersplenism 3 (2.72%), ITP 2 (1.8%) and aplastic anaemia 2 (1.8%).
Conclusions: Bicytopenia/pancytopenia is predominantly caused by treatable nutritional and infectious conditions with excellent prognosis. However, significant patients have life-threatening disorders like leukemia and aplastic anemia, which account for all mortality and morbidity.

Keywords: Bicytopenia, Pancytopenia, Bone marrow, Anaemia, Leukaemia

INTRODUCTION

Cytopenia is defined as reduction in either of the cellular elements of blood, i.e., RBC, WBC or platelets. Bicytopenia is reduction in any of the two cell lines and pancytopenia is reduction in all the three1. Pediatric patients frequently experience cytopenia, which are caused by neoplastic infiltration, immune-mediated bone marrow suppression, ineffective haematopoiesis, peripheral blood cell sequestration in hyperactive reticuloendothelial tissue and failure of hematopoietic progenitor production in the bone marrow.[2-4] The etiological spectrum in children varies widely ranging from transient marrow viral suppression to marrow infiltration by hematological and non-hematological malignancies. The common causes of bicytopenia are acute leukemia, idiopathic thrombocytopenic purpura, megaloblastic anemia and aplastic anemia and the common causes of pancytopenia are megaloblastic anemia, aplastic anemia and acute leukemia.[5] Clinically, anemia leads to fatigue, breathlessness and cardiac symptoms. Thrombocytopenia leads to bruising and mucosal bleeding and leucopenia leads to increased susceptibility to infections.[6] Peripheral smear studies and other complementary laboratory investigations aid in the diagnosis. A valuable and conclusive way of diagnosing and analysing hematologic and metastatic neoplasms as well as non-hematological diseases causing cytopenia is

bone marrow examination. Depending upon the etiology, bone marrow finding may vary from hypocellular as in aplastic anemia to normocellular with non-specific changes or hypercellular being replaced entirely by malignant cells.[7]

There is limited published literature describing bicytopenia and pancytopenia in children presenting to tertiary level hospitals from India. The present study was undertaken to find the clinico aetiological profile of bicytopenia and pancytopenia among pediatric patients in a tertiary care hospital located in Southern India.

METHODS

This cross-sectional study was conducted at the Department of Pediatrics of a tertiary care teaching hospital located in Vijayapura, Karnataka, over a period of 18 months from March 2024 to August 2025 after obtaining Ethical clearance from the Institutional Ethics Committee.

Inclusion criteria

Children aged 1 month to 12 years with previously undiagnosed bicytopenia and pancytopenia were included in the study.

Exclusion criteria

Children less than 1 month of age or more than 12 years of age, those diagnosed with aplastic anemia or leukemia, and individuals with a history of recent blood transfusion were excluded from the study.

Children with suppression of any two of the cell lines were categorized as bicytopenia and suppression of all three as pancytopenia. The cut-off taken to define cell line suppression were-hemoglobin <10 g/dl, total leukocyte count (TLC) <4×109/l and platelet count <150×109/l. After obtaining written informed consent from the parents or caregivers of children, basic patient information such as name, age, sex and demographic parameters along with a detailed clinical history for fever, pallor, Fatigue, skin rash, mucosal bleeds like epistaxis, gum bleed, melena and hematemesis were obtained on a predesigned proforma. A clinical examination was performed for the detection of pallor, jaundice, rash, hepatosplenomegaly, lymphadenopathy, bony tenderness, petechiae, purpura and joint swelling. A venous blood sample was obtained in all children under aseptic precautions. A complete hemogram including hemoglobin, TLC, platelet count, red cell indices, retic count and peripheral smear was done in all children by a designated pathologist who examined peripheral smears of all the patients. The following investigations were considered depending on the clinical presentations and hemogram findings- serum iron, serum folate level, serum B12 levels, serum ferritin levels, typhi-dot, Widal test, dengue serology (NS1 Ag and IgM ELISA), ELISA scrub typhus, Coombs test, blood culture, bone marrow examination, kidney function test, liver function test, prothrombin time, APTT, gene Xpert for M. tuberculosis, PS for malaria, HBsAg and HIV. The data was processed and analysed using Microsoft Excel software SPSS V.30. Categorical variables were summarized using frequency and percentage.

RESULTS

Out of 110 children, 68 (61.8%) had bicytopenia, and 42 (38.1%) had pancytopenia, with a male predominance observed in both groups.

Table 1: Demographic characteristics of children with bicytopenia and pancytopenia.

