ORIGINAL RESEARCH

Clinico-etiological profile of children presenting with pancytopenia in a tertiary care centre of North Karnataka region: A prospective observational study

[1]Dr. Goudappa R Patil, [2]Dr. Sachin Hatti, [3]Dr. Naveen Kumar B, [4]Dr. Sandeep H, [5]Dr. Nagaraj

[1,2]Assistant Professor, Department of Paediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi,Karnataka, India
[3]Senior Resident, Department of Paediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi, Karnataka, India
[4]Professor and Head, Department of Paediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi, Karnataka, India
[5]Post Graduate, Department of Paediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi, Karnataka, India

Corresponding Author
Dr. Goudappa R Patil
Assistant Professor, Department of Paediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi, Karnataka, India

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ABSTRACT

Objectives: To determine the clinical features, etiological and hematological spectrum of pancytopenia in children between the age of 1month to 18 years from Kalaburagi, Karnataka India. **Materials and methods:** A Prospective observational study, was conducted at the Department of Pediatrics, Gulbarga Institute of medical Sciences, Kalaburagi, Karnataka from 1st August 2021 to 31st July 2022(12 months). This study included 60 patients between the age of one month till 18 years with pancytopenia. Study participants were assessed for various parameters including their demographic details, clinical features, immunization history, and nature of the disorder. The prevalence of various etiologies (nutritional, neoplastic, infectious, autoimmune, and others) of pancytopenia was ascertained. **Results:** Of the 60 patients, 26(43.33%) were males and 34 (56.66%) were females with a mean age of 69.47 ± 7.12 months. Fever was present in 71.66%, arthralgias in 55%, weight loss in 15%, and failure to thrive in 18.33% of patients. The bone marrow examination revealed aplastic changes in 36 (37.50%), hyperplastic changes in 21 (21.87%), and normal cellularity in 40.62% of patients. Pancytopenicanemia was the most common nutritional cause of pancytopenia present in 21.66% of cases. Acute lymphoblastic leukemia (ALL) was the most prevalent neoplastic etiology present in 8.33% of patients. Aplastic anemia, miliary tuberculosis, parvovirus B19, systemic lupus erythematous and hemolytic anemia were other notable etiologies. **Conclusion:** Majority of the causes of pancytopenia among pediatric patients in our region are preventable. There is a need to be aware of such conditions and appropriate investigative modalities should be undertaken for the same.

Key words: Pancytopenia, aplastic anemia,bone marrow biopsy, pediatric age group

INTRODUCTION

Pancytopenia is an important clinico-hematological entity encountered in our day-to-day clinical practice. 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 the simultaneous presence of anemia (hemoglobin [Hb] less than the normal for age), leukopenia (total leukocyte count [TLC] ≤4 × 10^9/L, and thrombocytopenia (platelet count ≤150 × 10^9/L).[2] Presenting symptoms are usually attributable to anemia, leucopenia or thrombocytopenia.

The aetiology of pancytopenia varies widely in children, ranging from transient marrow suppression due to viral infection to marrow infiltration by life-threatening malignancy.[3] The bone marrow picture may vary depending on the aetiology, from normocellular with non-specific changes to hypercellular being replaced completely by malignant cells.[4] It is recommended that bone marrow aspiration

and biopsy be done simultaneously in cases of pancytopenia.

Although pancytopenia is a common clinical finding with extensive differential diagnosis, there is a paucity of data on children. There is a relatively little discussion of this abnormality in literature, although there have been several studies of the aetiopathogenesis of pancytopenia in adults but there is the lack of data on pancytopenia in paediatric age group, especially with regards to clinical and etiological findings, especially in North Karnataka region in India. This study has been done to identify preventable causes of pancytopenia.

MATERIALS AND METHODS

This is a Prospective observational study, which was conducted at the Department of Pediatrics, Gulbarga Institute of medical Sciences, Kalaburagi, Karnataka from 1st August 2021 to 31st July 2022 (12 months). All the indoor children admitted through OPD or emergency who meet the following criteria were enrolled for the study.

INCLUSION CRITERIA

- Children between 1 month to 18 years of age.
- Having blood investigation report of.

-Hemoglobin (Hb) <10 gm/dL,
-Total leukocyte count (TLC) <4000/mm^3 and
-Platelet count <100000/mm^3.

- Gave informed consent.

