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Original Research

Clinico-Hematological Study of Pancytopenia at a Tertiary Care Center

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ABSTRACT:

Background: Pancytopenia is a condition characterized by a triad of findings, which includes a reduction in all three major types of formed blood elements: erythrocytes (red blood cells), leukocytes (white blood cells), and platelets. The objective of the current study is to investigate the clinical profile of patients who present with pancytopenia. Additionally, the study aims to identify the underlying causes that lead to pancytopenia and explore the bone marrow morphology associated with various etiologies of pancytopenia. This research will contribute to a better understanding of this complex and often challenging medical condition. **Methods**: A study of 200 pancytopenia patients admitted to the general medicine department involved the selection of patients who underwent a thorough examination of their clinical history, physical condition, and subsequent laboratory tests. The data collected were then organized and presented in tables or graphs and subjected to analysis. **Results**: The study encompassed a total of 200 patients aged between 15 and 90 years. It was characterized by a male predominance, with a male-to-female ratio of 2.2:1. The most frequently observed clinical presentations were generalized weakness, which was present in 60% of cases, followed by fever in 48%. Among the common physical findings, pallor was detected in all patients, while splenomegaly was seen in 15 patients and hepatomegaly in 8 patients.When examining bone marrow aspiration cytology, the study revealed that 62% had a hypercellular marrow, 13% had a normocellular marrow, and 25% had a hypocellular marrow. Megaloblastic erythropoiesis with hypercellular marrow was observed in 78 cases. Additionally, 26 cases were diagnosed as acute leukemia, and 4 cases were diagnosed as myelodysplastic syndrome (MDS). Hypocellular marrow was diagnosed in 50 cases, out of which 36 cases were attributed to idiopathic aplastic anemia, 4 to scrub typhus, and 4 to systemic lupus erythematosus (SLE). Furthermore, 2 cases each of post-partum aplastic anemia, disseminated tuberculosis, and methotrexate-induced aplastic anemia were identified. **Conclusion**: The study's findings led to the conclusion that megaloblastic anemia stands out as the most prevalent and potentially reversible cause of pancytopenia.

Keywords: Pancytopenia, megaloblasticanemia, bone marrow

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INTRODUCTION

Pancytopenia is a condition characterized by a trio of abnormalities, involving a decrease in all three major components of the blood: red blood cells, white blood cells, and platelets. In adults, pancytopenia is recognized when hemoglobin levels fall below 13.5 gm/dl in males or 11.5 gm/dl in females, the white blood cell count drops below 4 × 109/L, and platelet counts dip below 150 × 109/ L. It can be attributed to a variety of causes, both related to blood formation (hematopoietic) and not (non-hematopoietic)[1]. Pancytopenia typically develops slowly, but it can present diagnostic challenges when it arises suddenly or is incidentally discovered.

It's important to note that pancytopenia is not a disease in itself; rather, it serves as an indicator of an underlying medical condition, often marked by symptoms and signs associated with anemia and low platelet counts. The causes of pancytopenia can be categorized into two main types: central and peripheral.[2]

1. Central pancytopenia involves conditions that affect the bone marrow itself. This can occur due to various factors such as exposure to toxins that damage the marrow, the replacement of normal marrow tissue with abnormal or malignant tissue, or the suppression of normal marrow growth and differentiation.

2. Peripheral pancytopenia, on the other hand, results from increased destruction of blood cells in the bloodstream.

Pancytopenia underscores the importance of thorough medical evaluation to identify the root cause and initiate appropriate treatment.

Potential mechanisms contributing to pancytopenia encompass the swift removal of faulty cells from circulation, the sequestration or destruction of cells through antibody actions, and the retention of normal cells within an enlarged and hyperactive reticuloendothelial system[3]. The diagnostic workup required to establish a pancytopenia diagnosis is often quite comprehensive, involving a detailed clinical history, medication history, physical examination, and standard hematological assessments, including a complete blood count (CBC), reticulocyte count, observation of peripheral blood smears, and bone marrow examination. Bone marrow examination, in particular, serves as a valuable diagnostic tool in medical practice and can unveil the underlying pathology in approximately 75% of pancytopenia cases. In select instances, additional tests and evaluations are necessary to reach a definitive diagnosis[4].

Despite these extensive diagnostic efforts, there remains a subgroup of patients with unexplained cytopenia, categorized under the label of "idiopathic cytopenias of unknown significance." The present study was initiated to examine the clinical characteristics of patients presenting with pancytopenia, pinpoint the root causes of pancytopenia, and scrutinize bone marrow morphology in various pancytopenia cases.

