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Original Article

Pancytopenia - A Study on Clinical and Etiological Profile at a Tertiary Care Institute

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Abstract

Introduction: Pancytopenia is a common hematological condition of varied etiology; however, only a few studies on pancytopenia from the northern regions of India have been published. Pancytopenia is the deficiency of all three cellular elements of blood, resulting in anemia, leucopenia, and thrombocytopenia. The frequency of underlying pathology causing pancytopenia varies considerably depending on various factors including age, geographic distribution, and genetic disturbances.

Purpose: The purpose of the study was to evaluate the clinical and etiological profile of patients presenting with pancytopenia to a tertiary care hospital of northern India.

Methods: A total of 66 patients were included in this study over a period of 18 months. Basic investigations were performed for each patient including hemoglobin, total leukocyte count, platelet count, and reticulocyte count. Absolute values including packed cell volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were calculated for every patient.

Results: A total of 66 patients were studied over a period of 18 months including 40 males and 26 females. Male to female ratio was 1.53:1. The most common cause of pancytopenia was megaloblastic anemia (MA) found in 23 patients (34.84%), followed by aplastic anemia in 5 patients (7.57%), undiagnosed cases in 5 patients (7.57%), tuberculosis in 4 patients (6.06%), multiple myeloma and myelodysplastic syndromes in 3 (4.54%) patients each, respectively.

Conclusion: MA is still the most common cause of pancytopenia in our setting. All patients with pancytopenia should be sought for MA as it is a potentially treatable condition.

Key words: Aplastic anemia, Leukemia, Megaloblastic anemia, Multiple myeloma, Pancytopenia

INTRODUCTION

Pancytopenia by itself is not a disease but is the result of various diseases.[1] The presenting symptoms can be due to anemia, leucopenia or, thrombocytopenia leading to fatigue, and dyspnea. Thrombocytopenia can lead to bruising and mucosal bleeding. Leukopenic features are uncommon as the presenting symptom, but during the course of the disease becomes a life-threatening condition.[2] In pancytopenia, all the three formed elements of blood are reduced below the normal range.[3] By definition hemoglobin <13.5 g/dl in males or 11.5 g/dl in females, the leukocyte count $<4 \times 10^9$/L and platelet count $<150 \times 10^9$/L constitute pancytopenia.[4] Peripheral pancytopenia may be a manifestation of a wide variety of diseases which can primarily or secondarily affect the bone marrow. The presenting symptoms are usually attributable to anemia or thrombocytopenia. Red blood corpuscles survive much longer than platelets or neutrophils. Thus, anemia develops slowly (unless there is significant bleeding) and the typical symptoms of tiredness, fatigue, puffiness of face, edema, lassitude, and effort intolerance may not be striking in the initial phase.[5] The platelet count is first to be affected. Mucocutaneous bleeding is typical of thrombocytopenia with petechial hemorrhages in skin and mucous membranes (commonest being epistaxis, hematuria, gastrointestinal bleeding, menorrhagia, and only rarely intracranial bleeding). The presence of spontaneous bleeding with platelet count

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$<20 \times 10^9$/l indicates severe marrow failure. Leukopenia is an uncommon initial presentation. Infections usually occur with commensal organisms of the skin or gastrointestinal tract. An early manifestation of neutropenia is often a sore throat or chest or soft tissue infection which typically shows an incomplete response to antibiotics.[6] The most common clinical manifestations of pancytopenia are usually fever (86.7%), fatigue (76%), dizziness (64%), weight loss (45.3%), anorexia (37.3%), night sweats (28%), pallor (100%), bleeding (38.7%), splenomegaly (48%), hepatomegaly (21.3%), and lymphadenopathy (14.7%).[7] Megaloblastic anemia (MA), hypersplenism (congestive splenomegaly, malaria, and leishmaniasis), aplastic anemia, myelodysplastic syndrome (MDS), subleukemic leukemia's, tuberculosis, and multiple myeloma are some of the etiologies presenting with pancytopenia. Identifying the etiopathology of pancytopenia is important for a given case for timely treatment of the disease.[8] Bone marrow examination is extremely helpful in evaluation of pancytopenia.[9] Bone marrow examination allows complete assessment of marrow architecture , pattern of distribution of any abnormal infiltrate and the detection of focal bone marrow lesions.[10,11] The most common causes leading to pancytopenia on bone marrow examination are aplastic (AA) bone marrow (29.05%), MA (23.64%), hematological malignancies, i.e., acute myeloid leukemia (21.62%), and erythroid hyperplasia (19.6%).[12] The aim of this study was to evaluate the clinical presentation and etiological profile of pancytopenic patients admitted at a tertiary care hospital of northern India.