EXCLUSION CRITERIA

- Children of age less than 1 month or more than 18years.
- Diagnosed cases of aplastic anemia and leukemia.
- History of recent blood transfusion.
- Receiving chemotherapy and radiotherapy.
- Not given consent.

After getting informed written consent from parents/guardians, patients were enrolled into study. Detailed history and clinical examination was done by pediatrician. Various clinical features like age at presentation, drug history, fever (>98.6˚F), visceromegaly including hepatomegaly (if liver palpable >2cm below costal margin), splenomegaly (if spleen palpable below left costal margin) and lymphadenopathy (if cervical lymph nodes >1cm large, axillary lymph nodes >1 cm large and inguinal lymph nodes >1.5 cm large) on clinical examination, bleeding manifestations in the form of gum bleed, epistasis, petechial rash, pallor, joint pains and bone pains was confirmed on history and clinical examination. All relevant investigations were done including complete blood picture, Peripheral film, Reticulocyte count, MP smear, Typhi dot, Widal Test, blood culture, lymph node biopsy, bone marrow aspiration and bone marrow biopsy. For the diagnosis of nutritional anemia, serum iron, serum ferritin, vitamin B12 and folic acid levels was noted. The investigative workup was directed by the suspected underlying pathology.

RESULTS

In the current study involving 60 patients, the mean age of the study participants was 69.47 ± 7.12 months with a range between one month and 12 years. Fever was present in 71.66%, arthralgias in 55%, weight loss in 15%, and failure to thrive in 18.33% of patients. Most of the patients had multiple symptoms during the presentation. The details of the study participants are delineated in Table 1

Table 1:Baseline characteristics of the study participants

Parameters		Frequency	Percentage
Gender	Male	26	43.33
	Female	34	56.66
Age groups	1 month till 1 year	8	13.33
	1-3 years	10	16.66
	3-5 years	18	30.00
	5-10 years	13	21.66
	More than 10 years	11	18.33
Immunization history	Complete	28	46.66
	Partial	19	31.66
	No	13	21.66
Presenting symptoms	Fever	43	71.66
	Pallor	36	60.00
	Arthralgias	33	55.00
	Failure to thrive	11	18.33
	Weight loss	9	15.00
	Tremors	5	8.33
	Jaundice	5	8.33
	Vomiting	9	15.00
Clinical features	Hepatomegaly	32	53.33
	Splenomegaly	30	50

	Lymphadenopathy	10	16.66
	Hyperpigmentation	5	8.33
	Bleeding	20	33.33

In all patients, a bone marrow biopsy was performed for a definitive diagnosis of pancytopenia. The bone marrow examination revealed aplastic changes in 36 (37.50%), hyperplastic changes in 21 (21.87%), and normal cellularity in 39 (40.62%) patients. Megaloblastic anemia was the most common nutritional cause of pancytopenia present in 21.66% of cases. ALL was the most prevalent neoplastic etiology present in 8.33% of patients. Miliary tuberculosis was the most common infective etiology with 5%. Other notable etiologies were aplastic anemia, myelofibrosis, and sideroblastic anemia. There was a wide spectrum of neoplastic and non-neoplastic etiologies of pancytopenia. The spectrum of hematological diseases is elucidated in Table 2.

Table 2: A tabulation of hematological diseases and the associated prevalence in children with pancytopenia

Type of disorder	Diagnosis	Frequency	Percentage
Nutritional	Iron deficiency anemia	6	10
	Megaloblastic anemia	13	21.66
	Mixed deficiency anemia	4	6.66
Infective	Parvovirus B19	1	1.66
	Leishmaniasis	1	1.66
	HIV	1	1.66
	Miliary tuberculosis	3	5.00
	Salmonella species	1	1.66
	Chronic granulomatous disease	1	1.66
	Complicated malaria	1	1.66
Autoimmune	Systemic lupus erythematosus	6	10.00
	Immune thrombocytopenic purpura	1	1.66
	Hemolytic anemia	4	6.66
Neoplastic	ALL	5	8.33
	AML	4	6.66
	Aplastic anemia	4	6.66
Others	Myelofibrosis	1	1.66
	Hypoplastic bone marrow	2	3.33
	Sideroblastic anemia	1	1.66

Discussion

Pancytopenia is a prevalent pathological finding that is frequently encountered in the pediatric age group. It has a multitude of underlying causes that determine the management and prognosis.[5]An appropriate clinical history, physical examination, laboratory investigations, and bone marrow examination are some necessary prerequisites for the assessment of the underlying etiology of pancytopenia.[6] Timely recognition of the underlying pathology may decrease mortality and morbidity.

