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A HOSPITAL'S STUDY OF THE CLINICO-HEMATOLOGICAL PROFILE OF PANCYTOPENIA IN CHILDREN

Dr. Sangita Kadu (Tehre)[1], Dr. Asha Harwani[2]

[1]Assistant professor, Department of Pathology, Dr Panjabrao Deshmukh alias Bhausaheb Memorial Medical College, Amravati.

[2]Assistant professor, Department of Pathology, Dr Panjabrao Deshmukh alias Bhausaheb Memorial Medical College, Amravati.

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Corresponding Author:

Dr. Asha Harwani

Assistant professor, Department of Pathology, Dr Panjabrao Deshmukh alias Bhausaheb Memorial Medical College, Amravati

ABSTRACT

BACKGROUND: In our routine clinical practice, we frequently run into the clinical condition pancytopenia. All three of the blood's key components—red blood cells, white blood cells, and platelets—decline in pancytopenia. Pancytopenia is a decline in any two of the three blood cell lineages, which includes all three. These may also result from iatrogenic causes, such as certain medications, chemotherapy, or radiotherapy for cancer. Depending on the etiology, the bone marrow image can range from normocellular with subtle alterations to hypercellular with a complete replacement of malignant cells. Clinically, these can result in fever, pallor, infection, acute sickness, or even death depending on the cause, severity, and length of the impairment. For targeted treatment and prognostication, it's critical to understand the precise cause.

AIM: The aim of the study was to describe the different etiologies of pancytopenia in pediatric patients based on clinical and hematological profiles including peripheral blood and bone marrow examination

MATERIAL AND METHOD: The current study was an observational hospital-based investigation conducted at the Pathology Department. Before beginning this investigation, the institutional ethical committee gave its written consent. Thirty kids, of either gender, who were admitted to the hospital and met the inclusion requirements, were included in the study after receiving their parents' written, informed consent. All children between the ages of one month and fifteen years who were admitted to the hospital with pancytopenia met the inclusion criteria for this study. At the time of presentation, a thorough history, clinical examination, and hematological parameters were noted. Hemoglobin, red cell indices, total and differential leukocyte counts, platelet count, peripheral blood smear morphology, and bone marrow aspiration/biopsy were all part of the hematological profile.

RESULTS: During the study period, 30 children of age group 1 month to 15 years who presented with pancytopenia were studied. They consisted of 20 males and 10 females. Fever (88%) was the commonest symptom at presentation followed by bleeding manifestations (78.5%), abdominal pain (35.7%), and weight loss (43.3%). All children with pancytopenia had pallor 30 (100%). Other findings were splenomegaly (64.2%), hepatomegaly (59.5%), lymphadenopathy, and hyperpigmented knuckles (38%). The most common condition causing pancytopenia in our study was megaloblastic anemia 14 (46.67%), followed by acute lymphoblastic leukemia 5 (16.67%), and 3rd was aplastic anemia 2 (6.67%).

CONCLUSION: Pancytopenia is a frequent hematological disorder that doctors deal with on a daily basis in both inpatient and outpatient settings. Patients who report with generalized weakness, easily fatigued, pallor, and bleeding symptoms or pyrexia should be suspected of having pancytopenia. Pancytopenia can be diagnosed by aspiration cytology, biopsy, and bone marrow exams. Megaloblastic anemia was revealed to be the most frequent cause of pancytopenia in this series, despite the fact that aplastic anemia and leukemia are thought to be prevalent causes.

KEYWORDS: Anemia, Hematological profile, Pancytopenia and Thrombocytopenia

INTRODUCTION

In our routine clinical practice, we frequently run into the clinical condition pancytopenia. Pancytopenia, a clinical trial brought on by primary or secondary bone marrow involvement, is not a disease.[1,2] Pancytopenia may result from straightforward, treatable causes such drug-induced hypoplasia and megaloblastic anemia, or it may result from fatal conditions like leukemia or bone marrow aplasia.[3] All three of the blood's key components—red blood cells, white blood cells, and platelets—decline in pancytopenia.[4] When hemoglobin is <12.0 gm/dl, total leucocyte count less than 4x109/L and platelet count <100x109/L.

