Original Article

Clinico-Hematological Study of Pancytopenia in Pediatric Age Group at a Tertiary Care Hospital in Kachchh District, Gujarat, India

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Abstract

Background: Pancytopenia is a common pediatric hematological finding seen on routine CBC reports. It is defined as a reduction in all three major formed elements of blood—erythrocytes, leucocytes, and platelets. It may result from a number of disease processes, either primarily or secondarily involving the bone marrow. Careful assessment of blood elements is often the first step in evaluating hematologic function and diagnosing disease, followed by bone marrow evaluation.

Materials and Methods: This was a hospital-based observational study conducted in the Department of Pathology, Bhuj, from January to June 2024. A total of 60 patients aged 6 months to 18 years with pancytopenia were enrolled in our study. All blood samples were evaluated using a cell counter, and a complete hemogram was obtained.

Results: Out of 60 patients, the majority were between 6 months and 6 years old. The male-to-female ratio was 0.7:1. The most common etiological factors were deficiency anemia, infections, and other causes. Generalized weakness and fever were the most common presenting symptoms. The most common signs were pallor and splenomegaly.

Conclusion: The present study concludes that clinical findings and peripheral blood pictures provide valuable information in the workup of patients with cytopenias. They aid in diagnosing the majority of pancytopenic children and help in planning further investigations.

Keywords:

Pancytopenia, anemia, peripheral smear, bone marrow evaluation

Introduction

Normal hematopoiesis occurs within a specialized microenvironment, where humoral factors also play an important role. Hematopoiesis markedly increases in response to increased demands. Mature blood cells derived from pluripotent stem cells are then released into circulation.

Pancytopenia is a common pediatric hematological finding seen on routine CBC reports. Pancytopenia is defined as a reduction in all three major formed elements of blood—erythrocytes, leucocytes, and platelets [1]. Pancytopenia is not a disease entity but a triad of findings that may result from a number of processes [1]. It may result from a number of disease processes—primarily or secondarily involving the bone marrow [2].

The underlying pathogenic mechanisms of cytopenias are variable and include a decrease in hematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective hematopoiesis with cell death, defective cell formation that is removed from the circulation, antibody-mediated destruction of cells, or trapping of cells in a hyperplastic and overactive reticuloendothelial system [3-5]. Other causes of suppressed hematopoiesis include nutritional deficiencies, as observed in vitamin B12, folate, and iron deficiency [3,4].

Pancytopenia is linked to organomegaly, and lymphadenopathy typically indicates the presence of cancer or bone marrow failure syndromes, although there are several other easily curable reasons that can present similarly [6]. The incidence of various hematological disorders causing pancytopenia varies due to differences in age groups, geographical distribution, nutritional status, prevalence of infectious disorders, and genetic predisposition [7]. The presenting symptoms, such as weakness, fatigue, dyspnea, fever, and bleeding manifestations, are usually attributable to the presence of anemia, leucopenia, or thrombocytopenia [8]. Leucopenia is an uncommon cause of initial presentation but can become the most serious threat to life during the course of the disorder.

Careful examination of the blood film is important if the reason for pancytopenia is not apparent from the clinical history. If this does not reveal the cause, bone marrow examination might be needed [9,10]. Careful assessment of blood elements is often the first step in evaluating hematologic function and diagnosing disease [7]. The peripheral blood picture and physical findings are useful in the work-up of patients with pancytopenia and in planning bone marrow investigations [11]. Bone marrow evaluation is an invaluable diagnostic procedure in medical practice, which may confirm the diagnosis of suspected cytopenia based on clinical features and peripheral blood examination or occasionally reveal a previously unsuspected diagnosis [12].

The severity of pancytopenia and the underlying pathology determine the management and prognosis of patients [11]. Aplastic anemia is the most common cause of pancytopenia according to worldwide research studies, which contrasts with studies done in India. The causes of pancytopenia in pediatric age groups are not well defined in India. However, megaloblastic anemia is the most common cause of pancytopenia according to previous Indian studies. Timely recognition of the underlying pathology will not only impact the mortality and morbidity of vulnerable pediatric patients but will also help in treating simple and easily manageable conditions like megaloblastic anemia, which can present with drastic symptoms but can be effectively treated.

