Original Article

Indian Journal of Medical & Health Sciences
Volume 8 Number 1, January – June 2021
DOI: https://dx.doi.org/10.21088/ijmhs.2347.9981.8121.1

Retrospective Clinico Hematological Study of 150 Cases of Pancytopenia in Tertiary Care Center

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Abstract

Context: Pancytopenia is not a disease but a clinic-hematological entity encountered in day to day practice. Bone marrow examination with peripheral blood finding and relevant biochemical test with radiological finding play important role in diagnosing and understanding the causes of pancytopenia which further determine the management and prognosis.

Aim: To obtain detailed clinical and hematological spectrum of the common disorders producing pancytopenia in patients attending our tertiary care center and its causes and diagnostic approaches.

Material and Method: The study was conducted in the department of pathology Katihar Medical College, Katihar. A retrospective study including 150 cases of pancytopenia in the duration of 2018 October to 2020 October.

Results: The age of the patients ranged from 2 to 80, 75% of patients out of 150 cases were of megaloblastic anemia followed by aplastic anemia (10%), kalazar (8%), acute leukemia (6%), malaria (4%), myelodysplastic syndrome (1%) and tuberculosis (1%).

Conclusion:The study concluded that bone marrow examination along with peripheral blood finding and radiological finding with biochemical finding helps to diagnose and understand the causes and management of pancytopenia.

Keywords: Pancytopenia; Anaemia; Kalazar; Tuberculosis

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How to cite this article:
Monilisha Jha, Izhar Alam, Neha Singh et al./Retrospective Clinico-Hematological Study of 150 Cases of Pancytopenia in Tertiary Care Center 2021;8(1):11-14.

Introduction

Pancytopenia is characterized by anemia, leucopenia and thrombocytopenia. It is generally due to decrease in hematopoietic cell production in the marrow resulting from infections, toxins, malignant cell infiltration, chemotherapies and radiation.[1] Pancytopenia is a manifestation of many serious and life threatening disease. Peripheral blood smear examination plays important role to correlate with etiology. Macroovalocytes with hypersegmented neutrophils in megaloblastic anemia, occasional blast cell in sub leukemic leukemia, leucoerythroblastic blood picture in myelofibrosis and Pelger-Huet neutrophils in MDS.[2] Bone marrow aspiration and bone marrow biopsy also play important role in understanding the etiology of disease. In some case bone marrow biopsy is more useful than aspirate like aplastic anemia, MDS, acute leukemia, hair cell leukemia and myelofibrosis.[2] Patient with pancytopenia presents with different clinical features. Marrow cellularity and composition in cases of pancytopenia differ in relationship to underlying pathological condition. The marrow is generally hypocellular in cases of pancytopenia caused by a primary production defect. Cytopenia's resulting from ineffective hematopoiesis, increased peripheral utilization or destruction of cells, and bone marrow invasive processes are usually associated with a normocellular or hypercellular marrow. [3] Aim of our study is to obtain detailed clinical and hematological spectrum of the common disorders producing pancytopenia in patients attending our tertiary care center and its causes and diagnostic approaches.

Material and method

This retrospective study was conducted in the central laboratory of pathology department of Katihar Medical College. The duration of study was October 2018 to October 2020, 150 cases of pancytopenia were included in the study.

Inclusion Criteria-Inclusion Criteria for this Study were

Patients with hemoglobin: <9 g/dl

Total leukocyte count: <4000/cu.mm

Platelet count: <140,000/cu.mm.

Exclusion Criteria-Exclusion Criteria for this Study were:

Diagnosed cases of malignancy, including leukemia receiving chemotherapy or radiotherapy.

Patientswere selected according to the guidelines of inclusion criteria. All the patients were subjected to examination of their complete blood count and peripheral blood smear examination. Bone marrow aspiration and/or bone marrow biopsy was done in cases where required. Marrow was examined for cellularity, myeloid: Erythroid ratio, erythropoiesis, myelopoiesis, megakaryopoiesis, other cells such as plasmacells, lymphocytes, blasts and parasites. Special investigations were done in cases where indicated. Patients were followed until discharge and response to therapy was noted. Most of the patients in this study were male.

Table 1: Common causes of pancytopenia with age and sex distribution in the study.

