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ORIGINAL ARTICLE

Prevalence of Pancytopenia/ Bicytopenia in Pediatric Population and its Association with Etiology Based on Bone Marrow Findings

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ABSTRACT

Background: An important clinico-haematological condition known as pancytopenia or bicytopenia is brought on by a multitude of disease processes that either directly or indirectly affect the bone marrow.
Aim: To ascertain the prevalence of cytopenias in the pediatric population presenting to a tertiary care hospital in Rawalpindi and its correlation with age and gender distribution, clinical presentation, and aetiology**.**
Study Design: Descriptive cross-sectional study.
Methodology: It was a descriptive cross-sectional study carried out at Holy Family Hospital in Rawalpindi's hematology division. Using non-probability consecutive sampling, 253 individuals referred for bone marrow testing were included in the study, of which 108 patients had pancytopenia and 108 had bicytopenia. Data was gathered on the patient's mode of presentation, clinical examination, full blood counts, and bone marrow analysis. The data were analyzed using SPSS 22, and descriptive statistics were computed. Using chi-square test with a P value of 0.05 was taken as significant.
Results: Bicytopenia was discovered in (133)52.6% of patients and pancytopenia in (120)47.4% of patients. 139 (55%) of the 253 instances involved men, while 114 (45%) were women. Fever 225 (89%), bleeding symptoms 52 (20.5%), and bruising 36 (14.2%) were the most frequent presenting complaints. The most frequent result on examination was pallor234, which was followed by hepatomegaly118 (46.64%) and splenomegaly114 (45.05%). In the total blood count, bicytopenia (133), 52.6%, and pancytopenia (120), 47.4%, were the most common findings.
Practical Implication: There is scarcity of such data on paediatric patients, and to the best of our knowledge, no study has analysed the paediatric bicytopenic / pancytopenic patient in our centre. Thus present study was planned inorder to determine the prevalence of different etiology of bicytopenia /pancytopenia and its association with clinico-haematological parameters.
Conclusion: It was discovered that bicytopenia/pancytopenia was frequently the reason for bone marrow testing. Three common underlying etiologies acute leukaemia, megaloblastic anemia, and aplastic anemia were discovered.
Keywords: Cytopenias, Bone Marrow, Pediatric Population, Clinico-haematological Parameters and Prevalence.

INTRODUCTION

According to literature review, bicytopenia, and pancytopenia have a wide etiological spectrum in children, ranging from viral infections to malignancies.[1] However, there is limited data describing the clinic-etiological profile of bicyto-penia and pancytopenia in children in recent times. Need of an hour is to correlate and compare these abnormal cell findings with clinical findings in order to reach correct diagnosis. There is a considerable overlap between the causes of bicytopenia and pancytopenia. Bone marrow aspiration and biopsy become essential when the cause of bicytopenia and pancytopenia is not apparent from clinical history and examination. Bone marrow pictures may vary depending on etiology, from normocellular with nonspecific changes to hypercellular being replaced completely by malignant cells[2].

In our routine clinical practice, pancytopenia is a significant clinico-haematological phenomenon. Its clinical pattern, therapeutic options, and outcome exhibit varied tendencies. Pallor is a significant and frequently seen symptom in pediatric practice. On the one hand, it might be caused by a straightforward ailment like nutritional anemia, but on the other, it might be the early sign of a fatal illness like leukaemia[3].

When a patient presents with pallor, a blood complete picture is typically performed. This can reveal pancytopenia (Anemia, Thrombocytopenia, Leucopenia), or bicytopenia (If only two parameters from the entire blood count are low)[4].

In haematology, a bone marrow examination is a crucial diagnostic technique. The diagnosis and treatment of hematological and, to some extent, nonhematological problems are handled frequently in hospitals using this straightforward and generally safe approach[5-7]. A very useful test that is now crucial for the diagnosis of haemtological problems is the bone marrow examination. The care and prognosis of the patients depend on the extent of pancytopenia and the underlying pathology. Bicytopenia, which affects 396(40%) or pancytopenia, which affects 175(17.7%) of the 990 children in an Indian study done in 2011; the male to female ratio was 2.9:1[4].