MATERIALS AND METHODS

An observational study on patients with pancytopenia was carried out with prior approval from the institute's ethical committee[5]. A total of 200 consecutive patients were selected based on specific inclusion and exclusion criteria. Informed consent was obtained from all the participating patients.

The study included individuals aged 15 years and above who presented with peripheral pancytopenia, defined as hemoglobin levels below 10 gm/dl, total leukocyte counts (TLC) below 4,000/µL, and platelet counts below 150,000/µL. These patients also expressed their willingness to undergo a bone marrow aspiration study as part of the diagnostic evaluation. Patients with pancytopenia in whom bone marrow examination was not necessary, not performed, or those who did not provide consent were excluded from the study. Additionally, patients who had already been diagnosed with a hematological disorder, malignancy, HIV infection, or were undergoing treatment with chemotherapy or other immunosuppressive agents were also excluded[6].

The selected patients underwent a comprehensive assessment, including a detailed clinical history, physical examination, and a range of laboratory investigations. These investigations consisted of a complete blood count (CBC), erythrocyte sedimentation rate (ESR), examination of peripheral blood smears, and measurement of reticulocyte counts. Bone marrow aspiration was performed for all patients, while bone marrow biopsy was conducted in selected cases. Various additional tests were carried out for all cases, such as viral studies (Hepatitis B surface antigen, Anti-HCV, and HIV), liver function tests (LFT), kidney function tests (KFT), chest X-ray (CXR), and abdominal ultrasound (USG)[7].

In certain selected cases, additional viral studies for hepatitis A, Epstein-Barr virus, and cytomegalovirus were performed, along with assessments of Vitamin B12 and folate levels, Coomb's test, antinuclear antibody (ANA), and anti-dsDNA levels. The data collected from patient histories, clinical examinations, and all investigations were compiled in tabulated or graphical formats and subsequently subjected to analysis.

RESULTS

In the study, a total of 200 patients within the age range of 15 to 85 years were included. The male population dominated with 138 males compared to 62 females, resulting in a male-to-female ratio of 2.2:1. Among the most common clinical presentations, generalized weakness was reported by 61% of patients, followed by fever in 47%[8]. The most prevalent physical finding was pallor, observed in all patients, and splenomegaly and hepatomegaly were noted in 15 and 8 patients, respectively.Hemoglobin (Hb) levels ranged from 1.9 gm/dl to 12.5 gm/dl, with the lowest Hb recorded in a 40-year-old female who was subsequently diagnosed with systemic lupus erythematosus (SLE). Total leukocyte count (TLC) varied between 1800 /cumm and 3700 /cumm, while platelet counts ranged from 10,000 to 90,000 /cumm.Bone marrow aspiration cytology revealed hypercellular marrow in 62% of cases, normocellular marrow in 13%, and hypocellular marrow in 25%. It was evident that there was a spectrum of diseases that could lead to pancytopenia with hyperplastic bone marrow

Indeed, there was a wide spectrum of diseases that could result in pancytopenia with a hypercellular bone marrow[9]. Among these cases, 78 patients displayed megaloblastic erythropoiesis with hypercellular marrow. In the remaining cases with hypercellular marrow and peripheral pancytopenia, 12 patients were found to have hypersplenism, and 4 patients had dimorphic anemia.In the context of hematological malignancies, the study identified 26 cases of acute leukemia, with the highest incidence observed in the age range of 15-24 (8 cases), followed by 4 cases each in the age ranges of 25-34 and 35-44, and 2 cases in the 45-54 age group. Additionally, 4 cases were diagnosed as myelodysplastic syndrome (MDS) and were recommended for karyotyping.The maximum concentration of hypoplastic marrow was observed in

the age range of 15-24, followed by 10 cases in the age range of 45-54[10]. Out of the 50 cases with hypocellular marrow, 36 were diagnosed as idiopathic aplastic anemia, while 4 cases each were attributed to scrub typhus and systemic lupus erythematosus (SLE). Two cases of post-partum aplastic anemia were reported in young females, and 2 cases of hypocellular marrow were found in patients suffering from disseminated tuberculosis. Two cases showed pancytopenia following methotrexate treatment for rheumatoid arthritis.Normocellular marrow was observed in 8 cases of dimorphic anemia, 4 cases of Kala-azar, 2 cases each of disseminated tuberculosis and falciparum malaria, and 2 cases each of metastatic adenocarcinoma and non-Hodgkin lymphoma (NHL). Furthermore, 6 cases exhibited bone marrow aspiration cytology results as normocellular marrow with reactive changes.

