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PANCYTOPENIA: A PROSPECTIVE STUDY OF 220 CASES IN WESTERN INDIA

Amit Agravat[1], Krupal Pujara[2], Gauravi Dhruva[3], Raghunath Baria[4]

[1]Professor, Department of Pathology, PDU Medical College and Hospital, Rajkot, India.
[2]Assistant Professor, Department of Pathology, PDU Medical College and Hospital, Rajkot, India.
[3]Professor and Head, Department of Pathology, PDU Medical College and Hospital, Rajkot, India.
[4]2nd year Resident, Department of Pathology, PDU Medical College and Hospital, Rajkot, India.

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Corresponding Author:
Dr Raghunath Baria, 2nd year Resident, Department of Pathology, PDU Medical College and Hospital, Rajkot, India.
Email: raghunathbaria03@gmail.com

Abstract

Background: Pancytopenia is a hematological condition which occurs commonly and etiology varies according to different geographic location. Finding out specific etiology is important for appropriate management. **Aims and Objectives:** The present study was undertaken to describe etiological factors which leads to pancytopenia in "Central Clinical Laboratory (CCL), Department of Pathology, P.D.U Medical College & Hospital, Rajkot". **Materials and Methods**: A prospective study was conducted for a period of six months between September 2023 to February 2024 in which 220 patients were included. After acquiring clinical history, complete blood count including peripheral smears was done. Afterward, bone marrow aspiration was performed and microscopically examined in selected cases. **Results**: Among 220 patients studied, 134(60.09%) were males and 86 (39.09%) were females. Mean age was 38 years. The most common cause of pancytopenia was found to be megaloblastic anemia in 68 patients (30.90%) followed by thalassemia in 26 patients (11%). Other common causes included alcoholic liver disease in 20 patients (9.10%) and acute myeloid leukemia in 16 patients (7.27%), severe sepsis in 16 patients (7.27%). **Conclusion:** Megaloblastic anemia was found to be the most common cause of pancytopenia in this study. Identifying of etiologies of pancytopenia can be helpful in defining diagnostic and therapeutic strategies, which contributes toward the better management of patients.

Key words: hematological findings, bone marrow examination, pancytopenia

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Introduction

Pancytopenia is a medical condition characterized by a deficiency of all three types of blood cells: red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes). Clinical features of pancytopenia are usually consequences of these factors or their combination leading to life-threatening infection or bleeding in the late stages of disease. In routine institutional hematology practice, the condition is frequent.[10] Various etiological factors have been implicated in the causation of pancytopenia. Factors include decrease in blood cell production, abnormal cells infiltration of bone marrow (BM), suppression of BM, ineffective hematopoiesis, antibody mediated destruction of cells, and sequestration of cells in the reticuloendothelial system.[11] Treatment and prognosis of patients depends on the cause and severity of the underlying disease.[12] Variation in etiology of pancytopenia is appreciated in different countries as well as in different regions of a single country. Aplastic anemia followed by malaria and leishmaniasis were the main causes of pancytopenia reported from Bangladesh.[15] In Europe and Israel, neoplasm and radiation have been found to be the most common cause of pancytopenia.[7]

