TO DETERMINE THE ETIOLOGY AND FREQUENCY OF PANCYTOPENIA IN PEDIATRIC POPULATION AND COMPARE IT WITH OTHER STUDIES

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ABSTRACT

Background: Peripheral pancytopenia is not a disease by itself; rather it describes simultaneous presence of anemia, leucopenia and thrombocytopenia resulting from a number of disease processes[1]. Only a few systemic studies have been published on the topic of pancytopenia, although extensive studies have been done for its different etiological factors like aplastic anemia, megaloblastic anemia, leukemia etc.

Thus this study was carried out to find out the frequency of different causes of pancytopenia and to compare the findings with those of other similar studies from this part of the world and worldwide.

Objective: To determine the etiology of pancytopenia on the basis of bone marrow examination in children from 1 month to 15 years.

Materials and Methods: This study was conducted in the department of Paediatrics, Hayatabad Medical Complex, Peshawar. it was an observational study. The study period started from January 2015 and ended on December 2015. All patient aged 1 month to 15 years having pancytopenia on peripheral smear were included. Patients beyond this age limits, already diagnosed cases, history of blood transfusion, patients on chemotherapy were excluded from the study. History, physical and systemic examination and haemotological parameters at presentation were recorded. Haemotological profile included peripheral smear and bone marrow aspiration/ biopsy.

Result: During the study period, out of 5,946 admission in the Paediatric Department of Hayatabad Medical Complex, 150 patients had pancytopenia on their peripheral blood smear (2.52%). Male to female ratio was 1.5: 1 and the nationalities were Pakistani (60%) and Afghani (40%). The most common etiology was acute leukemia (26.65%), followed by megaloblastic anemia (16.60%), aplastic anemia (13.20%), sepsis (8.00 %), Malaria (10.6 %), storage disorder Gaucher disease (6%) and ITP (4%). A few cases of leishminiasis were also diagnosed. Clinical presentations were pallor,fever, hemorrhages and hepatosplenomegaly.

Conclusion: Variation in etiology of pancytopenia is not only appreciated in different countries but also in different regions of a single country. Hence documentation of variation in the etiology of pancytopenia has an important role in formulating a comprehensive diagnostic and therapeutic strategies, unique to pancytopenic patients of a particular region.

INTRODUCTION

Pancytopenia is defined as the decrease in number of all the three formed elements of the blood and is a triad of findings that result from a number of disease processes. Etiological spectrum in paediatric population ranges from common condition like iron deficiency anemia to relatively rare congenital disorders like Fanconi's anemia.

A child presenting with pancytopenia should be evaluated for a possibility of acute leukemia and Aplastic anemia when associated with lymphadenopathy or visceromegaly. A child who is malnourished and presents with pancytopenia should be evaluated for megaloblastic anemia. Infections such as Bacterial sepsis, Malaria and leishmeniasis are other possible cause of pancytopenia, particularly in patient who presents with fever. Bone marrow examination is one of the most frequently done procedure in the Paediatric unit.

Though an invasive procedure, it can be easily performed even in the presence of severe thrombocytopenia with little or no risk of bleeding. Trephine biopsy is usually done when there is hypoplasia or aplasia on aspiration.

MATERAILS AND METHODS

This study was conducted in the department of Paediatrics Hayatabad Medical Complex Peshawar, on 150 cases who presented to this department with pancytopenia from January 2015 to December 2016.

All patients aged 1 month to 15 years, who had Pancytopenia on peripheral blood smear, and

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attendants consented for admission and bone marrow examination were included in the study.

The exclusion criteria were, patients beyond this age limits, diagnosed cases of aplastic anemia and leukemia, history of blood transfusion in the recent part, and those who were not willing for admission or for bone marrow examination. Pancytopenia was defined as hemoglobin (Hb) < 10 gm%, absolute neutrophil count (ANC) $<1.5 \times 10^9$ / L, platelets count $<100 \times 10^9$ / L. The patients who fulfilled the inclusion criteria were admitted in the ward and their detailed history was taken after obtaining consent from their parents.

