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CLINICO-ETIOLOGICAL PROFILE OF PERIPHERAL BICYTOPENIA AND PANCYTOPENIA IN CHILDREN DUE TO NON- MALIGNANT CAUSES: A PROSPECTIVE OBSERVATIONAL STUDY

Paediatric Medicine

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ABSTRACT

Background: Peripheral bicytopenia and pancytopenia in children are important hematological conditions that may arise from a wide variety of non-malignant causes. Early identification of etiology and clinical profile is essential for appropriate management and prognosis. Objectives: To evaluate the etiological profile of peripheral bicytopenia and pancytopenia in children due to non-malignant causes and to study their clinico-hematological profile. Methods: A prospective observational study was conducted in the Department of Pediatrics at a tertiary care teaching hospital in Surat, India. The study period was 15 months. A total of 121 children aged 6 months to 17 years diagnosed with peripheral bicytopenia or pancytopenia due to non-malignant causes were included. Detailed clinical history, physical examination, and laboratory investigations including complete hemogram, peripheral smear, viral markers, liver function tests, reticulocyte count, and bone marrow examination when indicated were performed. Results: Among the121patients included in the study, 78(64.4%) had bicytopenia and 43 (35.6%) had pancytopenia.The prevalence of bicytopenia and pancytopenia among non-malignant cases in the institute was 9.8%. Clinical features commonly observed included fever, pallor, bleeding manifestations, and hepatosplenomegaly. Laboratory investigations and etiological evaluation revealed that nutritional deficiencies, infections, and bone marrow suppression were among the most common non-malignant causes.Conclusion: Peripheral bicytopenia and pancytopenia in children are frequently associated with treatable non-malignant conditions. Careful clinical evaluation and appropriate hematological investigations help in early diagnosis and management, thereby reducing morbidity and mortality.

KEYWORDS

Peripheral Bicytopenia, Pancytopenia, Leukopenia, Anemia, Thrombocytopenia.

INTRODUCTION

Peripheral pancytopenia is defined as reduction in the cellular elements of blood, i.e. leukocytes, erythrocytes and platelets [1]. Peripheral bicytopenia is reduction in any of the two cell lines[2,3]. It has been observed in the Indian scenario that megaloblastosis (vitamin B12 and/or folate deficiency) is the commonest cause of pancytopenia [4-6]. According to etiology, degree and duration of impairment, clinically these can lead to fever, pallor, infection or serious illness and death. Knowing the exact etiology is important for specific treatment and prognostication [6]. However, major diagnostic problems occur when there are no specific features in the blood to suggest the diagnosis or when the clinical features are not sufficiently specific to point out the cause.

Materials and Methods

Study Design: Prospective observational study.
Study Setting: Pediatric department of a tertiary care teaching hospital in Surat, India.

Study Period: 15months.
Sample Size: The study included 121 children.

Inclusion Criteria: Children aged 6 months to 17 years diagnosed with peripheral bicytopenia or pancytopenias due to non-malignant causes were included in the study.

Exclusion Criteria: Patients with known hematological malignancy, patients receiving chemotherapy or radiotherapy, and patients not fulfilling inclusion criteria or lost to follow-up were excluded.

Data Collection: Detailed clinical history, physical examination findings, and laboratory investigations were recorded. Investigations included complete blood count using an automated hematology analyzer, peripheral smear examination, ESR, C-reactive protein, viral markers such as dengue and hepatitis, liver function tests, reticulocyte count and bone marrow examination where required.

Result:

During the study period of 15 months, 121 patients between 6 months to 17 years of age having peripheral bicytopenia or pancytopenia due to non-malignant causes were included. Prevalence of patients with peripheral bicytopenia and pancytopenia among the non-malignant cases in our institute was 9.8%. Of the 121 children 78 (64.4 %) had bicytopenia and 43 (35.6%) had pancytopenia.

TABLE 1 : GENDER DISTRIBUTION IN BICYTOPENIA AND PANCYTOPENA

PARAMETER	MALE	FEMALE	TOTAL	P VALUE
BICYTOPENIA	42 (53.8%)	36 (46.2%)	78	O.3415
PANCYTOPENIA	27 (62.7 %)	16 (37.3%)	43	
TOTAL	69 (57.0%)	52 (42.9%)	121	

TABLE 2 : COMPARISION OF AGE DISTRIBUTION AMONGST THE INFECTIOUS AND NON INFECTIOUS CAUSES OF BICYTOPENIA AND PANCYTOPENIA

Age group	Infectious		Non infectious		Total (n=121)
	BICYTOPENIA	PANCYTOPENIA	BICYTOPENIA	PANCYTOPENIA	
6 month-1 year	04	-	04	04	12
>1-5 year	08	07	01	07	23
>5-10 year	13	07	02	05	27
>10-17 year	45	04	01	09	59
Total	70	18	08	25	121

Maximum patients with infectious etiology were found in bicytopenia group. Whereas maximum patients with non-infectious etiology were found in pancytopenia group.