Materials And Methods

This study was conducted in the Department of Pathology in "Central Clinical Laboratory (CCL) Department of Pathology, P.D.U Medical College & Hospital, Rajkot", for a period of six months from September 2023 to February 2024 .**Inclusion criteria**: Within this period, patients who fulfilled the following criteria were provisionally selected: Simultaneous peripheral blood hemoglobin level <13.5 g/dl in males, or 11.5 g/dl in females, leukocyte count $<4 \times 10^9$/L, and the platelet count $<150 \times 10^9$/L were evaluated .**Exclusion criteria :**Patients who had received multiple blood/blood component transfusions within the previous 2 weeks, patients receiving erythropoietin and/or colony-stimulating factors, and patients who were too sick to undergo the proposed diagnostic workup were excluded from the study. **Data collection procedure**: A detailed clinical history was noted from each patient followed by a thorough physical examination. Specific features in respect of symptoms related to pancytopenia such as fatigue, palpitation, shortness of breath, fever, and easy bruising were enquired. A general survey of each patient was followed by a thorough systemic examination. Chest radiography and ultrasonography of abdomen were undertaken to note the condition of different organs. Blood samples were collected for complete blood count (CBC) and peripheral blood smear (PBS) examination. The smear was stained by Leishman stain for PBS examination and by new methylene blue to note the reticulocyte count. The blood collected in the ethylene diamine tetra acetic acid vial was analyzed with MINDRAY automated cell counter to obtain the CBC. Bone marrow aspiration (BMA) performed using Salah's BMA needle respectively. BMA smears were stained with Leishman stain. The BMA were studied in detail relevant data were recorded, tabulated and analyzed.

Results

A total 220 patients with pancytopenia were included in the study group. Out of these patients, 136 (60.09%) were males and 86 (39.09%) were females having male: female ratio 1.5:1. The age of these patients ranged from 3 month to 82 years.

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Table 1: Distribution of various etiologies of pancytopenia in cases

Etiology	Number of cases (%)
Megaloblastic anemia	68(30.90) %
Thalassemia	26(11.0) %
Alcoholic liver disease	20(9.10) %
Acute myeloid leukemia	16(7.27) %
Severe sepsis	16(7.27) %
Aplastic anemia	11(5.0) %
Auto immune hemolytic anemia	10(4.54) %
Chemotherapy	10(4.54) %
Paroxysmal nocturnal hemoglobinuria	7(3.18) %
SLE	7(3.18) %
Myelodysplastic syndrome	6(2.72) %
Lymphoma	6(2.72) %
P. vivax positive	6(2.72) %
Tuberculosis	4(1.81) %
Multiple myeloma	2(0.9) %
ITP	2(0.9) %
sickle cell anemia	1(0.45) %
Hemophagocytic lymphohistiocytosis	1(0.45) %
Total cases	220(100) %

Table 1: The most common cause of pancytopenia was found megaloblastic anemia in 68 patients (30.90%). followed by thalassemia in 26 patients (11%). Other common causes included alcoholic liver disease in 20 patients (9.10%) and acute myeloid leukemia in 16 patients (7.27%), severe sepsis in 16 patients (7.27%) respectively.

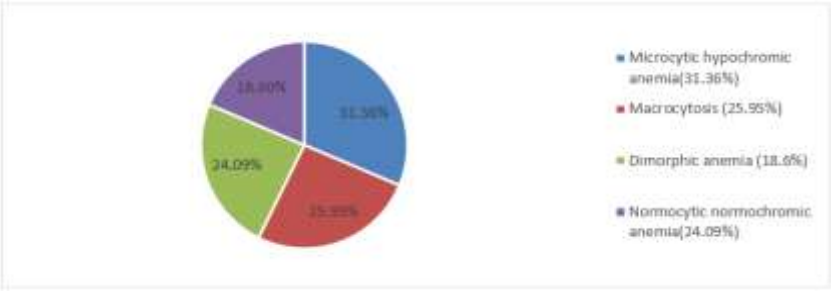

Table 2: Peripheral blood film findings in all cases

Table 2: The most common PBF finding was Microcytic hypochromia anemia 68(31.36%) followed by Macrocytosis 57 (25.95%), Dimorphic anemia 53 (18.6%) and Normocytic normochromic anemia 41(24.09%) respectively.