There are few studies that have examined the pediatric bicytopenic/pancytopenic patient in our center, and there is a dearth of such information on pediatric patients. This study's goal is to identify the prevalence of various causes of bicytopenia and pancytopenia and their relationships to clinico-haematological variables.

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METHODOLOGY

It was a descriptive cross-sectional study carried out at the Holy Family Hospital in Rawalpindi's department of haematology. Using non-probability consecutive sampling, all patients younger than 12 years of age, of either gender, with two or more cytopenias on blood counts, were chosen. The study excluded all bone marrows deemed unfit for opinion and diagnosed cases of malignancy, including leukaemia receiving chemotherapy or radiotherapy.

Records of children under the age of 12 who were sent to the department of haematology for a bone marrow examination between 1 June 2020 and 31 May 2022 were downloaded and examined. Causes, clinical, and bone marrow findings were thoroughly reviewed. At the time of presentation, a thorough history, clinical examination, and hematological data were documented. Haemtological testing includes bone marrow aspiration and biopsy, total and differential leukocyte counts, platelet count, and haemoglobin. Using an automated haematology analyzer, blood counts were performed (Beckman coulter-LH-750). Peripheral blood smear analysis was used to corroborate the platelet counts reported by the counter. Haemoglobin levels below 10, total leukocyte counts below 4, and platelet counts above 100 are all considered to be cytopenia. According to the clinical recommendation, a trephine biopsy and bone marrow aspiration

were performed. Standard procedures were used to perform the bone marrow procedure and further staining. Hematoxylin and eosin and May-Grunwald Giemsa were used to stain all of the trephine biopsies and bone marrow aspirate smears, respectively. When necessary, aspirate smears can be stained specifically with Sudan black B, periodic acid Schiff, and Perl's stain.[6]

Statistical Analysis: IBM SPSS version 21 was used to enter and analyze the data. For categorical variables, frequencies and percentages were calculated at the descriptive analysis for things like age, gender, fever, pallor, bruises, bleeding, bone pain, splenomegaly, hepatomegaly, lymphadenopathy, cytopenias, and their underlying causes. Hemoglobin, WBCs, ANC, and platelets were considered continuous variables, and their means and standard deviations were computed. The clinical and etiological profile was compared with cytopenias (Bicytopenia/Pancytopenia) at a univariable analysis using the chi-square test. P 0.05 was regarded as significant.

RESULTS

Descriptive Analysis: 253 pediatric cytopenia patients with a 1:1 ratio of bicytopenia and pancytopenia participated in this study. Patients between the ages of 1 and 12 were included, with the majority of patients (43.1%) and 43% (43.1% and 14.2%, respectively) belonging to the age groups of 1 to 5 years and 6 to 12 years. More than half of those who were male 139(55%) had average haemoglobin levels of 7 g/dl, ANC levels of 2.2%, WBC levels of 15.4*109/L, and platelet levels of 725*109/L. Most of the patients (89%) had pallid skin tones (n=225), and 92.5% of them had fevers. Only a small percentage of individuals (n=36) suffered bruising, bleeding, bone discomfort, or lymphadenopathy. Moreover, we discovered that almost half of the patients had hepatomegaly 118(47%) and splenomegaly 114(45.1%). Leukemia acute (28.5%), In terms of the mechanism of cytopenias' causation, megaloblastic anemia (17.4%) and aplastic anemia (11.5%) were calculated as being prevalent (Table 1).