Aim and Objective:

To identify the etiologies of pancytopenia in pediatric patients and correlate clinical presentations with hematological findings to aid in the management of pancytopenia.

Materials and Methods

Place of Study: The present study entitled “Clinico-hematological study of pancytopenia in pediatric age group at tertiary care hospital of Kachchh district, Gujarat state, India" was carried at the Department of Pathology in our institute.

Design of Study: Observational study. Study Period: Study conducted over a period of 6 total months (January to June 2024). Sample Size: 60 Patients of age group 6 month to 18 years admitted in our institute with a hematological diagnosis of pancytopenia during the study period. Selection of Data: Inclusion Criteria: Patients belonging to the age group of 6 months to 18 years. Hb < 10 gm %, leucocytes count < 4000/ cu mm, platelet count < 1.5 lac/ cu mm. Exclusion Criteria: Patient with diagnosed causes of pancytopenia. Patient on treatment of pancytopenia. Collection of Data: Clinical history and examination of all identified cases of pancytopenia were taken. 2 ml of anticoagulant blood was collected & evaluated in cell counter (Sysmex XN1000).

Complete hemogram obtained which include: Hemoglobin, RBC count, RBC indices include MCV, MCH, MCHC, and RDW, WBC count & differential count, Platelet count. Other investigations were done are: Peripheral smear examination, Malarial parasite detection Reticulocyte count, Following investigation done as & when require: Biochemical Tests: S. Vit B12 & folate, Iron study, S. LDH (Serum Lactate Dehydrogenase), Liver function test, Other Hematological Tests: Coagulation profile, Bleeding time & clotting time, Anti-human globulin test, Sickling & G6PD (Glucose-6-phosphatase deficiency) Deficiency, HPLC.

Results

In our study, 60 patients who presented with pancytopenia were studied. The following results were recorded and analyzed. In the present study, non-malignant conditions were more commonly seen than malignant conditions as the causative etiology of pancytopenia. Among non-malignant conditions, nutritional anemia was the most common, observed in 53.34% of cases, followed by infections in 38.33% of cases. Within nutritional anemia, megaloblastic anemia was the most prevalent, constituting 31.67% of the cases. Among infections, malaria (Figure 1) was the most frequently encountered, seen in 26.67% of cases.

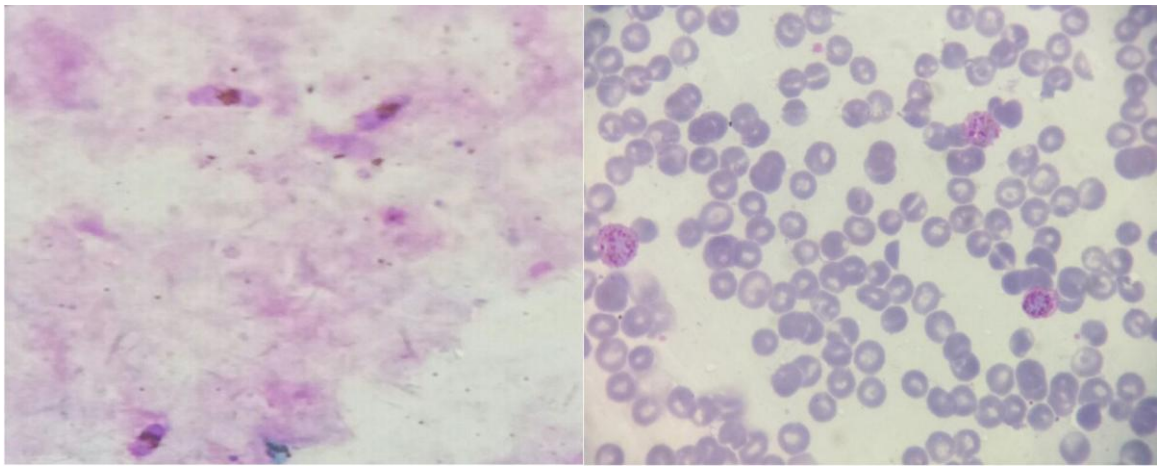

Figure 1: (a): Gametocyte of P. falciparum in thick smear (Field stain 100×), (b): Schizont form of P. vivax in peripheral smear (Field stain 100x)

Malignancy was seen only in 5% cases. In present study, megaloblastic anemia was most common cause of pancytopenia followed by malaria. (Table 1). Pancytopenia have shown highest incidence in the age group of 6 month- 6 years and its occurrence was less frequent in the age group of 7 years- 10 years. The incidence of pancytopenia showed slight preponderance among females. Approximately male to female ratio was 0.7:1. (Table 2).