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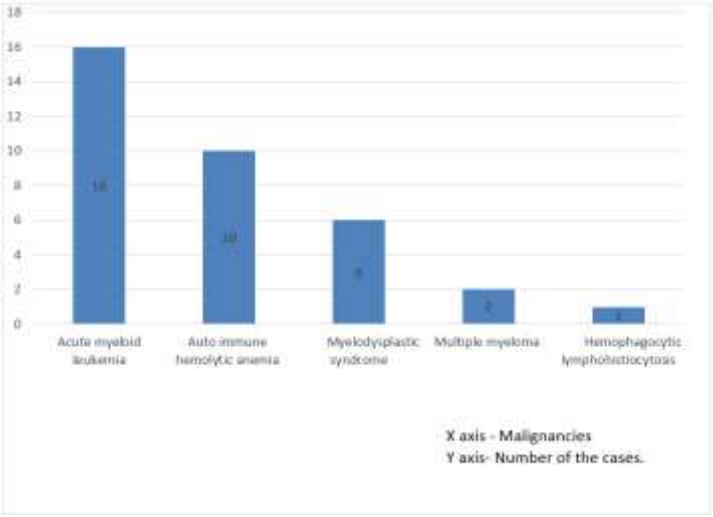

Table 3: Distribution of different haematology malignancies in the study subjects

Table 3: In this study, hematological malignancies accounted for 15.88% of cases of pancytopenia and included Acute myeloid leukemia (7.24%), Auto immune hemolytic anemia (4.54%), Myelodysplastic syndrome (2.72%), Multiple myeloma (0.90%), Hemophagocytic lymphohistiocytosis (0.45%).

Table 4: Age distribution of the study

Age distribution in year	**Female (n=86)**	**Male (n=134)**	**Total (n=220)**
< 20	20	29	49
21-30	21	18	39
31-40	18	22	40
41-50	12	20	32
51-60	11	24	35
>60	06	19	25
TOTAL	86	134	220

Table 4 shows the age distribution of male and female participants of the study. The study included 134 males and 86 females. The maximum number of participants belonged to the age group of <20 years (n = 49), followed by 31–40 years (n = 40), 21-30 years (n = 39), and >60 years (n = 25). The remaining participants were aged between 41 and 60 years.

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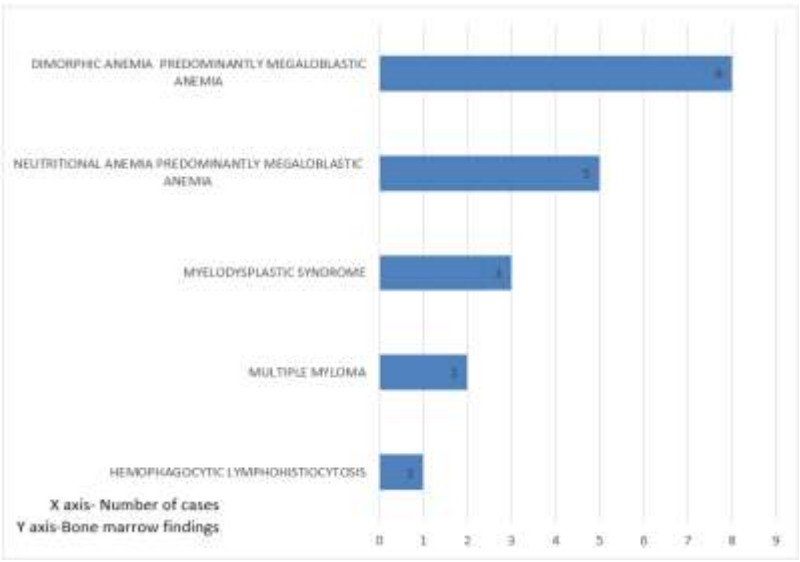

Table 5: Bone marrow examination findings in the study subject

Table 5 On BM examination, the most common finding was Dimorphic anemia predominantly megaloblastic anemia seen in 8 (3.63%) patients, Nutritional anemia predominantly megaloblastic anemia observed in 5 Patients (2.27%), myelodysplastic syndrome (MDS) observed in 3 Patients (1.36%), Multiple myeloma observed in 2(0.90%) patients and Hemophagocytic lympho histiocytosis observed 1(0.45%) patient.