Pancytopenia is a prevalent condition among hospital patients. Pancytopenia is not a sickness in and of itself; rather, it is a complication of several disorders.[5,6] Anemia, leucopenia, or thrombocytopenia may be the cause of the symptoms, which include weariness and dyspnea. Thrombocytopenia can cause mucosal bleeding and bruises. Leucopenic symptoms are uncommon when they first appear, but can develop into a life-threatening condition as the disease progresses.[7] All three blood components that are generated are decreased below the normal range in pancytopenia.[8] Pancytopenia may result from a variety of illnesses, and the sickness varies according to hereditary and geographic variances.[9] The causes of pancytopenia range from hematological malignancies and storage disorders that result in the replacement of bone marrow with malignant and storage cells to viral infections that produce self-limiting bone marrow suppression.[10] Fever, pallor, mucocutaneous hemorrhage, hepatosplenomegaly, and lymphadenopathy are some of the clinical signs of the condition that causes bone marrow suppression in children.[11] A prompt diagnosis based on suspected clinical symptoms is necessary for the initiation of treatment quickly and the avoidance of consequences.[12] Numerous causes of pancytopenia in children, including malaria, enteric fever, sepsis, and some cancers (ALL), are curable.[13] If the reason of pancytopenia was not obvious from the clinical history and examination, peripheral smear testing becomes necessary. If this does not identify the cause, a biopsy or bone marrow aspiration is required.[14] Clinical anemia results in exhaustion, shortness of breath, and heart problems. Leucopenia increases the risk of infection, while thrombocytopenia causes bruising and mucosal bleeding.[15] The prevalence of different pancytopenia causes varies according to distinct regional and genetic distributions.[16] The severity and etiopathogenesis of pancytopenia affect treatment and prognosis. The intensity of the type of cells lacking determines how pancytopenia presents clinically. An increased susceptibility to infection, weakness, dyspnea with exertion, pallor, headache, dizziness, purpura, melena, hematemesis, epistaxis, and other prepresentations are possible.[17,18]

Pancytopenia is brought on by hypersplenism and is sometimes due to hemolysis as well as splenic sequestration.[19] Cirrhosis, congestive heart failure, leukemia/lymphoma, hemoglobinopathies, and infections are among the major causes of hypersplenism. Pancytopenia can be a symptom of autoimmune diseases like systemic lupus erythematosus (SLE) when all three cell lines are impacted. When screening patients who have autoimmune diseases like rheumatoid arthritis, psoriasis, or SLE, it's critical to rule out underlying cancers like lymphoma because these patients are more susceptible to lymphoproliferative disorders.[20] Autoimmune cytopenias are also seen in autoimmune lymphoproliferative syndrome (ALPS) and common variable immunodeficiency disease (CVID).

By using peripheral smears, bone marrow aspirations, and/or bone marrow biopsies, the current study seeks to assess cases of pancytopenia and determine its origin in children, along with its clinical and hematological characteristics.

MATERIAL AND METHODS

The current study was an observational hospital-based investigation conducted at the Pathology Department. Before beginning this investigation, the institutional ethical committee gave its written consent. Thirty kids, of either gender, who were admitted to the hospital and met the inclusion requirements, were included in the study after receiving their parents' written, informed consent. All children between the ages of one month and fifteen years who were admitted to the hospital with pancytopenia met the inclusion criteria for this study. At the time of presentation, a thorough history, clinical examination, and hematological parameters were noted. Hemoglobin, red cell indices, total and differential leukocyte counts,

platelet count, peripheral blood smear morphology, and bone marrow aspiration/biopsy were all part of the hematological profile.