Table 1: Descriptive statistics of pediatric patients (n=253)

		n	%
Age	< 1year	36	14.2
	1-5 years	109	43.1
	6-12yeqrs	108	43
Gender	Male	139	55
	Female	114	45.1
Hb (g/dl)¥		7.0±2	
ANC (%)¥		2.2±3.1	
WBC (109/L)¥		15.4±38.5	
Platelets (109/L)¥		725±10748	
Fever	Yes	225	89
	No	28	11.1
Pallor	Yes	234	92.5
	No	19	7.5
Bruises	Yes	36	14.2
	No	217	86
Bleeding	Yes	52	21
	No	201	79.4
Bone pain	Yes	15	6
	No	238	94.1
Hepatomegaly	Yes	118	47
	No	135	53.4
Splenomegaly	Yes	114	45.1
	No	139	55
Lymph-adenopathy	Yes	50	20
	No	203	80.2
Cytopenia	Bicytopenia	133	53
	Pancytopenia	120	47.4
Etiology	Megaloblastic Anemia	44	17.4
	Aplastic Anemia	29	11.5
	Hemolytic Anemia	20	8
	Hypersplenism	17	7
	Storage disorder	8	32
	Visceral lishmenia	20	8
	Mixed Deficiency Anemia	7	3
	Others	36	14.2

Note: ¥mean ±SD, ANC= Absolute neutrophils counts, WBC= white blood cells, Hb= haemoglobin

Univariable Analysis: Cytopenias were substantially correlated with age (P-chi = 0.03); bicytopenia was more common in children aged 1 to 5 (47.3%), whereas pancytopenia was more common in children aged 6 to 12 (51%). On the other hand, patients under 1 year of age had a low prevalence of cytopenias (17.3% Bicytopenia and 11% Pancytopenia). Bicytopenia (87%) and Pancytopenia (72%) were considerably more common in those who had no bleeding symptoms (P-chi = 0.004) (Table 2).

Table 2: Comparison of Cytopenia with clinical characteristics

		Bicytopenia	pancytopenia	p- value
Age	< 1 year	23 (17.3)	13 (11%)	0.03‡
	1-5 years	63 (47.3%)	46 (38.3%)	
	6-12 years	47 (35.3%)	61 (51%)	
Gender	Male	67 (50.4%)	72 (60%)	0.12‡
	Female	66 (50%)	48 (40%)	
Fever	Yes	116 (87.2%)	109 (91%)	0.36‡
	No	17 (13%)	11 (9.2%)	
Pallor	Yes	124 (93.2%)	124 (93.2%)	0.63‡
	No	9 (7%)	10 (8.3%)	
Bruises	Yes	17 (13%)	19 (16%)	0.48‡
	No	116 (87.2%)	101 (84.2%)	
Bleeding	Yes	18 (14%)	34 (28.3%)	0.004‡
	No	115 (87%)	86 (72%)	
Bone pain	Yes	7 (5.3%)	8 (7%)	0.63‡
	No	126 (95%)	112 (93.3%)	
Hepato-megaly	Yes	62 (47%)	56 (47%)	0.99‡
	No	71 (53.4%)	64 (53%)	
Spleno-megaly	Yes	63 (47.4%)	63 (47.4%)	0.437‡
	No	70 (53%)	69 (58%)	
Lymph-adenopathy	Yes	23 (17.3%)	27 (23%)	0.29‡
	No	110 (83%)	93 (78%)	