In present study, the commonest mode of presentation was generalized weakness, which was present in patients constituting 58.33%. The other main symptoms were fever (53.33%). In present study, pallor was noted in all cases. Splenomegaly (35%), hepatomegaly (16.67%) was seen in cases of megaloblastic anemia, leukemia (Fig. 2), aplastic anemia and malaria. In present study, haemoglobin percentage varied from 2.5 – 9.8 gm %.

Most of patients had haemoglobin percentage between 4.1-7 gm %. Lowest value of 2.5 gm% was seen in iron deficiency anaemia. Total leucocyte count ranged from 1000 – 3900 cells/mm3. Most of patients had white cell count in range of 2501 – 4000 cells/mm3. Lowest count of 1000 cells/mm3 was seen in a case of megaloblastic anaemia. In our study, platelet count ranged from 7000 – 1, 40,000 /mm3. Most of patients had platelet count <50,000 /mm3. Lowest platelet count of 7000 /mm3 was seen in case

of megaloblastic anemia. In Peripheral smear examination majority of the cases showed macrocytosis (35%) (Fig. 3) followed by normocytic normochromic picture (30%).

Table 1: Distribution of various causes of pancytopenia

Serial no.	Causes	No. of cases	Percentage (%)
1.	**Non - malignant**	**57**	**95%**
	Nutritional anemia	**32**	**53.34**
	Megaloblastic anemia	19	31.67
	Iron deficiency anemia	10	16.67
	Nutritional anemia	03	5.00
	Infections	**23**	**38.33**
	Malaria	16	26.67
	Typhoid	02	3.33
	Dengue	02	3.33
	Pulmonary tuberculosis	02	3.33
	Parvovirus B19	01	1.67
	Aplastic anemia	**02**	**3.33**
2.	**Malignant**	**03**	**5**
	Acute leukemia	02	3.33
	Myelodysplastic syndrome	01	1.67
	Total	**60**	**100**

Table 2: Incidence of pancytopenia in different age groups

Serial No.	Age groups	Male	Female	No. of cases	Percentage (%)
1.	6 month – 6 year	12	13	25	41.67
2.	7 year - 10 year	02	03	05	8.33
3.	11 year- 14 year	06	08	14	23.33
4.	15 year – 18 year	05	11	16	26.67
	Total	**25**	**35**	**60**	**100**

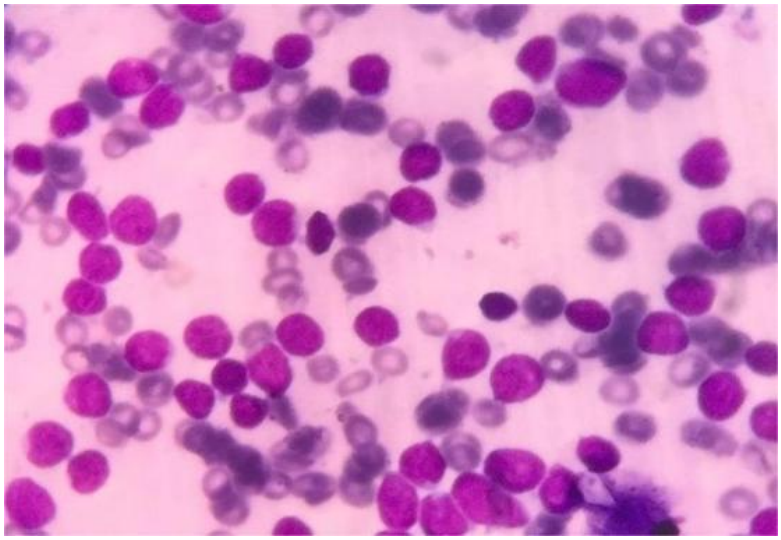

Figure 2: Bone marrow aspiration showing blasts in acute leukaemia (Field stain 100x)