Disease	Total case	Male	Female	Most Common Age Group
Megaloblastic anemia	105	65	40	20-40
Aplastic anemia	15	9	6	02-14
Kalazar	12	4	8	20-40
Acute leukemia	9	6	3	02-14
Malaria	3	1	2	20-40
MDS	3	2	1	20-40
Tuberculosis	3	2	1	20-40

Analysis of Hematological Investigations

The hemoglobin concentration was between 7 and 9 g/dl in 44% of cases. In 56% of the cases had hemoglobin <6 g/dl, which formed the major group of patients who had pancytopenia. The total leukocyte count was between 3300 and4000/cu.mm in 40% of cases. In 39% of the cases, the leukocytes count was between 2300 and 3300/cu.mm. In 21% of the cases, it was <2300/cu.mm. The platelet count was between 100,000 and 140,000/cu.mm in 19% of the cases. In 42% of cases, it was between 80,000 and 100,000/cu.mm, and in 39% of cases it was <80,000/ cu.mm.

The mean corpuscular volume (MCV) was increased in 49% of the total cases of pancytopenia, and megaloblastic anemia was the cause. It was decreased in 7% of cases and was found to be within the normal range in 44%of the cases. The reticulocyte count was within normal range in 60% of the cases. Twenty percentage of the cases showed a decreased reticulocyte count. An increased count was seen in 20% of cases and these were those cases with malaria and kala-azar, which represent a relative increase in pool of immature red blood cells (RBCs).

The predominant blood picture was macrocytic anemia constituting 42%, followed by normocytic anemia seen in 40% of the cases. Dimorphic picture was seen in18% of cases. Circulating megaloblasts were found in 26 patients with pancytopenia. Giant platelets were seen in 14 patients with pancytopenia. Hypersegmented neutrophils were seen in 47 cases. Relative lymphocytosis was seen in 16 (16%) patients. Malarial parasites were seen in 3 of the total cases.

Bone marrow examination was done in all the 150 cases. Bone marrow was hypercellular in 114cases, which included 105 cases of megaloblastic anemia. Cellularity was decreased in 30 cases, including 15 cases of aplastic anemia. Normal marrow cellularity was seen in three cases. Megaloblastic maturation, presence of blasts, abnormal plasma cells and presence of Leishman Donavan (L.D.) bodies were diagnostic features in bone marrow examination.

Myelodysplasia was seen in three case and showed dysplastic features in all the three lineages, however ring sideroblasts were absent. 80 patients responded to therapy and followed-up until there was substantial improvement. 19 cases were referred to advanced hematology centers for further treatment.

Table 2: Distribution of cases-presenting complaints and physical findings.

Symptoms	No. of cases	Most Common Cause	2nd Most Cause Common
Fever	65	Megaloblastic anemia	Hypoplastic anemia
Epistaxis	30	Megaloblastic anemia	ITP
Gum bleed	10	Hypoplastic anemia	ITP
Petechiae	15	Hypoplastic anemia	ITP
Rash	15	Hypoplastic anemia	ITP
Hematemesis	10	Hypersplenism	MDS, Megaloblastic anemia
Hematuria	10	Megaloblastic anemia	Aplastic anemia, ALL
Malena	5	Megaloblastic anemia	MDS, ALL
Bleeding per Rectum	5	Megaloblastic anemia	Dimorphic anemia
Pedal oedema	18	Megaloblastic anemia	Dimorphic anemia

Table continous ....

Facial oedema anemia	5	Megaloblastic	
Jaundice	8	Megaloblastic anemia	Hypoplastic anemia
Hepatomegaly	15	Megaloblastic anemia	B.M reactive to infection
Splenomegaly	45	Megaloblastic anemia	Hypersplenism, Dimorphic anemia
Lymphadeno-pathy	24	Megaloblastic anemia	ALL

For bleeding manifestations Epistaxis, hematuria, Malena and bleeding per rectum, most common cause was found to be megaloblastic anemia while hypoplastic anemia was common cause for gum bleed, petechiae and rash. Hematological parameters in 3 subgroups of pancytopenia observed were as follows.

Severe anemia (Hemoglobin less than 5 gm%) was found in more than 50% cases in megaloblastic anemia, hypoplastic anemia, dimorphic anemia and bone marrow reactive to chronic infection.

Moderate (Hemoglobin-5-8 gm %) and mild (Hemoglobin -8-9 gm %) anemia were found most commonly in megaloblastic anemia in 39.25% (35/105 cases) and 21 % (20/105 cases) respectively.