Note: ‡ Chi-square test applied

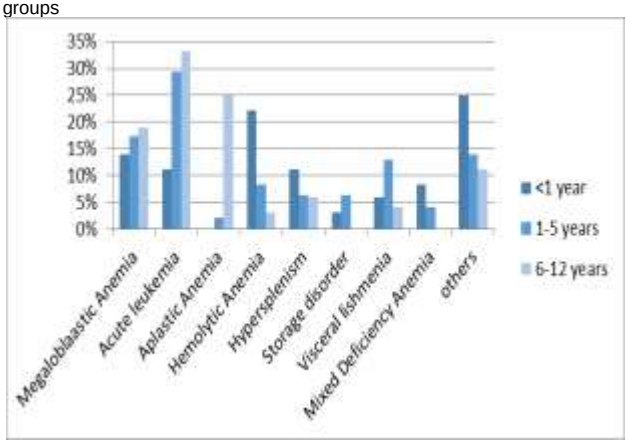
Bicytopenia and Pancytopenia with Etiology: In contrast, acute leukaemia had an almost identical ratio of bicytopenia (27%) and pancytopenia (30%), and aplastic anaemia was 19.2% higher in pancytopenia than in bicytopenia (5%). The significant association was evaluated in the manner of cytopenias' causation, and Megaloblastic Anaemia was higher (20%) in pancytopenia than in bicytopenia (15%) (Table 3)

Table 3: Comparison of Cytopenia with Etiology

	Bicytopenia	pancytopenia
Megaloblastic Anemia	20 (15%)	24 (20%)
Acute leukemia	36 (27%)	36 (30%)
Aplastic anemia	6 (5%)	23 (19.2%)
Hypersplenism	9 (7%)	8 (7%)
Storage disorder	6 (5%)	2 (2%)
Visceral lishmenia	10 (8%)	10 (8.3%)
Mixed deficiency anemia	5 (4%)	2 (2%)
Hemolytic anemia	15 (11.3%)	5 (4.2%)
Others	26 (20%)	10 (8.3%)

P value <0.001‡ Note: ‡Chi-square test applied

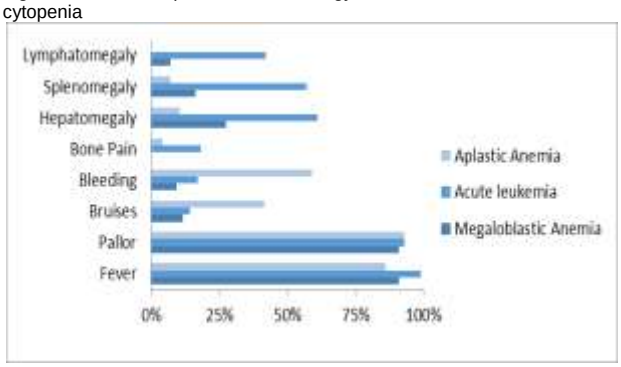
Figure 1: Relationship of Etiology of Cytopenia patients with different age groups



Etiology of cytopenias with different Age groups: Megaloblastic anaemia (19%), acute leukaemia (33.3%), and aplastic anaemia (25%) were found to be more prevalent in patients between the ages of 6 and 12 while hemolytic anaemia (22.2%) and hypersplenism (11.1%) were found to be more prevalent in patients under the age of one year old. This significant association was evaluated in terms of the causation of cytopenias with different age groups (P-chi = 0.001). (Figure 1).

Common Etiology of cytopenias with baseline characteristics: Megaloblastic anaemia (91% and 91%), acute leukaemia (99% and 93.1%), and aplastic anaemia (86%, 93.1%) all had high rates of fever and pallor skin tone. These associations were significant (P-chi = 0.006 and P-chi = 0.04, respectively). Aplastic Anemia patients frequently experienced bleeding and bruises (41.4% and 59%) with a correlation (P-chi = 0.001 and P-chi = 0.001 respectively). However there was a positive correlation between bone pain (18.1%), hepatomegaly (61.1%), splenomegaly (57%) and lymphatomegaly (42%) in acute leukaemia (P-chi = 0.001, 0.001, 0.001 and 0.001, respectively) (Figure 2).

Figure 2: Relationship of common Etiology with baseline characteristics of cytopenia



DISCUSSION

There aren't many studies analysing pancytopenic kids in the literature, and as far as we know, no information has been presented on the range of bicytopenia in kids in Rawalpindi. The referral-based structure of the patient group has also placed restrictions on the published studies on pancytopenia. The underlying aetiology of pancytopenia has been the subject of conflicting reports from around the globeas per literature review[8],

We examined the qualified individuals over the course of the five-year research period (0 months to 12 years patients). 400 patients in all were examined. Out of them, 253 patients' peripheral blood film reports and blood cp results revealed pancytopenia/bicytopenia.