MATERIALS AND METHODS

A total of 66 patients were identified over a period of 18 months (March 2016–September 2017) and were included in this study. In all patients, a detailed relevant history including the treatment history, history of drug intake, and any previous radiation exposure was obtained. Meticulous clinical examination of every patient was done for pallor, jaundice, hepatomegaly, splenomegaly, sternal tenderness, and lymphadenopathy. Basic investigations were performed for each patient including hemoglobin, total leukocyte count, platelet count, and reticulocyte count. Absolute values including packed cell volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were calculated for every patient. Chest radiography and abdominal ultrasonography were done in selected patients. Peripheral smear examination, and bone marrow examination was done in all patients, and wherever required, a trephine biopsy was also performed.

Inclusion Criteria

Patients with age >18 years, hemoglobin of <11.5 g per dl in women, and <13.5 g per dl in men, white blood cell count <4000 cells/cubic mm, and platelet count <1,50,000/cubic mm were included in this study.

Exclusion Criteria

Patients with a known hematological condition or patients on cancer chemotherapy and patients <18 years were excluded from the study.

Statistical Analysis

Data analysis was done with the use of IBM SPSS, version 21. Descriptive statistics were used to calculate the range, mean, and percentage.

RESULTS

This study was conducted on 66 patients admitted to the inpatient general medicine ward of a tertiary care institute presenting with pancytopenia and fulfilling the inclusion criteria. The most common symptom among the study patients was easy fatigability (77.21%) followed by fever (54.54%), palpitations (40.90%), anorexia (31.81%), and abdominal pain (27.27%). Hence, most of the patients presented with symptoms of anemia [Table 1]. The most common physical finding was pallor (81.81%), followed by splenomegaly (30.30%), and icterus (25.75%) as depicted in Table 2. The most common cause of pancytopenia was MA (34.84%), followed by aplastic anemia (7.57%), followed by undiagnosed cases of pancytopenia (7.57%), and tuberculosis (6.06%) as depicted in Table 3.

DISCUSSION

There are varying reports on the underlying aetiology of pancytopenia from various parts of the world. The frequency of pattern of disease causing them varies in different population groups and this has been attributed to differences in methodology and stringency of diagnostic criteria, geographical area , genetic differences, nutritional status, prevalence of infection and varying exposure to myelotoxic drugs among others.[3] Khunger *et al.*[4] in a study of 200 cases reported MA in 72% and aplastic anemia in 14% of cases. Savage *et al.* in Zimbabwe studied 134 patients ,identifying MA to be the most common cause of pancytopenia followed by aplastic anemia and acute leukemia. Vitamin B_{12} deficiency was recorded as the most frequent cause of pancytopenia in the young adults. It is commonly diagnosed as MDS ,because nuclear maturation abnormalities, dysplasia and megaloblastic changes are observed in all the three series during the evaluation of bone marrow smears. MDS can be distinguished with elevated blood lactic dehydrogenase and recovery of pancytopenia in first 2 weeks after Vitamin B_{12} substitution..[13] Common

Table 1: Symptoms of pancytopenia and their distribution among the study patients

Symptoms	Number of patients	% age
Easy fatigability	51	77.27
Fever	36	54.54
Palpitation	27	40.90
Anorexia	21	31.81
Abdominal pain	18	27.27
Weight loss	16	24.24
Bony pains	11	16.67
Vomiting	09	13.63
Cough	05	7.51
Diarrhoea	04	6.06