Inclusion criteria

- children below the age of 15 years.
- children having pancytopenia in complete blood count.

Exclusion Criteria

- Children who had received a blood transfusion in the previous 3 months.
- The patient not consenting to the participation in the study.
- The study excluded individuals with known acute leukemia and lymphoma, aplastic anemia, and malaria who were diagnosed before the study period and receiving regular therapy in our center at the time of the study.

Patients had thorough history, physical examinations, and food habits checks. The Sysmax automatic analyzer was used to create a whole hemogram. A pathologist analyzed the morphology of the RBC, macro ovalocytes, level of anisocytosis, poikilocytosis, atypical cells, hemiparasites, and blast cells in peripheral smears. Based on a clinical evaluation, bone marrow aspiration cytology was performed. Cellularity, myeloid to erythroid ratio, megaloblast, dysplastic cells, proportion of cells to fat spaces, aberrant fibrosis, and blast cells are all examined in the evaluation of bone marrow. Children with blast cells or abnormal cells in their peripheral smear had the procedure. By doing a morphological analysis on bone marrow smears or biopsy samples, the diagnosis was made. The chemiluminescence technique was used to evaluate the amounts of vitamin B12 and folic acid. Folic acid and vitamin B12 normal ranges were 211-911 pg/ml and >5.38 ng/ml, respectively. When necessary, pertinent investigations such as antibody titers for SLE, ELISAs for Dengue, and scrub typhus were also conducted.

Pancytopenia was defined as hemoglobin (Hb) ≤10 g percent, absolute neutrophil count (ANC) ≤1.5 109 /l, and platelet count (PC) ≤100 109 /l. Pancytopenia was labeled as severe if the patients had two or more of the following: Hb ≤7 g percent, ANC ≤0.5 109 /l, and platelet count ≤20 109 /l. At the presentation, the hematological values and the full clinical profile were noted. According to the clinical recommendation, a trephine biopsy and bone marrow aspiration were performed. The bone marrow treatment and further staining were completed using conventional techniques. Hematoxylin and eosin and May-Grunwald Giemsa were used to stain all of the trephine biopsies and bone marrow aspirate smears, respectively. When necessary, special staining was carried out on aspirate smears for myeloperoxidase, Sudan black B, periodic acid Schiff and Perl's stain, and reticulin stain on biopsy. For the aspiration and biopsy of the bone marrow, informed consent was obtained.

STATISTICAL ANALYSIS

The data was entered in Microsoft excel and further statistical analysis was done using the IBM SPSS software statistics 20 trial version.

RESULT:

During the study period, 30 children of age group 1 month to 15 years who presented with pancytopenia were studied. They consisted of 20 males and 10 females.

Table 1: Age and gender-wise distribution

Age group	Males	Females	Total no.
1 Month - 1 year	3	0	3 (10%)
1 year -5 years	8	3	11 (36.67%)
6 years- 12 years	6	6	12 (40%)
>12 years	3	1	4 (13.33%)
Total	20	10	30 (100%)

Table 2: Presenting complaints and physical findings in pancytopenia

Presenting symptoms and signs of pancytopenia	Number of patients
Fever	17 (56.67%)
Bleeding manifestations	15 (50%)
Petechial rashes	9
Hematemesis	07
Bleeding from gums	07
Malena	04
Pain Abdomen	11 (36.67%)
Pallor	30 (100%)
Splenomegaly	14 (46.67%)
Hepatomegaly	13 (43.33%)
Lymphadenopathy	12 (40%)
Hyperpigmented knuckles	12 (40%)
Petechial rashes	10(33.33%)
Bleeding gums	07 (23.33%)

Fever (56.67%) was the commonest symptom at presentation followed by bleeding manifestations (50%), abdominal pain (36.67%). All children with pancytopenia had pallor 30 (100%). Other findings were splenomegaly (46.67%), hepatomegaly (43.33%), lymphadenopathy, and hyperpigmented knuckles (40%).

