DOI: 10.7860/JCDR/2022/50969.16037

Original Article

Paediatrics Section

Aetiological Profiles of Pancytopenia in Children between 2 months to 12 years of Age- A Retrospective Study from a Tertiary Care Centre, Chennai, India

SWETHA KARUN THAPPA[1], DIVYA MASILAMANI[2], SUDHAKAR PRASANNA[3], ATHMARTHAN KRISHNASAMY[4], REJI MANJUNATHAN[5]

ABSTRACT

Introduction: Pancytopenia is a medical condition that generally exists among children in which the peripheral blood cell lineages are found to reduce in blood. The condition is diagnosed as a common haematological problem with an extensive differential diagnosis and vary according to the geographical distribution and genetic mutation. The condition is reversible and easily treatable if identified at the earliest.

Aim: To determine the frequency of aetiological spectrum of pancytopenia in children between the age of 2 months to 12 years from Chennai, Tamil Nadu, India.

Materials and Methods: A retrospective descriptive study was carried out at the Institute of Child Health, Madras Medical College, Chennai, Tamil Nadu, India, from January 2016 to December 2016. Out of 12,869 patients admitted, 91 children were identified with pancytopenia based on peripheral blood smear analysis. Complete blood count, peripheral smear, red blood cell indices, bone marrow examination, and serum vitamin B12 levels were analysed. The complete data was tabulated in Microsoft excel sheet and frequency(n) and percentage (%) analysis was performed.

Results: Total of 91 children with pancytopenia (45 males and 46 females, aged from 6 months to 12 years) were included in the study and analysed. Majority of the pancytopenia children belonged to the age group of 1 to 6 years (40, 43.9%). The identified common clinical presentations for admission included the unexplained fever (82.92%), pallor (10.8%), and bleeding (9.79%). The common major aetiologies were megaloblastic anaemia (23, 25.2%), acute lymphoblastic leukaemia (17, 18.6%), and aplastic anaemia (12, 13.1%). Infections due to microorganisms in children also cause pancytopenia and there was one child each with the infectious symptoms due to Human Immunodeficiency Virus (HIV), tuberculosis, and Epstein-Barr Virus (HBV).

Conclusion: Acute leukaemia and bone marrow failure were identified as the most common causes of pancytopenia in children. It is highly advisable to record the symptoms related with iron deficiency anaemia along with the symptomatic issues of certain viral and bacterial infections among children from the developing nations while diagnosing pancytopenia.

Keywords: Bone marrow, Megaloblastic anaemia, Nutritional anaemia

INTRODUCTION

Pancytopenia is a medical condition in which the peripheral blood cell lineages such as the erythrocytes, leukocytes, and platelets are reduced in blood [1]. Pancytopenia is diagnosed when the Haemoglobin (Hb) level is less than 10 gm%, the Absolute Neutrophil Count (ANC) is $<1.5\times10^9$/L and the platelet count is $<100\times10^9$/L. The condition is marked as severe, when the patient has haemoglobin (Hb) less than 7 gm%, ANC $<0.5\times10^9$L, platelet count 20×10^9/L, and the reticulocyte count is 1% [2].

The aetiological profiles of pancytopenia ranges from the simple drug-induced bone marrow hypoplasia and nutritional deficiencies to the fatal bone malignancies [3]. According to the geographical distribution and genetic mutations, the incidence of pancytopenia varies and is noted as a result of either failure of the production of haematopoietic progenitors in bone marrow, or malignant cell infiltration, or antibody-mediated bone marrow suppression [4]. The peripheral sequestration of blood cells in overactive reticulo-endothelial system or ineffective haematopoiesis and dysplasticare also known to cause pancytopenia in children [5]. The common clinical manifestations of pancytopenia are usually fever, anorexia, fatigue, dizziness, weight loss, pallor, bleeding, splenomegaly, lymphadenopathy, and hepatomegaly [6].