Demographic data		Bicytopenia (n=68) N (%)	Pancytopenia (n=42) N (%)
Gender	Male	38 (55.9)	22 (52.3)
	Female	30 (44.1)	20 (47.6)
Age group	1-12 months	12 (17.6)	8 (19)
	1-5 years	24 (35.2)	12(28.5)
	6-12 years	32 (47)	22(52.3)

Overall, 60 (54.5%) were males, and 50 (45.4%) were females, resulting in a male-to-female ratio of 1.2:1 as depicted in table 1, whereas that in bicytopenia and pancytopenia it was 1.26:1 and 1.1:1, respectively. It was observed that in both groups the majority of children were more than 5 years of age. In cases of bicytopenia 32 out of 68 (47%) and in cases of pancytopenia 22 out of 42 (52.38%) were more than 5 years of age. Both bicytopenia and pancytopenia presented with fever as the most common presenting symptom seen in 60 (88.2%) and 37 (88%) cases followed by fatigue in 32 (76.1%) and 28 (41.1%) cases respectively. Notably, bleeding manifestations were significantly more frequent in children with pancytopenia.

The commonest clinical signs observed in case of bicytopenia was pallor seen in 57(83.8 %) cases, followed by hepatomegaly 32(47%), splenomegaly 30 (44.1%), petechiae 20 (29.4%) and lymphadenopathy 12(17.6%). All 42 (100%) children with pancytopenia had pallor.

Other findings were splenomegaly 27 (64.2%), hepatomegaly 25 (59.5%), lymphadenopathy 16 (38%) and hyperpigmented knuckles 16 (38%) (Table 2). Anemia with thrombocytopenia 35 (41%) was the most common cytopenic profile in bicytopenia, followed by anemia with leukopenia 21 (30.8%) and leukopenia with thrombocytopenia 12 (17.6%) as shown in (Table 3). Among the 110 cases studied, 99 had non-malignant causes. Out of 68 cases of bicytopenia, 63 (94.11%) had a

non-malignant etiology. Among 42 cases of pancytopenia, 36 (85.71%) were non-malignant causes. It shows that malignancy is not a common cause of bicytopenia and pancytopenia in children. For the entire group with cytopenia, the etiologies noted were infections 48 (43.6%), followed nutritional anemia 43 (39%) and leukemia 11 (10%).

Table 2: Frequency of symptoms and signs observed in cases with bicytopenia and pancytopenia.

Clinical manifestations		Bicytopenia (n=68) N (%)	Pancytopenia (n=42) N (%)
Symptoms	Fever	60 (88.2)	37 (88)
	Bleeding manifestation	23 (33.8)	25 (59.5)
	Fatigue	28 (41.1)	32 (76.1)
	Pain abdomen	18 (26.4)	15 (35.7)
	Bone and joint pain	8 (11.7)	7 (16.6)
	Weight loss	22 (32.3)	18 (42.8)
Signs	Pallor	57 (83.8)	42 (100)
	Hepatomegaly	32 (47)	25 (59.5)
	Splenomegaly	30 (44.1)	27 (64.2)
	Lymphadenopathy	12 (17.6)	16 (38)
	Jaundice	2 (2.9)	1 (2.3)
	Bone tenderness	8 (11.7)	9 (21.4)
	Hyperpigmented knuckle	9 (13.2)	16 (38)
	Petechiae and purpura	20 (29.4)	15 (35.7)

Table 3: Distribution of type of cytopenia (n=110).

Type of cytopenia	Definition	Number	Percentage (%)
Bicytopenia	Anaemia+thrombocytopenia	35	51.47
	Anaemia+leukopenia	21	30.88
	Leukopenia+thrombocytopenia	12	17.64
Pancytopenia	Anemia+leukopenia+thrombocytopenia	42	38.18

Megaloblastic anemia was the most common cause of pancytopenia present in 17 (40.4%) of cases. Infections were the second most common cause in pancytopenia, with 16 (38%) cases, followed by leukemia 6 (14.2%), aplastic anemia 2 (4.7%) and CLD with PHTN 1 (2.3%).

Table 4: Etiological profile of children with bicytopenia.