Table 1: Signs and symptoms of the patients

S.No.	Signs&Symptoms	No.of patients'
1	Weakness	124
2	Fever	94
3	Vomiting	26
4	Palpitation	10
5	Bodyache	10
6	Giddiness	10
7	Lossofappetite	14
8	Dyspnea	8
9	Chestpain	02
10	Hemoptysis	04
11	Recurrentnasalbleed	06
12	PVbleeding	02
13	Melena	04
14	Epigastricpain	08
15	Loosemotion	08
16	Oralulcers/glossitis	04
17	Facialswelling	02
18	Hepatomegaly	16
19	Splenomegaly	30
20	Lymphnode	04
21	Jaundice	06

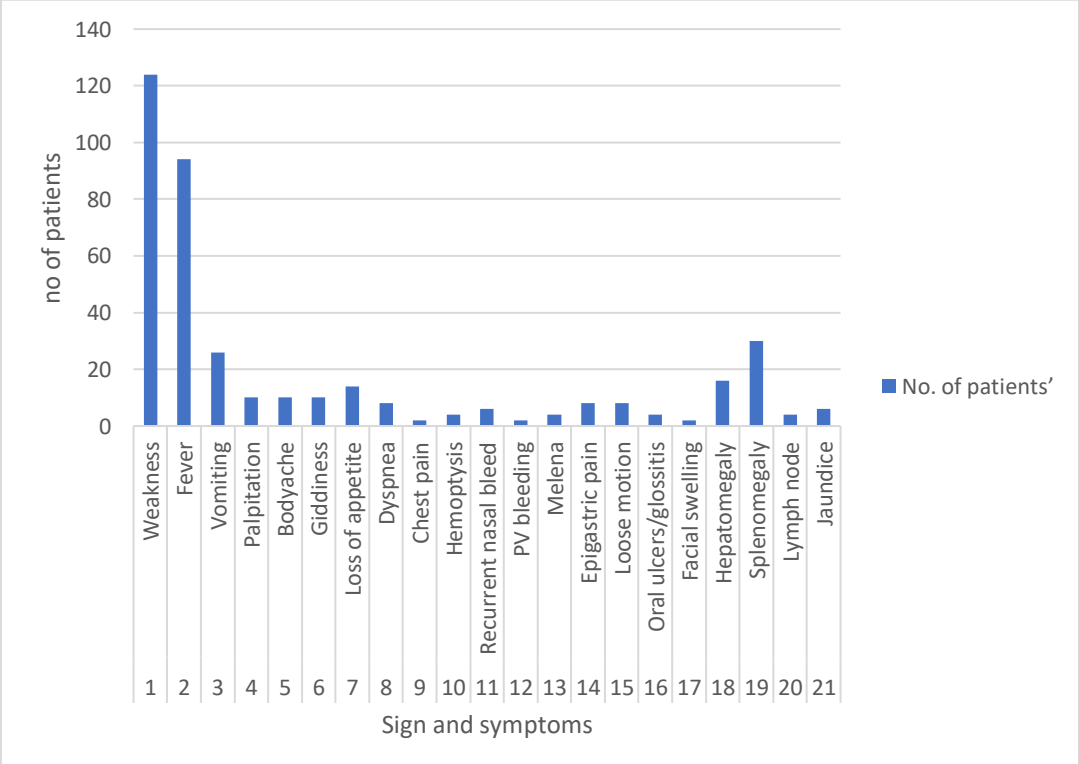

Table-2: Various causes of pancytopenia

Diagnosis	Cellularity	Male	Female	Total
Megaloblastic anemia	Hypercellular	54	24	78
Acute leukemia	Hypercellular	18	08	26
Hypersplenism	Hypercellular	10	02	12
Dimorphic anemia	Hypercellular	-	04	04
Myelodysplastic syndrome	Hypercellular	04	-	04
Non Hodgkins Lymphoma	Normocellular	02	-	02
Dimorphic anemia	Normocellular	04	04	04
Disseminated tuberculosis	Normocellular	02	-	02
Falciparum malaria	Normocellular	02	-	02
Leishmaniasis	Normocellular	04	-	04
Metastatic	Normocellular	-	02	02
Idiopathic aplastic anemia	Hypocellular	28	08	36
Scrub typhus	Hypocellular	04	-	04
SLE	Hypocellular	-	04	08
Drug induced	Hypocellular	-	02	02
Post-partum aplastic anemia	Hypocellular	-	02	02
Disseminated tuberculosis	Hypocellular	02	-	02
Undiagnosed	Normocellular	04	02	06