The optimal diagnostic approaches behind pancytopenia diagnosis remain undefined even though the condition recognised from common haematological problems. The clinical reasons behind pancytopenia may vary in different regions due to geographical variations and genetic differences, thus having epidemiological importance. The most common cause for pancytopenia is linked with megaloblastic anaemia in the population located at Uttarakhand and Karnataka [7-9]. On the contrary, the data published by Graham S et al., proved that normoblasts erythroid hyperplasia (30%) also could be a significant reason behind pancytopenia among children from the state of Karnataka [10]. A retrospective study done by Kumar V et al., from New Delhi reported that pallor (70.9%) is the most common clinical feature for pancytopenia [11], whereas in eastern India, the aplastic anaemic condition (36.9%) is identified as the major culprit behind pancytopenia (18.7%) [12].

Thus, due to the varied data in the existing literature, it was decided to conduct a retrospective descriptive study to assess the main aetiology and clinical profiles behind paediatric pancytopenia condition. Because the clinicians should be aware of the different causes of pancytopenia present in the definitive region, delay in diagnosis can be prevented along with unnecessary investigation. The present study also identifies the easily treatable and reversible causes of pancytopenia among vulnerable paediatric patients for a better prognosis.

MATERIALS AND METHODS

This was a retrospective descriptive study done at the Institute of Child health, Madras Medical College, Chennai, Tamil Nadu, India, from 01 January 2016 to 31 December 2016. The ethical approval was obtained from the Institutional Ethical Committee, held at Madras Medical College (EC Reg. No. ECR/270/Insti. TN/2013, No-13122016).

Study Procedure

A total of 12,869 children admitted at the Paediatric Department, from 2 months to 12 years of age, were screened. A total of 91 cases among the screened population were noted with pancytopenia based on the peripheral blood smear evaluation. The details of the complete clinical profiles and haematological parameters during the admission were recorded.

Inclusion criteria: Children in the age group of 2 months to 12 years and identified with pancytopenia based on their peripheral blood smear evaluation were included in the study.

Exclusion criteria: Children who received blood transfusion were excluded from the study.

A complete analysis of Hb, total leukocytes count, differential leukocytes, platelet count, Absolute Neutrophil Count (ANC), peripheral smear, red blood cell indices, serum vitamin B12 along with bone marrow examination were performed as per Institution's protocol. The other investigations included the identification of various viral markers such as HIV, Hepatitis B surface antigen (HBsAg), Hepatitis C Virus (HCV), Parvovirus, EBV, and Cytomegalovirus (CMV). The levels of serum Lactate Dehydrogenase (LDH), serum ferritin, serum fibrinogen along with gene experts were also examined.

STATISTICAL ANALYSIS

Descriptive statistics were used and the proportions and percentages of each diagnosis were calculated along with the exact 95% confidence interval by the R (Ross Ihaka and Robert Gentleman) statistical Environment, version 3.5.1 (Vienna, Austria).

RESULTS

During the study period, the number of admissions at the Institute were 12,869. Among them, 91 were noted with pancytopenia. Thus, the frequency of incidence was 0.70%. There were 45 males (49.45%) and 46 females (50.54%), and the male female ratio was 1:1.02 [Table/Fig-1]. Pancytopenia was more common among the children who were in between of the ages of 1 to 6 years (40, 43.9%).

Age group	Males (n=45)	Females (n=46)	N (%)
<1 year	8	7	15 (16.4%)
1-6 years	19	21	40 (43.9%)
>6 years	18	18	36 (39.5%)

[Table/Fig-1]: Age and gender distribution (N=91).

[Table/Fig-2] represents the common complaints and symptoms related with the admission of children at the hospital. The most frequent complaint was associated with fever. Total 63 children (69.2%) were reported with fever. Considering the aetiological pattern of the pancytopenia cases [Table/Fig-3], megaloblastic anaemia was found as the single most common cause of pancytopenia among children (23, 25.2%).