A thorough physical and systemic examination was conducted and all the clinical data was collected on the study proforma. Laboratory investigation done in all patients included complete blood count {Hb, total leukocyte count, differential leukocyte count (DLC) platelet count, reticulocyte count and ANC}, peripheral blood smear and bone marrow examination. Bone marrow biopsy was performed whenever aspiration was inconclusive. Other investigation that were performed in selected cases were peripheral smear for malarial parasite, blood culture in suspected case of septicemia. Data was expressed in percentage.

RESULTS

One hundred and fifty patients with pancytopenia on their peripheral blood smear made a frequency of 2.52% out of the total admission of 5,946 during the study period. Out of these 150 cases, there were 90 (60.00%) male and 60(40.00%) female patients with male to female ratio of 1.5:1. Most cases were in between 5-12 years age group (n=80, 53.33%), while 70 (46.66%) were between 1 month to 4 years.

The most common etiology of pancytopenia in this study was acute leukemia (26.6%). Acute lymphoblastic leukemia (ALL-L1) accounts for (19.66%,) while acute myeloid leukemia M_2 and M_3 account for (7.66%). Lymphoma accounts for only 1.3% of the total cases. Out of the non-malignant condition, Megaloblastic anemia was on the top; accounting for (16.66%), followed by Aplastic anemia (13.33%). Infective condition like malaria including both falciparum and vivax accounts for (10.00%) and bacterial sepsis accounts for (8.6%) of the total cases.

Storage disorder like Gauchers disease was also diagnosed on the basis of bone marrow and made (6.00%) of the total case which is the highest cases disgnosed in this study when compared with other native studies from the same area. Congenital pancytopenia, Anemia of chronic disorder, idnopathic thrombocytopenia, Haemophagocytosis, Chediack-Highashi syndrome, and Viscual leshminas were also diagnosed on bone marrow examination in this study.

Majority of these patients presented with anemia, bleeding tendendencies and fever. Children with malignancies had varying degree of hepatosplenomegaly and lymphadenopathy. Children with megaloblastic anemia had different grade of malnutrition. Grade III malnutrition kwashiorkor and marasmus was present in 72.00% while grade II and I malnutrition was present in 28.13%.

DISCUSSION

Etiological spectrum of pancytopenia n=150

Disease	No of Cases	Percentage
NON-MALIGNANT CAUSES		
Megaloblastic Anemia	25	16.6%
Aplastic Anemia	20	13.33
Malaria (falciparum/ vivax)	15	10.00%
Bacterial Sepsis	13	8.66%
Gauchers Disease (Storage disorder)	9	6%
Idiopathic thrombocytopenic purpura	7	4.66%
Congenital Pancytopenia	6	4%
Visceral Leshminiasis	2	1.33%
Chediack higashi syndrome	1	0.60
No cause identified	10	6.66%
MALIGNANT ETIOLOGY		
Acute lymphoblastic leukemia	40	26.637
Lympho	02	1.33

Comparison of frequencies of etiology of Pancytopenia of different studies conducted in Pakistan with the present study

Etiology	Shazia Memon et al N=230	Muddassar Sharif N=105	Present study N=150
Megaloblastic anemia	13.04%	44.9%	16.66%
Aplastic anemia	23.9%	13.3%	13.33%
Malaria	8.69%	19.0%	10%
Bacterial infection/ enteric fever	10.8%	-	8.66%
Acute leukemia	8.69%	10.5%	26.63%
ITP	-	5.7%	4.66%
Visceral leishminiasis	-	1.9%	1.33%
Guchers disease	-	2.9%	6%
Iron deficiency anemia	8.69%	1.9%	-
Lymphoma	2.17%	1.9%	1.33%
Thalassemia	-	1.0%	-

Pancytopenia is a common finding in Paediatric admitted patient, which require proper evaluation and treatment. Bone marrow examination is one of the most important investigation to diagnose these patients[2]. In our study one hundred and fifty patient presented with pancytopenia and 140 (93.44%) patients were diagnosed on bone marrow examination and trephine biopsy, showing a very high diagnostic yield for pancytopenia.