Table 3: Hematological parameters in three subgroups of pancytopenia

Parameters	Megaloblastic anemia	Leukemia	Aplasticanemia
Hb(gm/dl)	1.9-7	2-6.1	1.0-6.7
TLC (mm^3)	800-3800	400-3700	600-3000
Platelets(mm^3)	14,000-19,000	11,000-97,000	14,000-49,000

17 children (45.2%) had Hb levels of 4 to 7gm/dl. The lowest level of hemoglobin was 1.0 gm/dl, this child had aplastic anemia. The majority of children (67%) had leukocyte counts in the range of 2000- 4000/mm^3. The lowest level was noted in the case of leukemia which was 400/mm^3. 15 children (38%) had platelets value of 19,000 to 49,000.

Table 4: Bone marrow cellularity in cases of pancytopenia

Bone marrow findings	No. of patients
Normocellular marrow	3 (10%)
Hyper cellular marrow	25 (83.33%)
Hypocellular marrow	2 (6.67%)
Total	30

We found hypercellular marrow in 25 (83.33%) cases and megaloblastic anemia (46.67%) was the most common cause of hypercellularity. The most common cause of hypocellularity was aplastic anemia, all 2 (6.67%) children had hypocellular bone marrow.

Table 5: Etiological profile of pancytopenia

S. No.	Etiology	N (%)
1.	Megaloblastic anemia	14 (46.67%)
2.	ALL	5 (16.67%)
3.	Aplastic anemia	2(6.67%)
4.	AML	1(3.33%)
5.	Scrub typhus	2(6.67%)
6.	Falciparum malaria	2(6.67%)
7.	CLD with PHTN	2(6.67%)
8.	Dengue	1(3.33%)
9.	SLE	1(3.33%)
	Total	30

The most common condition causing pancytopenia in our study was megaloblastic anemia 14 (46.67%), followed by acute lymphoblastic leukemia 5 (16.67%), and 3rd was aplastic anemia 2 (6.67%). In this study infectious cause of pancytopenia was, scrub typhus (6.67%) and falciparum malaria (6.67%) dengue 1(3.33%). Other causes were portal hypertension and SLE.

DISCUSSION

We frequently face the clinical condition of pancytopenia, which has a number of etiological causes. It can be brought on by a decline in bone marrow activity or a rise in blood cell apoptosis. **Jha et al.2008**[21] from Nepal studied the causes of pancytopenia in 148 patients. In their investigation, megaloblastic anemia, seen in 35 instances (23.6%), hypoplastic bone marrow, seen in 43 cases (29%), and hematological malignancy, seen in 32 cases (21.6%), were the most frequent causes of pancytopenia. The most frequent etiology mentioned by them was megaloblastic anemia (30.2%) in adults and hypoplastic bone marrow (38.1%) in children. In a bone marrow aspiration research conducted in their pediatric unit, megaloblastic anemia was identified as the most common diagnosis and the primary cause of cytopenia and pancytopenia.[22] Another study from Pakistan by **Memon et al.2008**[23] on 230 pancytopenia children found the most common causes of pancytopenia as aplastic anemia, megaloblastic anemia, leukemia and infections. In their study, children with pancytopenia frequently presented with pallor, fever, petechial hemorrhages, visceromegaly, and nose and gastrointestinal bleeding.

Bhatnagar et al.2005[24] who retrospectively analyzed 109 pediatric patients presenting with pancytopenia, found megaloblastic anemia as the single most common etiological factor causing pancytopenia in 28.4% of children, followed by acute leukemia and infections in 21% of patients each, and aplastic anemia in 20% cases. **Gupta et al.2008**[25] reviewed 105 children aged 1.5–18 years with pancytopenia. In their study, aplastic anemia was the most common cause of pancytopenia (43%), followed by acute leukemia (25%). Infections, of which kala-azar was the most prevalent, were the third most frequent cause of pancytopenia. They discovered megaloblastic anemia in 6.7% of the kids. Their cohort's most frequent presenting complaints were fever and increasing pallor (81.4%), followed by bleeding signs (72.9%).