Platelet count less than 50, 000 /cumm were found in 85%, 69.2% and 66% cases of hypoplastic anemia, dimorphic anemia and megaloblastic anemia respectively.

Discussion

Reviewed retrospectively all 150 cases of pancytopenia in a time span of two years. Clinical details - age, sex distribution, presenting symptoms and signs were noted from medical records, hematological parameters, findings of leishman stained peripheral blood picture and bone marrow aspiration smears were reviewed. The underlying cause of pancytopenia was studied in all cases and observations were compared to other studies published in literature. The age of patients ranged from 2 to 80 years with mean age of 28 years.

Table 3: Age, sex distribution compared to those in other studies of pancytopenia.

Authors	No. of cases	Age range (Y)	M:F
Khunger JM et al (2002)[4]	200	2-70	1.2:1
Kumar R et al (2001)[5]	166	12-73	2.1:1
Khodke K et (2001)[6]	50	3-69	1.3:1
Tilak V et al (1999)[7]	77	5-70	1.14:1
B N Gayatri et al (2011)[8]	104	2-80	1.2:1
Rajendra Kumar et al (2013)[9]	155	2-80	1.12:1
Present study	150	2-80	1.45:1

Variations in the frequency of the various diagnostic entities causing pancytopenia have been attributed to difference in methodology and stringency of diagnostic criteria, geographic area, period of observation, genetic differences and varying exposure to myelotoxic agents, etc.[5]

The commonest cause of pancytopenia reported in various studies throughout the world has been aplastic anemia.[7] This is sharp contrast with results of our and other studies conducted in India where the commonest cause was found to be megaloblastic anemia.[4,5,6] This seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

Megaloblastic anemia constituted 70% cases in our study as compared to 72% reported by Khunger JM et.al and 68% by Tilak V et al and 41.5% by Rajendra et al. All of the studies have stressed the importance of megaloblastic anemia being major cause of pancytopenia. It is a rapidly correctable disorder and should be promptly notified.[5,7]

Although bone marrow aspiration studies are uncommon in suspected cases of megaloblastic anemia. But, if the diagnosis does not appear clear and hematological assays are not available, bone marrow aspiration is indicated. As facilities of folic acid and vitamin B 12 levels are not routinely available in most centers in India.Prevalence of aplastic anemia varies from10%to52% among pancytopenic patients.[6] The incidence of hypoplastic with the corresponding figure in study done by Rajendra et al 12% (20/155) and Khodke K et al, and the Khunger JM et al.[9,6,4] A higher incidence viz 29.5% was reported by Kumar R et al.[5]

Table 4: A comparison of the first and second most common causes of pancytopenia in different studies.

Study	Country	Year	No. of cases	Commonest cause	2nd Commonest cause
International agranulocytosis anemia study group[10]	Israel & Europe	1987	319	Hypoplastic anemia	MDS
Keisu & Ost[11]	Isreal & Europe	1990	100	Neoplastic disease radiation (32%)	Hypoplastic anemia (19%)
Hossain et al[12]	Bangladesh	1992	50	Hypoplastic anemia	Chronic malaria & chronic kalaazar
Verma & Dash[13]	India	1992	202	Hypoplastic anemia (40.6%)	Megaloblastic anemia (23.26%)

Table continous ....

Tilak & Jain[7]	India	1999	77	Megaloblastic anemia	Hypoplastic anemia
Kumar et al[5]	India	1999	166	Hypoplastic anemia	Megaloblastic anemia
Khodke et al[6]	India	2000	50	Megaloblastic anemia	Hypoplastic anemia
Bajracharyarya1[4]	Nepal	2005	10	Hypoplastic anemia	Megaloblastic anemia
B N Gayathri et al[8]	India	2007	104	Megaloblastic anemia	Hypoplastic anemia
Rajendra kumar et al(2013)[9]	India	2013	155	Megaloblastic anemia	Hypoplastic anemia
Present study	India	2020	150	Megaloblastic anemia	Hypoplastic anemia

Conclusion

Pancytopenia is a common condition whenever patient suspected with unexplained anemia, prolonged fever, tendency to bleed, lymphadenopathy and hepatosplenomegaly. In our country main cause of pancytopenia being fortunately megaloblastic anemia, which responds very well to treatment if diagnosed correctly in time. Detailed hematological investigation along with proper history and bone marrow examination can conclude the diagnosis which helps in the proper management of the patients.

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