CHART:1 PERIPHERAL BLOOD FINDINGS IN CHILDREN WITH BICYTOPENIA

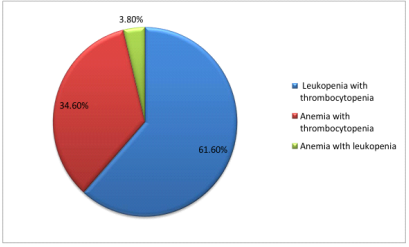


TABLE 3: COMPARISION OF PRESENTING SYMPTOMS IN BICYTOPENIA AND PANCYTOPENIA

PRESENTING SYMPTOMS	TOTAL (121)	BICYTOPENIA (n=78)	PANCYTOPENIA (n=43)	P VALUE
1) Fever	103 (85.1%)	68 (87.1%)	35 (81.4%)	0.2472
2) Abdominal pain	29 (24%)	19 (24.3%)	10 (23.3%)	0.8676
3) Vomiting	50 (41.2%)	30 (38.4%)	20 (46.5%)	0.2517
4) Bleeding manifestation	**27 (22.3%)**	**10 (12.82%)**	**17 (39.53%)**	<0.0001
a) Petechial rashes	09 (7.4%)	02 (2.6%)	07 (16.3%)	
b) Hematemesis	01 (0.8%)	-	01 (2.3%)	
c) Melena	04 (3.3%)	03 (3.8%)	01 (2.3%)	
d) Bleeding gums	05 (4.1%)	02 (2.6%)	03 (7.1%)	
e) Epistaxis	08 (6.6%)	03 (3.8%)	05 (11.6%)	
5) Leg pain	22 (18.18%)	08 (10.3%)	14 (32.6%)	0.0001
6) Jaundice	03 (2.47%)	02 (2.6%)	01 (2.3%)	0.6056
7) Loss of appetite	41 (33.8%)	21 (26.9%)	20 (46.5%)	0.0032
8) Abdominal distension	09 (7.4%)	05 (6.4%)	04 (9.3%)	0.3452
9) Body ache	47 (38.8%)	25 (32.1%)	22 (28.2%)	0.5371
10) Loose stool	12 (9.9%)	08 (10.3%)	04 (9.3%)	0.8094

Out of total 121 patients, 103 patients presented with fever followed by vomiting in 50 patients and body ache in 47 patients.

The main presenting symptoms in bicytopenia patients was fever in 68 (87.1%) patients, followed by vomiting 30 (38.4%) and abdominal pain 19 (24.3%) . Other common symptoms were body ache , loss of appetite , joint pain, abdominal distension and petechial rashes.

The main presenting symptom in pancytopenia was fever in 35 (81.4%) cases followed by vomiting 20 (46.5%) and leg pain 14 (32.6%). Other common 63 symptoms consisted of bleeding manifestation , appetite and abdominal pain and distension . Bleeding tendency, leg pain and loss of appetite was present in more patients with pancytopenia than bicytopenia and this difference is statistically significant. Out of total 27 patients with bleeding manifestations, 17 were from pancytopenia group.

CHART:2 FREQUENCY OF SYMPTOMS IN BICYTOPENIA

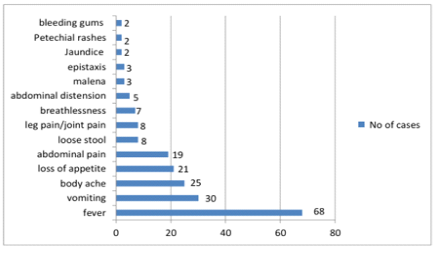


CHART:3 FREQUENCY OF SYMPTOMS IN PANCYTOPENIA

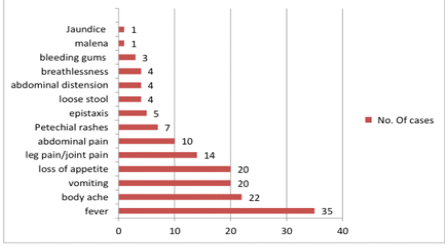
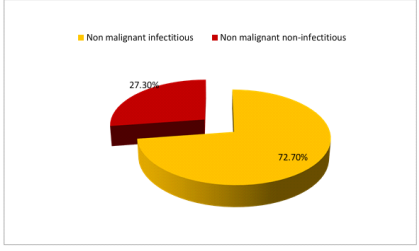


CHART: 4 ETIOLOGICAL PROFILE OF BICYTOPENIA AND PANCYTOPENIA PATIENTS



In our study, all patients with infectious etiology had acute infection.