A few number of studies evaluating the spectrum of pachytopenia in children have been published in the literature. Many short-lived illnesses and serious, life-threatening disorders are characterized by pancytopenia. Different population groups exhibit the disease's pattern more frequently, which has been linked to variations in myelotoxic medication exposure, infection prevalence, and nutritional state.[25] Numerous investigations on the range of pancytopenia have been carried out all around the world. Megaloblastic anemia was the most common cause of pancytopenia in a research from Zimbabwe that included 134 patients with the condition. Aplastic anemia and acute leukemia were the next most common causes.[24]

A retrospective study done by **Bhatnagar et al.2015**[24] on 109 pediatric patients presenting with pancytopenia, found megaloblastic anemia (28.4%) is the most common etiological factor causing pancytopenia in children followed by acute

leukemia (21%) and infections (20%). **Gupta et al2008**[25] reviewed 105 children with pancytopenia at BHU and found aplastic anemia (43%) followed by acute leukemia (25%) and infections (most common kala-azar).

Khunger et al 2002[4] an India study of 200 cases reported megaloblastic anemia in 72% and aplastic anemia in 14%. **Savage et al1999**[26] in Zimbabwe studied 134 patients identifying megaloblastic anemia to be the most common followed by aplastic anemia and acute leukemia. **Khan et al2012**[27] in Pakistan showed acute anemia to lead followed by aplastic anemia and then megaloblastic anemia. **Imbert et al1989**[28] in France studied 213 cases and found malignant myeloid disorder in 42%, lymphoid disorder in 18%, and aplastic anemia in 10%. **Naseem et al2011**[29] showed fever (65.5%) most common followed by pallor and hepatomegaly. When peripheral blood was examined, it revealed macrocytes with hyper-segmented neutrophils, which allowed for the diagnosis of megaloblastic anemia. In all series of cells, there is a depression because DNA maturation is being delayed. Megaloblasts and enhanced erythropoiesis were present in the hypercellular bone marrow aspirate.[30]

The study may have been biased because of the number of cases that were likely caused by infections that were common during the specific season and required hospital admissions. In our investigation, infections, acute leukemia, and aplastic anemia were the most frequent etiologies of pancytopenia in children, which indicates considerable underlying disease. Palor was the most typical examination finding in children with pancytopenia, according to several investigations. According to several research conducted worldwide, acute leukemia, megaloblastic anemia, and aplastic anemia are the most frequent etiologies of pancytopenia. Pancytopenia that is accompanied with organomegaly, fever, pallor, and bleeding indicates underlying bone marrow diseases or cancers that call for a complete workup. Examinations of the bone marrow and peripheral smears aid in the diagnosis of such conditions.

CONCLUSION:

Pancytopenia is a frequent hematological disorder that doctors deal with on a daily basis in both inpatient and outpatient settings. Patients who report with generalized weakness, easily fatigued, pallor, and bleeding symptoms or pyrexia should be suspected of having pancytopenia. Pancytopenia can be diagnosed by aspiration cytology, biopsy, and bone marrow exams. Megaloblastic anemia was revealed to be the most frequent cause of pancytopenia in this series, despite the fact that aplastic anemia and leukemia are thought to be prevalent causes. Many of these individuals can arrive at the hospital's emergency room bleeding severely from thrombocytopenia and pancytopenia. The damaged bone marrow will rapidly improve and the related issues will stop with immediate vitamin B12 and folic acid treatment. Early diagnosis of these illnesses will undoubtedly reduce morbidity and death in pediatric kids at risk. Additionally, illnesses including enteric fever, malaria, and fulminant sepsis in underdeveloped nations require cautious evaluation because these conditions may unnecessarily stump attending clinicians.

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