DISCUSSION

Pancytopenia is a frequently encountered issue in clinical practice, and it presents a considerable challenge due to its diverse range of potential underlying causes[11]. Various studies from around the world have reported a significant variation in the prevalence of different etiological factors responsible for pancytopenia. This variability is likely influenced by a multitude of factors, including geographic location, the demographic characteristics of the patient population being studied, nutritional status, the prevalence of infectious diseases, exposure to chemicals and toxins, and numerous other factors that may not be well-documented. These factors collectively contribute to the complex and varied landscape of pancytopenia's differential diagnosis[12].In our study, we evaluated patients spanning the age range of 15 to 85 years and noted a male predominance, consistent with findings from other similar studies. Among males, the age group most frequently affected was 15-24 years, accounting for 28% of cases. For females, the highest incidence was observed in the 25-34 age group, with 22 cases. Generalized weakness emerged as the most common clinical presentation, affecting 61% of cases, followed by fever in 47%. Bleeding manifestations from various sites were noted in 8% of cases. Pallor, a prominent physical sign, was observed in 100% of the cases, while splenomegaly was present in 15% and hepatomegaly in 8%.

Interestingly, these observations align with findings from studies conducted by B. N. Gayathri et al., Rangaswamy M et al., and Chandra K et al[13]., where fever and generalized weakness were also identified as common symptoms, and pallor was the most frequently observed physical sign. However, Khodke K. et al. reported fever as the primary presentation in only 40% of cases, followed by weakness in 30% and bleeding manifestations in 20%. In the study by Chandra K et al., bleeding manifestations were more prevalent, occurring in 24.4% of cases, which is notably higher than in the present study. Additionally, they reported a higher incidence of splenomegaly (33.7%) and hepatomegaly (22.8%) in their cases. These variations highlight the differences in the frequency of underlying causes of pancytopenia in specific regions.Numerous studies conducted by different authors in the past two decades from various geographical regions within the Indian subcontinent consistently support the fact that B12 deficiency is the primary cause of megaloblastic anemia in developing countries, including India. These studies collectively emphasize the significance of this nutritional deficiency as a major contributor to megaloblastic anemia. The overall incidence of megaloblastic anemia in these studies varies from 22.3% to 72%. Aplastic anemia, on the other hand, was found to be the second most common cause of pancytopenia, with an incidence ranging from 10% to 52.7% in patients presenting with pancytopenia.[14]

In the present study, B12 deficiency-induced megaloblastic anemia was identified as the leading cause of pancytopenia, followed by hypoplastic/aplastic anemia. This pattern was particularly prominent in the age group of 15-24 years, with a male predominance observed in both conditions. These findings corroborate the results of other researchers, such as B. N. Gayathri et al., Khodke K et al., and Khunger et al[15]., who also reported B12 deficiency as the most frequent etiological factor and hypoplastic/aplastic anemia as the second most common cause of pancytopenia in their respective studies[16]. This collective body of research underscores the critical role of B12 deficiency in megaloblastic anemia and its implications for the population in the Indian

subcontinent.The incidence of aplastic anemia appears to be higher in Asian countries when compared to Western regions, including the Indian subcontinent. Several factors likely contribute to this difference, including lower socioeconomic status, increased exposure to pesticides due to a greater reliance on agriculture, as well as exposure to various chemicals, toxins, and pathogens. The present study noted a male predominance in cases of hypocellular marrow where no specific cause could be established, categorizing them as idiopathic aplastic anemia.[17,18] This male predominance in aplastic anemia cases aligns with findings in studies from the Philippines and Nepal, which also reported a higher incidence of aplastic anemia among males when compared to females.

In contrast, a study conducted in Pakistan by Das Makheja K et al[19]. found an equal incidence of aplastic anemia among both males and females. These variations in gender distribution in aplastic anemia cases highlight the complexities of this condition and the potential influence of regional, environmental, and genetic factors on its prevalence.

CONCLUSION

Pancytopenia is a complex clinical condition with a multitude of potential underlying causes, some of which are reversible while others are not. Among these causes, megaloblastic anemia stands out as the most prevalent and treatable contributor to pancytopenia. This study underscores the importance of understanding the diverse etiologies that can lead to pancytopenia, particularly within a specific geographical region. Such knowledge is crucial for healthcare professionals as it enables them to narrow down the list of potential diagnoses and expedite focused and effective management strategies for patients presenting with pancytopenia.

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