ORIGINAL ARTICLE

ETIOLOGICAL SPECTRUM OF PANCYTOPENIA IN PAEDIATRIC PATIENTS

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ABSTRACT

Objective: To determine the etiological pattern of pancytopenia in pediatric age group patients presenting to a tertiary care hospital at Peshawar

Material and Methods: This descriptive study was conducted from January 2016 to December 2017. During this two-year duration, 100 pediatric patients with clinical diagnosis of pancytopenia were enrolled in the study fulfilling the inclusion and exclusion criteria. Non-probability consecutive sampling technique was used. A detailed clinical evaluation was done in all diagnosed cases of pancytopenia. Hematological profile included hemoglobin, red cell indices, total and differential leukocyte counts, platelet count, peripheral blood smear, bone marrow aspirate and trephine biopsy were carried out.

Results: In this study 66% were male and 34% were female with male to female ratio of 1.94: 1. The mean age of patients enrolled was 07.173 years$\pm$3.7702 SD where 35% of all cases were in the age range of 01-05 years.Mean hemoglobin level was 6.631gm%$\pm$ 2.0273 mean total leucocyte count was 2910.21 (SD + 1399.452)X 103/µl, and platelet count was 57750.00 (SD + 40776.646) X103/µl. Majority of the patients (51%) had acute lymphoblastic leukemia, followed by aplastic aneamia(20%) and hypoplasia (12%).

Conclusion: Acute lymphoblastic leukemia is the commonest cause of pancytopenia followed by aplastic aneamia and bone marrow hypoplasia as per this study findings.

Keywords: Lymphoblastic, Leukemia, Aplastic, Anemia, Gaucher, Hemolytic, Megaloblastic, Pancytopenia.

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INTRODUCTION

Pancytopenia is described as reduction in all three cellular lines of blood. It is a pathological manifestation due to variety of disease processes affecting the bone marrow either primarily or secondarily[1,2]. Common causes of pancytopenia are aplastic anemia, megaloblastic anemia, myelodysplastic syndrome, hypersplenism, acute leukemias, paroxysmal nocturnal hemoglobinuria, multiple myeloma and some infections e.g. HIV, miliary tuberculosis, Leishmaniasis and Brucellosis[3,4]. Some other causes are radiotherapy, chemotherapy and hypersplenism[5]. Clinical presentation of Pancytopenia can be due to symptoms due to anemia, leucopenia and thrombocytopenia[6]. The commonest cause of pancytopenia is aplastic anemia worldwide but megaloblastic anemiahas been reported as top cause in India[7]. Although pancytopenia is very common, but the causes are reported in limited number of studies[8]. In a recent study from Pakistan, it was reported that Leukemia is the commonest cause of Pancytopenia in pediatric age group in 28% patients, followed by lymphoma in 24%, aplastic anemia in 20%, megaloblastic anemia in 8%, enteric fever in 8%, malaria in 6.4% and sepsis in 5.6% cases[9]. In another study done in Pakistan aplastic anemia (38.3%), megaloblastic anemia (24.7%) Hypersplenism (16%) and acute leukemia (13.6%) were the most frequent reason of cytopenia[10]. In pancytopenia, peripheral blood smear examination is imperative if the cause of pancytopenia cannot be

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ascertained from history and clinical examination. If peripheral blood smear examination does not give conclusive diagnosis than bone marrow aspiration and trephine biopsy is required[11]. In peadiatric population with pancytopenia, the commonest cause like leukemia must be considered along with aplastic anemia and myelodysplastic syndrome. Furthermore, multiple infections including Cytomegalovirus (CMV), Epstein Barr virus (EBV),Human Immunodeficiency Virus(HIV), Rubella, Influenza, Para-influenza, and Hepatitis-A virus (HAV) and vitamin B12 deficiency may also lead to pancytopenia. A bone marrow aspirate and trephine is goldstandard diagnostic test for pancytopenia[12].