None of them had chronic etiologies. The non-malignant infectious causes were significantly more in bicytopenia (89.74%) compared to pancytopenia (41.46%). Most common infectious cause of bicytopenia was dengue fever (56.4%) as Surat is endemic for dengue fever followed by malaria (15.4%). The most common infectious causes of pancytopenia were septicaemia (13.9%) and dengue fever (13.9%).

However non-malignant non-infectious etiologies were significantly more in pancytopenia group (58.14%) compared to bicytopenia group (10.26%). Most common cause of non-malignant non-infectious cause of bicytopenia was severe acute malnutrition (5.1%) and of pancytopenia was megaloblastic anaemia (23.2%) followed by hypersplenism (18.6%). In patients with nutritional causes, 1 patient with bicytopenia was having iron deficiency anaemia and 10 patients with pancytopenia were having Megaloblastic Anemia.

TABLE 4: ETIOLOGICAL PROFILE OF BICYTOPENIA AND PANCYTOPENIA

ETIOLOGY	TOTAL	BICYTOPENIA (n=78)	PANCYTOPENIA (n=43)	P VALUE
INFECTIOUS (TOTAL)	**88 (72.7%)**	**70 (89.74%)**	**18 (41.86%)**	**<0.0001**
Dengue fever	50 (41.3%)	44 (56.4%)	06 (13.9%)	
Septicaemia	8 (6.6%)	02 (2.6%)	06 (13.9%)	
Enteric fever	7 (5.8%)	06 (7.7 %)	01 (2.3%)	
Malaria	17 (14.0%)	12 (15.4%)	05 (11.6%)	
AGE	6 (4.9%)	06 (7.7%)	-	
NONINFECTIOUS (TOTAL)	**33 (27.3%)**	**08 (10.26%)**	**25 (58.14%)**	**<0.0001**
Aplastic anaemia	3 (2.5%)	-	03 (6.9%)	
Chronic liver disease	1 (0.8%)	01 (2.3%)	-	
Hereditary spherocytosis	1 (0.8%)	-	01 (2.3%)	
Nutritional	11 (9.1%)	01 (2.3%)	10 (23.2%)	
SAM	5 (4.1%)	04 (5.1%)	01 (2.3%)	
Hypersplenism	8 (6.6%)	-	08 (18.6%)	
Homocystinuria	1 (0.8%)	01 (2.3%)	-	
Hypothyroidism	1 (0.8%)	01 (2.3%)	-	
Sickle cell anaemia (n=2)		-	02 (4.7%)	

TABLE 5: OUTCOME IN CHILDREN WITH BICYTOPENIA AND PANCYTOPENIA

OUTCOME	BICYTOPENIA (n=78)	PANCYTOPENIA (n=43)	TOTAL (n=121)	P VALUE
Death	00	03 (6.98%)	03 (2.48%)	0.0129
Recovered	76 (98.72%)	29 (67.44%)	105 (86.78%)	
On treatment and follow up	02 (1.28%)	11 (25.58%)	13 (10.74%)	
Total	78 (100%)	43(100%)	121 (100%)	

Of the total 121 cases, 105 (86.78%) children recovered and 3 (2.48%) cases died. 13 (10.74%) cases were undergoing treatment .Among these 13 patients, 8 patients with thalassemia were discharged after blood transfusion, vaccination advice and routine growth monitoring; 3 patients with aplastic anaemia were discharged after symptomatic treatment, blood products and continued medications. 1 patient with hypothyroidism was discharged after starting treatment of hypothyroidism and follow up protocol was explained. 1 patient with hereditary spherocytosis was discharged after splenectomy.

Since outcome in children with bicytopenia and pancytopenia depends on the etiology, among these 13 patients, 10 patients recovered completely on follow up but 3 patients with aplastic anaemia were still on treatment and regular follow up.

More subacute and chronic etiologies were found in pancytopenia group compared to bicytopenia. As discussed previously, the common infectious conditions causing bicytopenia were dengue fever 44 (56.4%), malaria 12 (15.4%) septicaemia 02(2.6%) and enteric fever 6 (7.7%). Of the total 50 cases of dengue fever, 49 cases recovered completely and 1 case died due to refractory shock, uncontrolled GI bleeding. 69 Of the total 8 cases of septicaemia, 2 (25%) cases died during treatment and 4(75%) cases recovered after treatment. The cause of death in septicaemia was shock and disseminated intravascular coagulation.