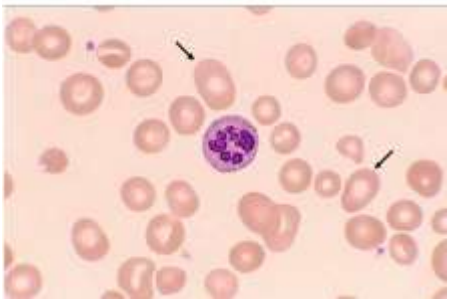

Figure 1: Peripheral smear showing macrocytic anemia with hyper segmented neutrophils with macro-ovalocyte.[1]

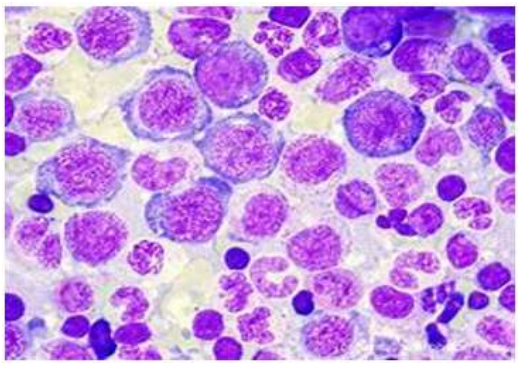

Figure 2: Bone marrow showing megaloblasts with sieve-like nuclear chromatin

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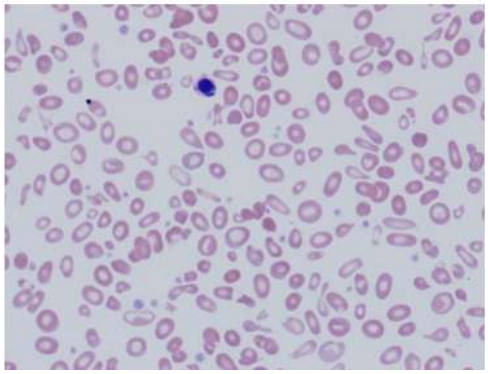

Figure 3: Thalassemia minor Peripheral smear showing microcytic hypochromic red cells with minimal anisocytosis. RBCs are closely packed indicating elevated red cell count.

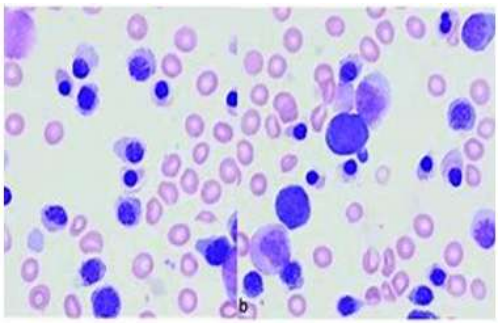

Figure 4: Representative bone marrow smears from a patient with beta-thalassemia major. Bone marrow smears showing erythroid hyperplasia with erythroblasts.

Discussion

Study	**Country**	**Year**	**Number of cases**	**Commonest cause**
International agranulocytosis and aplastic anemia group[6]	Israel & Europe	1987	319	Hypoplastic anemia (52.7%)
Keisu M*et al.*[7]	Israel & Europe	1990	100	Neoplastic disease, radiation (32%)
Tilak *et al.*[3]	(Chandigarh), India	1999	77	Megaloblastic (68%)
Khodke et a[9]	(Tamil Nadu), India	2000	50	Megaloblastic anemia (44%)
Jha A *et al.*[4]	(Tribhuvan), Nepal	2008	148	Hypoplastic anemia (29.05%)
Dr. Pinal Shah[23]	Surat (Gujarat), India	2016	40	Megaloblastic anemia (35%)
Present study	Rajkot (Gujarat), India	2024	220	Megaloblastic anemia (30.90%)

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Pancytopenia is a common hematological condition often encountered in day-to-day clinical practice. It is characterized by decrease in all the three cell lines of blood viz., red blood cells, leucocytes, and platelets. Pancytopenia is defined as hemoglobin level < 13.5 g/dl in males, or 11.5 g/dl in females, leukocyte count < 4×10^9/L, and the platelet count < 150×10^9/L were evaluated. Severe pancytopenia is defined as absolute neutrophil count < 500 / cmm, platelet count < 20,000 / mm, corrected reticulocyte count < 1 %. Male patients slightly outnumbered the female with male to female ratio 1.5:1 and this was similar to study of Makaju *et al.* 1.5:1, Jha *et al.* (1.3:1) [1-2]