Causes	Bicytopenia (n=68) N (%)
Iron deficiency anaemia	12 (17.6)
Megaloblastic anaemia	9 (13.2)
Mixed nutritional anaemia	5 (7.3)
Dengue	9 (13.2)
Sepsis	9 (13.2)
Enteric fever	8 (11.7)
Scrub typhus	6 (8.8)
Leukaemia	5 (ALL=3 and AML=2) (7.3)
Thalassemia with hypersplenism	3(4.4)
ITP	2 (2.9)

In this study infectious causes of pancytopenia were, sepsis 8 (19%), scrub typhus 3 (7.1%), dengue 3 (7.1%), falciparum malaria and miliary tuberculosis 1 (2.3%) each. The commonest cause of Bicytopenia was infection 32 (47%), followed by nutritional anemia (iron deficiency, megaloblastic, mixed nutritional seen in 26 out of 68 (38.2%), leukemia 5 (7.35%), thalassemia with hypersplenism 3 (4.4%) and immune thrombocytopenic purpura 2 (2.9%).

Of the 99 non-malignant cases, 48 (43.6%) were infectious in origin. Sepsis was the commonest infectious cause of bicytopenia and pancytopenia comprising 17 (15.4%) cases.

Table 5: Etiological profile of children with pancytopenia.

Causes	Pancytopenia (n=42) N (%)
Megaloblastic	17 (40.4)
Sepsis	8 (19)
Leukaemia	6 (ALL=5 and AML=1) (14.2)
Dengue fever	3 (7.1)
Scrub typhus	3 (7.1)
Aplastic	2 (4.7)
CLD with PHTN	1 (2.3)
Plasmodium malaria	1 (2.3)
Tuberculosis	1 (2.3)

Other common infectious causes of bicytopenia and pancytopenia included dengue fever 12 (10.9%), scrub typhus 9 (8.1%), enteric fever 8 (7.2%), malaria 1(0.9%) and military tuberculosis 1(0.9 %) altogether comprising 31 out of 48 cases. The non-malignant and malignant etiology of bicytopenia and pancytopenia has been summarized in (Table 4 and Table 5). Altogether there were 11 (10 %) cases of leukemia, acute lymphoblastic leukaemia consisted of the majority of cases, with 5 (4.54%) cases presenting with pancytopenia and 3 (2.72%) cases presenting with bicytopenia. Three (1.8 %) patients had acute myeloid leukaemia, Two (1.8%) presented with bicytopenia and one (0.9%) as pancytopenia.

Table 6: Diagnostic yield of bone marrow aspiration/ biopsy (n=21).

Bone marrow findings	No. of patients	Final diagnosis
Hypercellular marrow	11	ALL=8, AML=3
Erythroid hyperplasia	5	Megaloblastic anaemia
Hypocellular marrow	2	Aplastic anaemia
Normocellular	2	Normal
Megakaryocytic picture	1	ITP

On peripheral smear examination, circulating blasts were seen in all cases of leukaemia, after which a bone marrow aspiration study was done along with special stains such as MPO and PAS stain to differentiate between ALL and AML. Bone marrow aspiration was done in 23 cases. Bone marrow examination revealed hypercellularity with malignant infiltration in 11 (10%) cases, out of this 8 had acute lymphoblastic leukaemia and 3 had acute myeloid leukaemia, 5 (4.5%) cases showed erythroid hyperplasia consistent with megaloblastic anemia, hypocellular marrow was observed in both cases of aplastic anemia. One (0.9%) patient showed a megakaryocytic picture consistent with idiopathic thrombocytopenic purpura. One (0.9%) case with aspiration showed iron-deficient anaemia and 2 (1.8%) children had normocellular marrow (Table 6).

DISCUSSION

In our study it was seen that males were 60 (54.54%) and outnumbered females 50 (45.45%). Similar finding was reported by Sharif et al, in which males were (53.3%), and females were (46.7%).[8] The age group most commonly affected in our study was 6-12 years of age (51.61%), followed by 1-5 years of age (38.70%). A possible explanation can be that infection was the most common etiology of cytopenia in our study. Similar to our study, Sharif et al and Yalaki et al has observed that children more than 5 years of age were most commonly affected (39%).[8,9] Bhatnagar et al, found median age to be 6 years.[10] In contrast , a study conducted by Rathod et al, it was seen that 6 months to 6 years were most commonly affected (39%), followed by 7 to 10 years of age (34%).[11] Singh et al, observed that most of patients belonged to age group of 1-5 years (51.6%).[12] Our study has noted that Bicytopenia 68 (61.81%) was more common than pancytopenia 42 (38.18 %) in these patients. Similar findings were noted by Sharif et al, in which bicytopenia was seen in (62.9%) and pancytopenia in (37.1%).[8] similar findings were also noted by Naseem et al in their study that 69.4% children had bicytopenia and 30.6% had pancytopenia.[7] In contrast a study done by Bhatnagar et al, found that majority 54.5% of patients had pancytopenia and 45.5% had bicytopenia.[12] Overall, fever (88.18%) was the most common symptom in our study, similar to other studies analysing the etiology of cytopenia Naseem et al, Vijayakrishnan et al.[7,13] Overall, most common sign noted was pallor (90%), followed by hepatosplenomegaly (51.81%). Similarly, many studies have revealed fever and pallor as the most common clinical feature among patients with bicytopenia /pancytopenia.[8,9] Our study observed that the most common cause for bicytopenia was infections (41.1%), followed by nutritional anemia (38.2%). Yalaki et al has noted that in bicytopenia patients the most common etiology was infection (64.2%), followed by ALL (14.2%).[11] This is contrary to the study done by Naseem et al, in which, the most common cause of bicytopenia was acute leukaemia.[7]