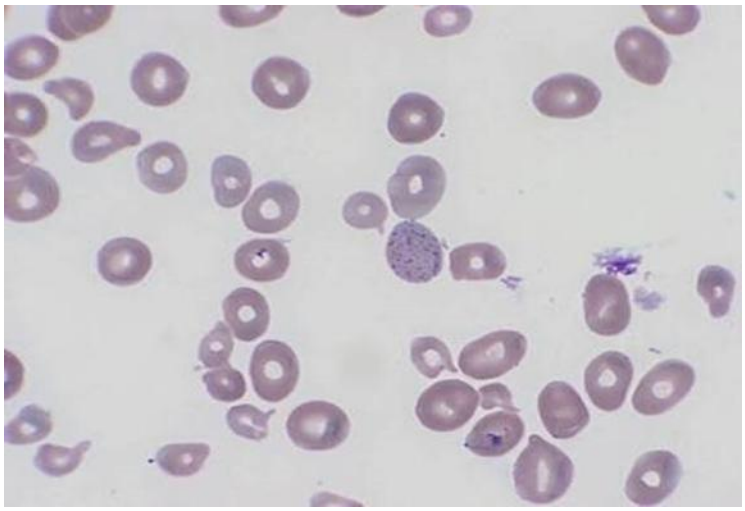

Figure 3: Peripheral smears showing macrocytes and basophilic stippling in case of Megaloblastic anemia (Field stain 100 x).

Bone marrow aspiration has been performed in 20 patients. Bone marrow aspirations in present study of pancytopenia showed three distinct cellularity- hypercellularity, hypocellularity & normocellularity. Hypercellular bone marrow was observed in 9 patients. In the present study of pancytopenia, megaloblastic anaemia (Fig. 3,4) was seen in 55.56% of total cases of pancytopenia with hypercellular marrow. In present study, 6 patients out of 20 cases of pancytopenia showed hypocellular marrow. Among hypocellular marrow most common causes was aplastic anemia (33.3%) and iron deficiency anemia (33.3%).

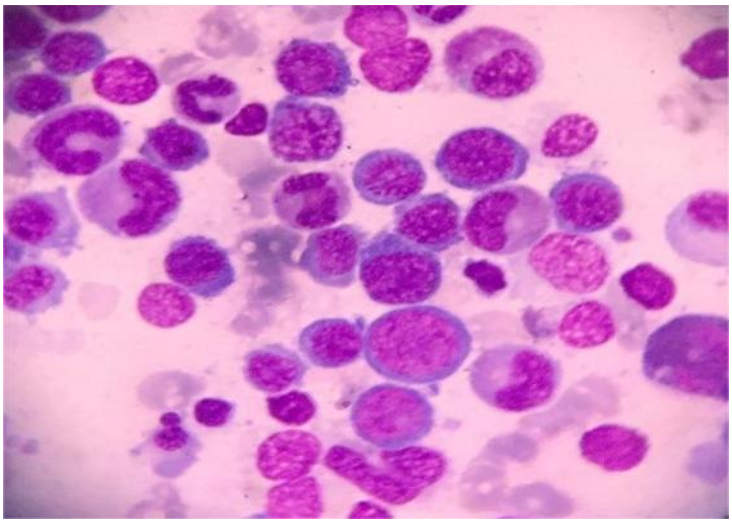

Figure 4: Bone marrow aspiration showing erythroid hyperplasia with Megaloblastic erythropoiesis (sieve like nuclear chromatin) (Field stain 100x)

Discussion

In our study, statistical data on age, sex, presenting complaints, systemic examination, peripheral smear examination, biochemical analysis, and bone marrow aspiration (as and when required) were studied and compared with those published in the literature.

In the present study, the M:F ratio was 0.7:1; there was no significant difference in incidence between males and females, which was in accordance with Dubey SRK et al. [13] (0.88:1). The present study found that the majority of patients were between the age group of 6 months to 6 years (41.67%), which was comparable with Syed Nadeem et al. (2017) [14] (47%) and Singh G et al. (2016) [15] (51.6%).

The variations in the frequency of various diagnostic entities causing pancytopenia have been attributed to differences in methodology, stringency of diagnostic criteria, geographic area, period of observation, genetic differences, prevalence of infection, and varying exposure to myelotoxic agents. The most common cause of pancytopenia reported in various studies worldwide has been aplastic anemia. This is in sharp contrast with the results of our study, where the most common cause of pancytopenia was megaloblastic anemia (31.67%).