Acute leukaemia was the most frequent cause among the 253 cases evaluated in our Centre, followed by megaloblastic anemia and aplastic anemia in terms of frequency. The most frequent clinical manifestations were hepatomegaly, pallor, and fever. On the other hand, in a study from Zimbabwe that included 134 individuals with pancytopenia, megaloblastic anemia was found to be the most common cause, followed by aplastic anemia and acute leukaemia[8,9s].

In contrast to our investigation, one researcher looked into 148 patients' causes of pancytopenia. In their investigation, hypoplastic bone marrow, which was present in 43 instances (29% of the total), megaloblastic anemia, 35 cases (23.6%), and haemtological malignancy, 32 cases (21.6%), were the most frequent causes of pancytopenia. The most frequent etiology mentioned by them10 was megaloblastic anemia (30.2%) in adults and hypoplastic bone marrow (38.1%) in children[10].

On the other hand, megaloblastic anemia was discovered by another researcher in a retrospective analysis of 109 pediatric patients with pancytopenia to be the most common etiological factor in 28.4% of cases11, followed by acute leukaemia, infections, and aplastic anemia[9,11]. In bone marrow aspiration research conducted in their pediatric unit, megaloblastic anemia was identified as the most common diagnosis and the main cause of bicytopenia and pancytopenia.

Similar studies were conducted on 105 pancytopenia-afflicted children between the ages of 1.5 and 18 months. Aplastic anemia (43% of cases) and acute leukaemia (25% of cases) were the most frequent causes of pancytopenia in their investigation. Infections, of which kala-azar was the most prevalent, were the third most frequent cause of pancytopenia. Similarly their cohort's most frequent presenting complaints were fever and increasing pallor (81.4%), followed by bleeding signs (72.9%).[12-14]

The typical haemtological parameters were found to be non-specific and to significantly overlap with the main causes of cytopenias. However, in individuals with megaloblastic anemia and leukaemia, the peripheral blood films were helpful in identifying the cause. In most cases of leukaemia and megaloblastic anemia, a bone marrow aspirate was found to be sufficient for diagnosis; however, a biopsy was necessary for the diagnosis of aplastic anemia[11].

Other causes of pancytopenia, such as visceral leishmaniasis, hemophagocytosis, storage disorders, and hemolytic anemia's, were also detected in this study in addition to the common causes of pancytopenia, such as acute leukaemia, megaloblastic anemia, and aplastic anemia. When analyzing cases of bicytopenia or pancytopenia, it is important to keep in mind the less prevalent causes of cytopenias as well. It is also crucial to underline the value of peripheral blood smear testing in cases of bicytopenia[12].

In our study, acute lymphoblastic leukaemia was the primary illness that led to bicytopenia in the majority of cases. Pediatric patients with this condition typically respond well to chemotherapy, therefore early detection is crucial. A practitioner should be aware of the underlying cause since it will help with the examination of children who have pancytopenia or bicytopenia in the future.

Limitations of study: This study was conducted only on a small size of population, therefore to generalize the results for larger groups, the study should be performed on a larger scale. Financial constrains and

CONCLUSION

Patients who were older than one year old were more likely to experience cytopenias. The majority of people had acute leukaemia, megaloblastic anemia, and aplastic anemia, which were contributing factors to pancytopenia. Furthermore, the prevalence of these typical causes of cytopenias was particularly high in individuals between the ages of 6 and 12. Regrettably, instead of cytopenias (Bicytopenia/Pancytopenia), we discovered a relationship between significant symptoms and prevalent causes of cytopenias.

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JA&ZS: Statistics application, analysis literature review, help in write up, **SD&MI:** Literature review help in write-up'
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