This was because that study was a retrospective study where records of children less than 12 years of age referred for bone marrow examination to a different institute were analysed. Among infectious causes of bicytopenia commonest etiology was dengue and sepsis (13.23 %) followed by enteric fever 8 (11.7%) and scrub typhus 6 (8.8%). Similar findings were noted in a study by Sharma A et al, sepsis causes pancytopenia through several mechanisms (marrow suppression, hypersplenism and consumptive coagulopathy), which usually act in combination.[14] Anemia with thrombocytopenia being the most common presentation among bicytopenia. Similar findings were seen in other studies where Sharma A et al and Vijayakrishnan et al.[13,14] Megaloblastic anemia (20%) followed by infections was the most common etiology of pancytopenia observed in our study. Similar to the studies done by, Rathod et al, Kumari et al, Bhatnagar et al and Chand et al.[9,15,10,16] But in contrast the etiological pattern noted for pancytopenia in children by various others authors were megaloblastic anaemia followed by aplastic anaemia.[9,17,18]

Among infectious causes of pancytopenia commonest etiology was sepsis 8 (19%) followed by dengue fever (7.1%) and scrub typhus (7.1%). Other less common etiology was malaria 1 (2.3%) and miliary TB 1 (2.3%). These findings were similar to study done by Sharma A et al, another study was done in India by Bhatnagar et al which showed that enteric fever was the commonest

etiology of pancytopenia among the infectious etiology.[10,14] Ineffective erythropoiesis, leucopoiesis and thrombopoiesis due to increased programmed cell death in absence of vitamin B12 or folic acid and decreased survival of precursors in peripheral blood are most commonly implicated in causing pancytopenia in megaloblastic anemia.[19,20] In this study, altogether there were only 11 (10%) cases of leukaemia. This is contrary to the study done by Naseem et al, in which, the most common cause of bicytopenia was acute leukaemia and the commonest etiology of pancytopenia was aplastic anemia.[7] It was seen that out of the 11 cases of hematological malignancy identified by bone marrow examination in our study, only 6 cases were picked up by peripheral smear examination. In a study done by Thiagarajan et al, it was seen that peripheral smear was able to pick up only 7 out of 11 cases of hematological malignancy.[21]

Limitations

Our study had several important limitations, such as the non-inclusion of socioeconomic and cultural parameters, which greatly affected the etiologies of cytopenia. This study included patients from a single center; a multicentric study from different hospitals would have enabled us to describe the prevalence of these etiologies in a precise manner. Another limitation of this study was that it was conducted over a limited period of time, which is not sufficient to predict the outcome in children with acute leukaemia and other chronic disorders. The comparison of hematological profiles in etiological groups was not done in this study. Investigations like viral antigen and antibody testing and genetic analysis for storage disorders were not done due to the economic constraints of the patients, so in a few cases, an etiological diagnosis could not be made.

CONCLUSION

Bicytopenia and pancytopenia is a common hematological problem encountered in pediatric clinical practice and should be suspected on clinical grounds when a child presents with unexplained anemia, prolonged fever and tendency to bleed. The etiological spectrum of cytopenia in children is varied. The causes range from infections including sepsis, dengue fever and enteric fever to serious illnesses including acute leukemia. This study demonstrated that most illnesses that cause bicytopenia and pancytopenia are curable and have a favourable prognosis, but unexplained cases should undergo bone marrow examination. So, whenever there is high index of clinical suspicion of hematological malignancy and peripheral smear is unable to pick up the findings, it is advisable to do bone marrow examination for timely diagnosis and prevent morbidity and mortality in vulnerable pediatric patients. Nonetheless, the results of our study necessitate dietary modification with iron and vitamin B12 supplementation in children in developing countries to prevent nutritional causes of cytopenia.

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