Pudasaini et al[3] and Bashawri[4] et al reported pancytopenia as the commonest indication for bone marrow examination in Paediatric patients. While Damulak[5] et al reported anemia as a common indication for bone marrow examination in pediatric patients.

In this study the frequency of pancytopenia was 2.53%. The frequencies shown in other studies were quite variable. The frequency from study conducted in Rawalpindi Military Hospital[6] in the year 2000 was 0.8%, while a study by Shazia Memon[7] at al from Hyderabad in 2008 reported 3.57%. While Kanchanalak et al[8] and Adil et al[9] reported 1.2% and 12.6% respectively.

In this study acute leukemia is the most common malignant disease diagnosed and classified on the basis of bone marrow examination. According to this study acute leukemia accounts for 26.6%. Out of 26.6%, 19.66% accounts for ALL-type 1 while acute myeloid leukemia M_2 and M_3 accounts for 7.66%. Worldwide the highest incidence is seen between ages 2 and 5 years[10]. All is the most common childhood cancer constituting about 23-30% of cases before age 15[11].

Epidemiological studies suggest that environmental factors on their own make only a minor contribution to disease risk, but it may interact with genetics. Genome-wide association studies have found association with a number of genetic nucleotide[12] polymorphism. Sine this study involve patient from other nationalities also, therefore the frequency of leukemia is much high.[13] Afzal et al reported 11.6% frequency of acute leukemia from Lady Reading Hospital Peshawar.

Among the non-malignant condition. Megaloblastic anemia was most important condition diagnosed as a cause of pancytopenia in this study. Megaloblastic anemia accounts for 16.66%. Vitamin B_{12} deficiency and folate deficiency can be caused by multiple factors[14] among the nutritionally deprived children.

Poor dietary intake, impaired absorption due to malabsorption and competitive parasites[15] could be some of the factor leading to megaloblastic anemia in these malnourished children.

Another study from Pakistan show a percentage of 13.04%, while a study from a Nigeria by Timothy Amos Ekwere shows a 6.4% of megaloblastic anemia[16]. The higher percentage in this study could be due to higher number of malnourished children included in this study who presented with pallor and bleeding tendency with peripheral pancytopenias.

Bone marrow aplasia and hypoplasia accounts for 13.33% as a cause of pancytopenia in this study. This figure is low when compared with other local and international studies. Shazia et al shows a figure of 23.9% while a study from Peshawar by Afzal khan et al and Zahid Gul et al shows a figure of 20.2% and 28.5% respectively. In this study many disease entities apart from malignancy, bone marrow aplasia and nutritional anemia emerged as a cause of pancytopenia.

Various infection as a cause of pancytopenia have been variedly documented. Malaria including both falciparum and vivax accounted for 10.00% as a cause of pancytopenia. Aouba reported haemophagocytic

syndrome resulting due to P. vivax infection as a cause of pancytopenia. Bacterial sepsis accounts for 8.6% as a cause of peripheral cytopenia, which is a well documented entity in the literature. Bone marrow undergo histiocytic hyperplasia along with haemophagocytosis or complete necrosis. Varying degree of cytopenias have been reported in other studies as well[17].

In this study, blood culture of 2 patients grow MRSA, 1 patient had grown MSSA, 2 patients had gram negative sepsis while the blood culture in the rest of the patients were negative. Shazia et al reported fulminant sepsis as a cause of pancytopenia in 8.69% while Garewal et al reported bacterial sepsis in 2 patients.

CONCLUSION

Pancytopenia is common in clinical Paediatrics. Documentation of its etiology is important in formulating a comprehensive diagnostic and therapeutic strategies.

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