Bone marrow study (aspiration/biopsy) a simple and commonly performed procedure in pediatric medical practice for both hematological and non-hematological disorders[13]. There is a relatively scarceliterature on pancytopenia in pediatric age group especially with regards to clinical and etiological findings in South-East Asia[14]. With inconsistent findings enlisting top causes of pancytopenia in local literature, there is need to explore this pathologic entity with regard to etiological causes.

MATERIAL AND METHODS

This descriptive study was conducted at Pediatrics department, Lady Reading Hospital, Peshawar Pakistan.The study was conducted from January, 2016 to December, 2017 with a total of 100 cases. Patients diagnosed as pancytopenia having hemoglobin (Hb) <9 gm%, total leukocyte count (TLC) <4,000/mm3 and platelet count of<100 x103/µl in the age range of 1 month to 15 years were included. Patients with pancytopenia who had received chemotherapy or immunosuppressive drugs, who had inconclusive blood and bone marrow examination and those not willing for bone-marrow aspiration were excluded. Ethical approval was obtained from the hospital ethical committee and all cases meeting the inclusion criteria were enrolled through OPD and hospital ward admissions. The procedure and use of research study were explained to the guardians of patients and an informed written consent was obtained. A detailed history and physical examination were performed. Hematological profile including Hb%, red cell indices, TLC and DLC and smear morphology were requested from the hospital laboratory. Blood smear for Malaria and IgM and IgG antibodiesor Salmonella typhi were also requested for selected cases with high clinical suspicion of the above diseases. Bone-marrow aspiration and trephine biopsy were performed where indicated. About 2 ml anticoagulated blood was taken and sent for complete hemogram to the hospital pathology lab for Hb%, TLC, DLC, platelet count, packed cell volume, and red cell indices. Bone-marrow biopsy was performed with the standard technique using a 16 G needle from posterior iliac crest of the patients under aseptic conditions using local anesthesia. Slides were sent to hospital pathology lab and stained using standard Wright's staining procedure. The demographic information of patients was recorded using a pre-designed proforma. Data was analyzed using SPSS version 24. Mean and standard deviation was calculated for quantitative continuous variables like Hb%, TLC and platelet count. Gender, age and cause of pancytopenia were calculated as categorical variables and expressed as percentages. The results were presented in the form of graphs and tables.

RESULTS

Out of 100 cases, 66 (66%)were males and 34 (34%) were female children with a male to female ratio of 1.94: 1. Age range was 03 months to 13 years. Mean age was 07.173 $\pm$ 3.7702 years. 06 cases (06%) were in the age range of 01-12 months, 35 (35%) cases were in the age range of 01-05 years, followed by 34 (34%) in the age range of 06-10 years, 25 (25%) were in the age range of 11-15 years as shown in Table 1. Hemoglobin levels obtained were from 2.6gm% to 8.9gm% with mean level of 6.631 (SD $\pm$ 2.0273).TLC levels were in the range of 210 to 3870/µl with mean of 2570.21 (SD + 1300.452)/µl (S.D), and platelet count was in the range of4x103/µl to 89.750x103/µl / with mean level of 57.750 (SD+ 40.776.646)x103/µlas shown in Table2.

Acute lymphoblastic leukemia was found to be the commonest cause of pancytopenia as seen in 51 (51%) cases.Aplastic aneamia was seen in 20 (20%) cases followed by hypoplasia in 12 (12%) cases. These three causes together accounted for 73% cases while the rest 27% cases were caused by megaloblastic anemia, peripheral destruction, Gaucher's and hemolytic anemiaas shown in table 3.