We compared our study with other studies conducted in India, where megaloblastic anemia was the major cause of pancytopenia (Table 3).

Megaloblastic anemia is a rapidly correctable disorder and should be promptly diagnosed and treated. The incidence of mixed nutritional deficiency anemia was 5% in our study, which was comparable to the findings of Shazia Memon et al. [22]. In the present study, the incidence of aplastic anemia was 3.33%, which correlated with the study by Singh G et al. [15], where aplastic anemia was seen in 1.1% of cases.

Table 3: Various causes of pancytopenia compared to other studies

Author	**Year**	**Place**	**Study population**	**Number of cases**	**common causes**
Dubey SRK et al[13]	2016	India (Kanpur UP)	Children	170	Megaloblastic anaemia (47%), aplastic anaemia (25.8%), leukemia (17.6%)
Syed nadeem et al[14]	2017	Pakistan	Children	200	Megaloblastic anaemia (32%), aplastic anaemia (22%) & acute leukemia (18%)
Singh G et al[15]	2016	India	Children	153	Severe acute malnutrition (27.3%), leukemia (18.2%), dengue and thalassemia with hypersplenism (9.1%)in each, aplastic anaemia (1.1%)
Waris et al[16]	2017	Pakistan	Children	69	Aplastic anaemia (42%), acute leukemia (22%) & megaloblastic anaemia (10%)
Rathod GB et al[17]	2015	India (Gujarat)	Children	200	Megaloblastic anaemia (26.5%), aplastic anaemia (20.0%), leukemia (17.5%)
Anwar Zeb Jan et al[18]	2013	Pakistan	Children	205	Aplastic anemia (28.3%), leukemia (23.9%) & megaloblastic anemia (19.5%)
Amieleena et al[19]	2012	India (Uttarkhand)	Children	91	Megaloblastic anaemia (31.8%), malignancies (25.2%), infectious disease (19.7%) & aplastic anaemia (18.8%)
Bhatnagar et al[20]	2005	India	Children	109	Megaloblastic anaemia (28%), Aplastic anaemia and infections (21% each)
Anjali Kale et al[21]	2024	India	Children	130	Megaloblastic anaemia (43.08%), Acute leukemia (22.30%), Aplastic anemia (12.30%) and infections.
Present study	2024	India	Children	60	Megaloblastic anaemia (31.67%), Malaria (26.67%) & IDA (16.67%), Aplastic anaemia & Malignancies (3.33% each)

Conclusion

Pancytopenia is a common occurrence in the pediatric age group. The clinical presentation of pancytopenia in children can be non-specific, often leading to delays in diagnosis. The overlap of symptoms with other conditions, such as fever, fatigue, or bleeding, complicates accurate diagnosis. There is no universally agreed-upon approach for diagnosing and treating pancytopenia in pediatric populations. This lack of standardization can lead to inconsistent management practices. The present study analyzes the clinico-hematological and etiological profile of pancytopenia in children. The clinical findings and peripheral blood picture provide valuable information in the workup of patients with cytopenias, aid in pointing toward a diagnosis in the majority of pancytopenic children, and help in planning further investigations. Bone marrow examination was an essential tool for diagnosing various etiologies of pancytopenia. Although bone marrow aspiration is uncommon in suspected nutritional deficiency anemia, it is indicated when the diagnosis is not straightforward or when the patient requires urgent treatment and hematological assays are not available. As facilities for estimating folic acid, vitamin B12 levels, and serum ferritin are now available in most centers in India, the need for bone marrow aspiration has decreased. The present study concludes that the maximum age distribution was observed in the 6-month to 6-year age group. Non-malignant conditions were more common than malignant ones. Among non-malignant conditions, deficiency anemia was the most common, followed by infections. In deficiency anemia, megaloblastic anemia was more common than iron deficiency anemia. Among infections, malaria was most commonly associated with pancytopenia. Aplastic anemia and acute leukemia were less common. As most cases are easily treatable and non-malignant, early attempts should be made to confirm the etiology as soon as possible so that prompt treatment can begin early. Early management of nutritional anemia and malaria at the village level, by strengthening the healthcare system at primary health centers, can help reduce the incidence of pancytopenia.

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Competing Interests: Nil

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