The general clinical examination [Table/Fig-4] revealed that majority of the children with pancytopenia had pallor (73, 80.2%). The system examination highlighted that hepatosplenomegaly and no organomegaly were seen in equal number of children (36, 39.6%). Among the 91, 35 children (38.5%) were noted with mild anaemia and 47 were identified with mild neutropenia (51.6%).

Clinical features	N (%)
Fever	63 (69.2%)
Fever+Pallor	7 (7.6%)
Fever+Bleeding manifestations	6 (6.59%)
Fever+Bone pain	4 (4.3%)
Fever+Fatigue	4 (4.3%)
Bleeding manifestations	3 (3.2%)
Pallor	3 (3.2%)
Poor weight gain	1 (1.09%)

[Table/Fig-2]: Clinical features and symptoms.

Diagnosis	N (%)
Megaloblastic anaemia	23 (25.2%)
Acute Lymphoblastic Leukaemia (ALL)	17 (18.6%)
Aplastic anaemia	12 (13.1%)
Iron deficiency anaemia	6 (6.5%)
Idiopathic Thrombocytopenic Purpura (ITP)	6 (6.5%)
Acute Myeloid Leukaemia (AML)	5 (5.4%)
Malaria	4 (4.3%)
Haemophagocytic Lymphohistiocytosis (HLH)	4 (4.3%)
Systemic Lupus Erythematosus (SLE)	2 (4.3%)
Glycogen Storage Disease (GSD)	2 (2.1%)
Enteric fever	2 (2.1%)
Parvovirus	2 (2.1%)
Drug Induced pancytopenia	2 (2.1%)
Osteopetrosis	1 (1.09%)
Human Immunodeficiency Virus (HIV)	1 (1.09%)
Tuberculosis (TB)	1 (1.09%)
Epstein-Barr Virus (EBV)	1 (1.09%)

[Table/Fig-3]: Aetiological profile.

Thrombocytopenia was noted in all the 91 children, among which the 35 (38.46%) showed moderate thrombocytopenia. The Mean Corpuscular Volume (MCV) of 42 children (46.1%) was found to be within the range of 80-100 fL. The mean corpuscular Hb of 55 children (60.4%) was within the range of 22 to 25.9 g/dL and the mean corpuscular Hb concentration value of 65 children (71.5%) was in between the range of 27 to 31.9 g/dL. Bone marrow cellularity and aetiology of the pancytopenia children are given in [Table/Fig-5]. Most of the children (31, 34.06%) were noted with normal bone marrow characteristics.

Clinical examination of all subjects	
I. General examination	N (%)
Pallor	73 (80.2%)
Pallor+Bleeding manifestations	10 (10.9%)
Pallor+Lymphadenopathy	8 (8.7%)
II. System examination	
Splenomegaly	2 (2.1%)
Hepatomegaly	17 (18.6%)
Hepatosplenomegaly	36 (39.6%)
Nil	36 (39.6%)

[Table/Fig-4]: Examination details (N=91).

Bone marrow	N (%)
Normal	31 (34.06%)
Hypocellular marrow with blasts	12 (13.1%)
Hypercellular marrow with blasts	12 (13.1%)
Hypocellular	11 (12.08%)

Hypercellular marrow with megaloblastic features	11 (12.08%)
Hypercellular	6 (6.49%)
Cellular marrow with megakaryocytosis	4 (4.3%)
Cellular marrow with macrophage predominance	4 (4.3%)

[Table/Fig-5]: Bone marrow examination details (N=91).