DISCUSSION

Childhood pancytopenia can be caused by different diseases, including hematological and non-he-

Table 1: Demographic features of Cases(n=100)

Variables	Frequency	Percentage	
Age ranges:			
01 - 12 months	06	06%	Minimum = 3 months
01 - 05 years	35	35%	Maximum = 13 years
06 - 10 years	34	34%	Mean = 7.173 years
11 – 15 years	25	25%	Std. deviation = + 3.7702
Gender:			
Male	66	66%	Male to female ratio=1.94: 1
Female	34	34%	

Table 2: Laboratory findings in Cases (n=100)

Variables	Minimum	Maximum	Mean	Std. Deviation
Hemoglobin (gm %)	2.6	8.9	6.631	2.0273
Total leucocyte count (/mm3)	210	3870	2570.21	1300.452
Platelet count (x103/µl)	4.000	89.750	57.750	40.776

Table 3: Etiological pattern of Pancytopenia (n=100)

Etiology	Frequency	Percentage
Acute lymphoblastic leukemia (ALL)	51	51%
Aplasia	20	20%
Hypoplasia	12	12%
Megaloblastic anemia	09	09%
Peripheral destruction	05	05%
Gaucher disease	02	02%
Hemolytic anemia	01	01%

matological entities. Overlapping phenotypes and pathophysiology poses a major diagnostic challenge. However, an accurate and rapid diagnosis is essential for the patient management, surveillance, and genetic counseling. Bone-marrow analysis is needed for the diagnostic work-up of cytopenias affecting one or more lineages[15,16].

Pancytopenia is more common in male children as evident from a local study with male to female ratio of 1.60:117 and our study also showed a male predominance with male to female ratio of 1.94:1. Male predominance is also documented insome other studies conducted in South Asian countries and Yamen[18-22]. This male predominance could be due to some social/ cultural taboos making health-care utilization on priority basis by the families for male children as compared to female.

Average age of the patients in our study was 7.173 + 3.7702 with minimum age of 3 months and maximum age was 13 years and this has been reported in some other studies that the highest incidence of pancytopenia is age group of less than 20 years[23,24]. Similarly some other local studies also reported average age of the patient as 7.46 (SD ±3.8) years with range 2 months-15 years 25, and mean age of 7.69 (SD ± 2.36) years 26 and mean age of 5.7 (SD ±3.6) years with arange from 2 months-12 years[27]. In our study 35% cases were in the age group1-5 years and nearly the same results were also reported from other local studies[28,29]. These findings suggest that 1-5 yearsof age is the most vulnerable period for pancytopenia.

In our study laboratory results showed that hemoglobin (Hb) mean level was 6.631 (+ 2.0273) gm%, Total leucocyte count (TLC) mean level was 2570.21 (+1300.452)/mm 3 and platelet count mean level was 57.750.00 (+ 40.776.646) x103/µl. Similar results were also reported in a study, in which mean hemoglobin was 6.87 ± 2.00 g/dL, TLC 0.85 ± 0.31 x 103, and platelet count 68.75 ± 20.01/µl[30]. Variations in etiology of pancytopenia are reported from different countries but also in different regions of a single country. Some

other regional studies have also reported megaloblastic anemia as the commonest cause of pancytopenia[31] while some studies show hypersplenism, infections and aplastic anemia to be the most frequently responsible diseases[32,33] for pancytopenia. In our study ALL accounted for 51% cases of pancytopenia which are higher and the top most cause as shown in a study another local study[10], but our results are higher from other regional and international studies[34,35] which needs further exploration.

LIMITATIONS

Culture for Salmonella typhi could not be done and its diagnosis was made on the basis of serology. Primary etiology of aplastic anemia and bone marrow hypoplasia could not be traced back.

CONCLUSION

Pancytopenia is a common condition in pediatric patients and acute lymphoblastic leukemia (ALL) is the commonest cause at our set up.

RECOMMANDATIONS

A comprehensive clinical, hematological workup and bone-marrow study of patientsis helpful in diagnosing the cause of pancytopenia.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Hussain M: Writing, abstract is methodology analysis corrections & references.

Irshad M: Main Idea, manuscript writing Review of Article.

Ullah I: Methodology final review & correction

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.