Data are expressed as numbers (%); % age=percentage

Table 2: Signs of pancytopenia and their distribution among the study patients

Signs	Number of patients	% age
Pallor	54	81.81
Splenomegaly	20	30.30
Icterus	17	25.75
Hepatomegaly	16	24.24
Petechiae	15	22.27
Lymphadenopathy	14	21.21
Ascitis	10	15.15
Glossitis	08	12.12
Edema	06	9.09
Heart Murmur	04	6.06

Data are expressed as numbers (%); %age=percentage

Table 3: Etiological profile among the study patients with gender distribution

Etiology	Males	Females	Total number of study patients	% age
Megaloblastic anemia	14	09	23	34.84
Aplastic anemia	03	02	05	7.57
Undiagnosed	03	02	05	7.57
Tuberculosis	02	02	04	6.06
Multiple myeloma	02	01	03	4.54
Myelodysplastic syndromes	02	01	03	4.54
Acute leukemia	02	01	03	4.54
CLD	02	01	03	4.54
Lymphoma	02	01	03	4.54
Drug-induced	01	01	02	3.03
Malaria	02	00	02	3.03
Connective tissue disorder	00	02	02	3.03
HIV	01	01	02	3.03
Myelofibrosis	01	01	02	3.03
Hypersplenism	01	01	02	3.03
Dengue	01	00	01	1.51
Septicemia	01	00	01	1.51

Data are expressed as numbers (%); % age=Percentage; CLD: Chronic liver disease, HIV: Human immunodeficiency virus

clinical presentations in our study patients were pallor, fever, petechial hemorrhages, and organomegaly. Khan and Hasan showed 81% cases with pallor followed by fever and bleeding manifestation[13] as the most common presentations in their study. Naseem *et al.* showed fever (65.5%) was the most common presentation followed by pallor and hepatomegaly.[14]

A total of 66 pancytopenia patients were studied in our study. Males outnumbered females, with 60.06% males and 39.39% females. Male to female ratio in the study was 1.53:1. The age of the patients ranged from 25 to 80 years. Most of cases were within the age group of 40 to 60 years, comprising a total of 47 patients. The most common presenting symptom was easy fatigability (77.27%), followed by fever (54.54%) and palpitations (40.9%). Clinical examination showed pallor in 81.81% of patients, splenomegaly in 30.30% of patients, icterus in 25.75% of patients, and hepatomegaly in 24.24% of patients, respectively.

MA was the most common cause of pancytopenia in the present study, accounting for 34.84% of total patients followed by aplastic anemia in 7.57% of total patients, whereas tuberculosis, multiple myeloma, chronic liver disease, lymphoma, and infections (malaria and dengue) accounted for the rare causes. Dahake *et al.*, in their study, found MA in 34% of cases.[15] Similar results were found in studies by Khodke *et al.* and Manzoor *et al.*, where the incidence of MA was found to be at 44% and 56%, respectively.[16,17] In another study by Kim *et al.* that evaluated the etiology of pancytopenia with 77 patients' bone marrow biopsies in India, MA was reported to be the most common cause (68%), whereas aplastic anemia (7.7%), MDS, and hemophagocytic syndrome, respectively, were rare causes.[18] Jha *et al.* found 23.64% and Bhatnagar *et al.* found 28.4% cases of MA in their studies.[12,19] In the study conducted by Bhatnagar *et al.*, the most common symptoms were weakness (97.8%), and breathlessness (75%), and signs were pallor (98.3%) and splenomegaly (25.5%). Bone marrow aspiration revealed most common cause of pancytopenia was megaloblastic anemia (25%) followed by dimorphic anemia (17.2%) and infections (17.2%).[19]

CONCLUSION

MA is still the most common cause of pancytopenia in our setting. All patients with pancytopenia should be sought for MA as it is a potentially treatable condition. The finding of hypersegmented neutrophils in the peripheral smear will guide the diagnosis. In Indian scenario, while evaluating etiology of pancytopenia, MA should always be kept in mind and it responds well to treatment. Pancytopenia should be evaluated aggressively as a significant number of patients have malignant condition in which early and aggressive treatment is warranted. Peripheral smear and bone marrow examination would help in identifying the etiology of pancytopenia in almost all patients. Bone marrow examination is necessary in the evaluation of patients with pancytopenia.

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