The age of the patients ranged from 3 month to 82 years, the most common age group being < 20 years. Das Makheja *et al.* also reported 21–30 years as the most common age group for the presentation of pancytopenia [[11]. In other studies, 12–30 and 21–40 years age groups were the most common age groups for presentation of pancytopenia [9,16]. The incidence of megaloblastic anemia varies from 0.8% to 32.26% of all panctytopenic patients. [3,6-8]

In present study megaloblastic anemia is still the commonest cause of pancytopenia. This constituted 30.90% of total cases of pancytopenia. Findings are similar to other studies tilak and khodke *et al.* in which megaloblastic anemia is a common cause of pancytopenia.[3,9] While this findings are sharp contrast with various studies from the world in which aplastic anemia is commonest cause this may be due to high prevalence of nutritional anemia in Indian subjects leads the increased frequency of megaloblastic anemia.[3].Pancytopenia was aplastic/ hypoplastic anemia in present study (5%) which was correlated with Tilak *et al.* and khodke *et al.*.[3,9] Jha *et al.* and Pathak *et al.* have aplastic anemia as common cause of pancytopenia.[1,2] Few studies from India and Indian subcontinent reported Aplastic anemia as the leading cause of pancytopenia in their study [16-20]. Jha A *et al.*, Ghartimagar D *et al.*, reported Hypoplasia of marrow as the leading cause while in present study 13%patient had hypocellular marrow [4,21]. This variation could be due to local food preferences, poverty, prevalence of infections, geographical location, climate season. In a study by Keisu *et al.* neoplastic disease was the commonest cause of pancytopenia.[3] 6 (2.72%) case of myelodysplastic syndrome was diagnosed in our study. It was the second most common cause of pancytopenia in studies by international agranulocytosis and aplastic anemia group.[6].

In this study, hematological malignancies accounted for 15.88% of cases of pancytopenia and included Acute myeloid leukemia (7.24%), autoimmune hemolytic anemia (4.54%), myelodysplastic syndrome (2.72%), multiple myeloma (0.90%), hemophagocytic lymphohistiocytosis (0.45%). Vaidya [9] also reported a similar prevalence of hematological malignancies, however, Jha *et al.*. observed a higher percentage of hematological malignancies in their study [2]. The prevalence of acute leukemia contributing to pancytopenia in this study was comparable to previous similar studies [9,12].

In this study bone marrow aspiration was conducted in 19 patients (8.61%). Megaloblastic anemia can be caused by deficiency of vitamin B12 or folic acid in diet and severity of anemia depends on ineffective erythropoiesis [22]. On Bone marrow examination, the most common finding was Dimorphic anemia predominantly megaloblastic anemia seen in 8 patients (3.63%), Nutritional anemia predominantly megaloblastic anemia observed in 5 Patients (2.27%), myelodysplastic syndrome (MDS) observed in 3 Patients (1.36%), Multiple

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myeloma observed in 2 patients (0.90%) and Hemophagocytic lympho histiocytosis observed 1patients (0.45%).

Conclusion

Pancytopenia is a common condition having reversible causes such as Vit B12 deficiency to difficult conditions like Malignancies and Aplastic anemia. If not diagnosed early it can lead to devastating complications, investigations involve multiple tests along with painful marrow aspiration. Megaloblastic anemia was the most common cause of pancytopenia in this study and also in some other studies in Indian subcontinent as well. Vit B12 and folic acid supplementation can reverse this condition. The present study concludes that primary hematological investigations along with bone marrow aspiration in pancytopenic patients are helpful to understand disease and to diagnose the causes of pancytopenia. These are pivotal to plan out further investigations and management.

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