The results of this study show that pancytopenia can occur in a variety of conditions in the pediatric population of our country. The male-to-female ratio in our study was 1:1.3. A similar study reported a ratio of 1:1.25 in their study with a non-significant female dominance.[6] In contrast, another study reported a male predominance.[7] These differences in gender predominance may be due to genetic differences, geographic differences, and differential nutritional status. These differences in gender predominance may be due to genetic differences, geographical variance, and disparity in nutritional status.

The most commonly presenting symptoms were fever, pallor, arthralgias and weight loss. Similar presenting complaints have also been reported in the literature.[8-10] These symptoms indicate a discrepancy in the cellularity of the bone marrow, resulting in a reduction of three of the cell lineages. The decreased total counts make the patient susceptible to various infections and decreased Hb leads to pallor and arthralgias. Hepatomegaly, splenomegaly, lymphadenopathy, and bleeding were common clinical features noted in patients.Similar features were reported in other studies from developing countries.[10,11]

Megaloblastic anemia was the most common nutritional cause of pancytopenia in children in our study, with a prevalence of 21.66%. Malnutrition in children, especially in developing countries, is the major cause of megaloblastic anemia, which ultimately translates into pancytopenia. Resource deprivation, unhealthy dietary habits, and poverty in developing countries also lead to other nutritional etiologies like iron deficiency anemia and mixed deficiency anemia.[8] Adequate supply of vitamin B12-enriched foods and supplementation of vitamin B12 and folic acid can help reduce these causes.

Miliary tuberculosis was reported to be the most common infective cause of pancytopenia in our

population. Miliary tuberculosis can be a fatal infectious etiology that can be prevented with immunization and timely diagnosis and treatment with antituberculosis drugs.[9]

We also reported other etiologies like malaria, leishmaniasis, Salmonella, chronic granulomatous diseases, Parvovirus B19 and HIV as infectious causes of pancytopenia. Other studies also reported malaria, visceral leishmaniasis, brucellosis, and sepsis as the common infections etiologies of pancytopenia.[10-12]This represents the broad spectrum of infectious etiologies of pancytopenia in children. In addition, neoplastic causes of pancytopenia in children should not be overlooked. Although neoplastic causes of pancytopenia in children are more common in developed countries, their prevalence is also increasing in developing countries. In the present study, ALL was described as one of the major neoplastic causes of pancytopenia. A study from India reported comparable findings with ALL being a common neoplastic cause of pancytopenia among the pediatric age group.[13]Other studies from developing countries report the prevalence of ALL to be between 13% and 23%. [8,10]Some other less common causes of pancytopenia reported in our study were aplastic anemia, myelofibrosis, and sideroblastic anemia.

A limitation of our study is the inclusion of only one study center. A multicenter study from different hospitals would have allowed us to accurately describe the prevalence of these etiologies. The failure to include socioeconomic and cultural parameters is also a limitation of the study. Nonetheless, the results of our study necessitate dietary modification with iron and vitamin B12 supplementation in children in developing countries to prevent nutritional causes of pancytopenia. In addition, the development of cancer screening programs and timely bone marrow examinations in children with suspected neoplastic causes may contribute to timely diagnosis and prevent mortality.

Conclusion

There is a broad etiologic spectrum of pancytopenia in the pediatric population that includes nutritional, infectious, autoimmune, and neoplastic etiologies. Of these, megaloblastic anemia is the most common nutritional cause and miliary tuberculosis is the most common infectious cause. ALL is the most common malignant cause of pancytopenia. Infectious causes of pancytopenia can be prevented by improving vaccination programs and empiric antibiotic therapy. Nutritional causes can be reduced by improving dietary habits and supplementation with vitamin B12 and iron. In conclusion, although aplastic anemia and leukemia are considered common causes of pancytopenia, megaloblastic anemia was the most common cause of pancytopenia in this series. Early detection of these diseases will certainly have an impact on morbidity and mortality in vulnerable pediatric patients. It is important that these disorders be recognized as common causes of pancytopenia so that appropriate investigative and therapeutic measures can be initiated promptly and relatives are not told a uniformly poor prognosis.

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