DISCUSSION:

In the present study, it was observed that 78 patients had bicytopenia, of which 53.8% patients were male and male to female ratio was 7:6. There is slight male predominance in children with bicytopenia in our

study. This result is similar to the study done by Zahide et Al[8].In our study, out of all the children admitted with bicytopenia, 61.6% had leukopenia with thrombocytopenia and 34.6% had anaemia and thrombocytopenia while only 3.8% had anaemia with leukopenia. So leukopenia with thrombocytopenia was the most common type of bicytopenia observed in the present study.

In the study conducted by Shano naseem et al, anaemia with thrombocytopenia was the most common type of bicytopenia observed. The reason for this disparity could be due to difference in the epidemiology of both the studies[2]. Study conducted by Shano Naseem et at was in northern India, while present study was conducted in south Gujarat. In present study 39.7% patients had anaemia, 67.9% patients had leukopenia and 96.1% patients had thrombocytopenia. While in Zahide Yalaki study, 85.7% patients had leukopenia, 57.1% patients had anaemia and 71.4% patients had thrombocytopenia[8].

In present study, 58% cases of pancytopenia were due to non-malignant non infectious etiology while 41.9% were due to non-malignant infectious etiology. In present study the common causes of pancytopenia were megaloblastic anaemia (23.2%), hypersplenism (18.6%), dengue fever (13.9%) and septicaemia (13.9%). In present study, the common infections causing pancytopenia were septicaemia and dengue fever followed by malaria. The common non-infectious conditions causing pancytopenia were megaloblastic anaemia (23.2%) followed by hypersplenism (18.6%) , aplastic anaemia (6.9%) and hereditary spherocytosis (2.3%).

Many studies have been conducted in various parts of the world to study pancytopenia and each study found different underlying etiology for pancytopenia. Shano Naseem et al, from India in their study , found that aplastic anemia was the most common etiology for pancytopenia. In present study also aplastic anemia is the 3rd most common non-malignant non-infectious etiology for pancytopenia. Bhatnagar et al, from India in their study, found that megaloblastic anemia was the most common etiology for pancytopenia, followed by infections and aplastic anaemia. They found that enteric fever was the commonest infectious cause for pancytopenia. Most common cause of pancytopenia in present study is also megaloblastic anaemia followed by hypersplenism and infection.

Gupta et al, from India in their study, found that aplastic anaemia was the most common etiology for pancytopenia. They found infections as the third most common etiology for pancytopenia. Imbert et al, from France in their study, found that aplastic anaemia was the most common non-malignant etiology for pancytopenia. They found vitamin deficiency as the second most common non malignant etiology for pancytopenia Jha et al, from Nepal in their study, found that aplastic anaemia followed by megaloblastic anaemia were the common etiologies for pancytopenia
patients[9].

TABLE 6: COMPARISON OF ETIOLOGICAL SPECTRUM IN PATIENTS WITH PANCYTOPENIA

STUDY	Study population	Etiology	
		Non Malignant	Malignant
Present study(n=43)	Children	1) Megaloblastic anemia (23.2%) 2) Hypersplenism (18.6%) 3) Dengue fever (13.9%) 4) Septicemia (13.9%)	–
Shano Naseem et al (n=139)	Children	1) Aplastic anemia (33.8%) 2) Megaloblastic anemia (13.7%)	1) Acute leukemia (66.9%) 2) Juvenile myelomonocytic leukemia (1.7%)
Bhatnagar et al(n=109)	Children	1) Megaloblastic anemia (35.84%) 2) Aplastic anemia (20%)	1) Acute lymphoid leukemia (17.4%) 2) Myelodysplastic syndrome (2.8%)
Gupta et al (n=105)	Children	1) Megaloblastic anemia (37.9%) 2) Mixed nutritional deficiency anemia (16%)	1) Acute leukemia (12.43%) 2) Myelodysplastic syndrome (11.24%)
Imbert et al (n=213)	Adults	1) Aplastic anemia (10%) 2) Vitamin deficiency (7.5%)	1) Malignant myeloid disorder (42%) 2) Malignant lymphoid disorder (18%)
Jha et al (n=148)	Adults and children	1) Aplastic anemia (29%) 2) Megaloblastic anemia (23.6%)	1) Acute myeloid leukemia (13.5%) 2) Acute lymphoid leukemia (6.1%)

CONCLUSION:

Peripheral bicytopenia and pancytopenia in children are frequently associated with treatable non-malignant conditions. Before going for the investigations for the more chronic and serious conditions like malignancy, suspecting and managing acute infections according to local epidemiology should be part of the initial approach in patients with bicytopenia and pancytopenia. Careful clinical evaluation and appropriate hematological investigations help in early diagnosis and management, thereby reducing morbidity and mortality.

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