DISCUSSION

Pancytopenia is considered as a foreground for many life-threatening conditions among the children and the pattern of diseases causing the condition varies in different population [1]. Hence, the present study tried to focus on the aetiological profiles of pancytopenia among south Indian children from Chennai. The study accounted 12,869 admitted children at the hospital, Chennai, and among them 91 children were identified with pancytopenia on the basis of clinical backgrounds such as fever, pallor, and bleeding. The calculated frequency of pancytopenia among the study population is 0.70%, which is comparatively lesser than the earlier reported data [13-15]. The maximum children noted with pancytopenia in the present study were in the age range of 1-6 years. Prolonged fever for weeks is the first stage of identification of pancytopenia among children and in the present study it was noticed that most of the children were admitted due to prolonged fever (69.7%) [3,16-18]. Megaloblastic anaemia has emerged as a recognisable cause of pancytopenia among 23 children (25.27%) and is seen to be within the range of the findings as reported by various studies (11 to 47%) [19-21]. Many reports identified leukaemia and aplastic anaemia as the main clinical reasons behind pancytopenia in children [22-24]. In the present particular study, the authors could identify acute leukaemia (24.1%) followed by aplastic anaemia (13.1%) as the major causes of pancytopenia in children located at southern part of India.

The most common physical finding for pancytopenia in the present study was pallor (80.2%). Hepatosplenomegaly has contributed 39.6% of the total cause and is in accordance with the previous examination done by Bhatnagar SK et al., [22]. Iron deficiency is also considered as one of the reasons behind pancytopenia in children [2,17,25]. In this study, six children were identified with pancytopenia only because of iron deficiency. Idiopathic thrombocytopenia purpura contributed only to 6.5% of cases and has been marked as a least accountable haematological problem. This finding is in contradiction with the earlier report in which all the patients were presented with various infections and contributed to a total of 11.87% of pancytopenia [17]. Various infectious conditions due to microorganism also induce pancytopenia in children. Pancytopenia was also noted as a result of either hypo-or hyper-cellular morphology in bone marrow with varying common causes [5]. An earlier report by Santra G and Das BK found 50% of pancytopenic children with hypocellular marrow [26]. Bone marrow examination data indicated that 34.06% of the children had normal cellular morphology of bone marrow.

At the same time, 12 children each (13.1%) were noted with hypo and hyper-cellular marrow with blasts. Hence, considering the cellular morphology of bone marrow along with other noted clinical symptoms of pancytopenia will support the physicians to identify the condition at the earliest for the better prognosis.

Limitation(s)

The study was conducted on a limited population sample.

CONCLUSION(S)

The present study concluded that the pancytopenia is more common among those children who are in between the ages of 1-6 years. Megaloblastic anaemia, pallor, bone marrow disorders and hepatosplenomegaly are the more common causes of pancytopenia in children from southern region of India. The data suggests that the infectious rate of the children due to various microorganisms should be included for an early detection and management of pancytopenia in children even though they contribute less to the pancytopenia frequency when considering mass population, because it is important to be awared of the frequent conditions behind pancytopenia within the given geography for a prompt and appropriate investigation and therapeutic measures.

Authors contribution: SKT and DM conceptualised the idea and collected the data. SP and AK, interpreted the data and reviewed the manuscript. RM analysed the data and drafted the manuscript. All the authors read and accepted the final version of the manuscript. Both SKT and DM equally contributed towards the publication.

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PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Paediatrics, Institute of Child Health, Madras Medical College, Chennai, Tamil Nadu, India.
2. Assistant Professor, Department of Paediatrics, Government Erode Medical College and Hospital, Perundurai, Tamil Nadu, India.
3. Associate Professor, Department of Paediatric, Chengalpattu Government Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
4. Senior Resident, Department of Paediatrics, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
5. Research Scientist, Department of Multi-disciplinary Research Unit, Chengalpattu Government Medical College, Chengalpattu, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Reji Manjunathan,
Research Scientist, Department of Multi-disciplinary Research Unit,
Chengalpattu Government Medical College, Chengalpattu, Tamil Nadu, India.
E-mail: rejimanjunath@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 21, 2021
- Manual Googling: Nov 24, 2021
- iThenticate Software: Dec 27, 2021 (9%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 19, 2021**
Date of Peer Review: **Oct 09, 2021**
Date of Acceptance: **Dec 18, 2021**
Date of Publishing: **Feb 01, 2022**