



Original Research Article

A prospective clinico-etiological study of 100 cases of pancytopenia in a tertiary care hospital in Eastern India

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ABSTRACT

Background: Pancytopenia is a hematological entity which is relatively common. Its evaluation is important for arriving at an early and correct diagnosis, to aid in appropriate management.

Materials and Methods: It was an observational study conducted in the Department of General Medicine and Clinical Hematology of our institute from June 2019 to May 2020. Clinical, hematological and biochemical parameters of 100 pancytopenic patients were evaluated and descriptive statistics was used.

Results: The age ranged from 18-75 years. The commonest presentation was easy fatigability and fever. Besides pallor, splenomegaly and hepatomegaly were the presenting signs. Megaloblastic anaemia was detected in 64% followed by aplastic anaemia in 12% and acute leukemia in 6% patients. Among infective etiologies, two cases of malaria (*P. falciparum*). And each case of HIV, tuberculosis and dengue were seen. Lowest Hb% of 1.8 gm/dl, lowest total leucocyte count (TLC) of 500cells/cmm and lowest total platelet count (TPC) of 4000 cells/cmm was noted in a case of aplastic anemia. Macrocytic anemia was predominant blood picture. Hypercellular marrow was noted in 70(70%) cases and common cause was megaloblastic anemia, followed by leukaemia. Hypocellular marrow was noted in 12(12%) patients with aplastic anemia being commonest cause.

Conclusion: In our study diagnosis of pancytopenia and its causes were ascertained by hematological investigations. An early and prompt treatment was given according to the cause and severity. Most of the cases had good prognosis due to a treatable cause.

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1. Introduction

Pancytopenia is a hematological disorder involving in a decrease in the three blood cell lineages like erythrocytes, leucocytes and thrombocytes.¹ It can manifest as a laboratory finding of many diseases. The etiology of pancytopenia has a wide age, sex and geographical variation which includes megaloblastic anemia, anemia of nutritional origin, aplastic anemia, blood cancer,

myelodysplastic syndromes(MDS), multiple myeloma, lymphoma, sepsis, alcoholic diseases, viral diseases like HIV and hepatitis, autoimmune diseases, endocrinological disorders and infiltrating diseases of the bone marrow (Gaucher's disease).² The usual attributable clinical features are unexplained weakness, lethargic, getting easily fatigued, difficulty in breathing, fever and other bleeding manifestations occurring as a result of decreased hemoglobin concentration, decreased white blood cells and a decrease in platelet concentration. Initial presentation of leucopenia is uncommon but can be serious life

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threatening.¹ Physical findings and peripheral blood picture provide valuable information in the work up of pancytopenic patients and help in planning investigations on bone marrow samples.³ During the diagnostic process, patients undergo laboratory tests, radiological imaging and invasive procedures in case they are needed. Bone marrow evaluation is an invaluable diagnostic procedure in practice of medicine which may confirm the diagnosis of suspected cytopenia, from the clinical features and peripheral blood examination or occasionally give a previously unsuspected diagnosis.⁴

Studies done elsewhere in the world show aplastic anemia and hypoplastic anemia as the most common cause of pancytopenia which is contrast with the studies done in India.⁵ Previous studies done in India stress the importance of megaloblastic anaemia as being the major cause of pancytopenia.^{3,6} Although it is a common clinical pattern with an extensive differential diagnosis, there is a relatively little discussion of this abnormality in major textbooks of internal medicine and haematology. It has been observed in the Indian scenario that megaloblastic anemia (vitamin B12 and/or folate deficiency) is the commonest cause of pancytopenia.⁷

The aim of the present study was to evaluate the cases of pancytopenia by peripheral smear and/or bone marrow aspiration and/or bone marrow biopsy and to find out the etiology of pancytopenia along with clinical, hematological, and histomorphologic features. This data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia and treat treatable cause like megaloblastic anemia.

2. Materials and Methods

This was an observational study done in the Medicine and Clinical Hematology Department of our institute in Cuttack, Odisha during period from June 2019 to May 2020 involving 100 numbers of patients. Informed written consent was taken from individual participants in local odia language in the study.

Patient of the age group 18-75 years admitted to the General Medicine ward and Clinical Hematology ward with laboratory report showing pancytopenia as defined by haemoglobin percentage (Hb%) below 13.5gm/dl for male and below 11.5gm/dl for female, total leukocyte count(TLC) below $4 \times 10^9/L$ and total platelet count(TPC) below $150 \times 10^9/L$ were included.⁸ Patients with age <18 years, on radiotherapy and chemotherapy, and those who had undergone treatment for pancytopenia were excluded from the study.

From all the patients a written informed consent for considering themselves as a participant in the study was obtained after having fully understanding the tests and protocols of the study as well as risk to the patients. In all patients, a complete relevant medical history including age,

sex, history of smoking, alcoholism, history of any drug ingestion, ingestion of or exposure to potentially harmful toxic chemical agents, irradiation, history of complaints of pain in bones, rise in temperature, night sweats, malaise, loss of weight and itching was taken. A detailed meticulous physical examination of every patient was done for pallor, jaundice, hepatosplenomegaly, lymphadenopathy, sternal tenderness and gum hypertrophy. An extensive correlation as regards to the clinico-pathological point of view was undertaken in all cases before arriving at a definite diagnosis.

Patients were subjected to hematological tests like complete blood count profile (CBC), peripheral smear (PS) comment, reticulocyte count and bone marrow (BM) aspiration study. In case of failed aspiration due to dry or bloody tap, a bone marrow trephine biopsy was done from the usual site of the posterior superior iliac spine wherever indicated. Additionally, serum vitamin B₁₂, blood culture, ELISA for HIV, Hepatitis B and C viruses, chest X ray, bone radiographs, abdominal ultrasonography, erythrocyte sedimentation rate (ESR), urinary Bence Jones proteins, serum electrophoresis was done wherever indicated.

Other investigations like ESR, urine and stool examination, liver and renal function tests, other serological investigations were also done when required. The investigations were carried out with a focus on the suspected pathology and the provisional diagnosis. Investigative work up was done as directed by provisional diagnosis.

2.1. Statistical analysis

Collected data was analyzed by frequency tables and percentages. Data were entered using Microsoft excel and analyzed.

3. Results

In our study the commonest finding was megaloblastic anemia constituting (64%) of all causes of pancytopenia. Aplastic anemia (12%) was second most common cause followed by acute leukemia (6%), liver cirrhosis (4%), myelodysplastic syndrome (MDS) (4%), multiple myeloma (MM) (3%), systemic lupus (2%), malaria (2%). One case each of HIV, tuberculosis and dengue presented with pancytopenia [Figure 1].

The age of the patients ranged from 18 to 75years, majority (24%) in the range of 18 to 30. There was male predominance with male constituting (59%) and female (41%). Easy fatigability (95%), fever (28%) and breathing difficulty (20%) were the common symptoms of presentation. Bleeding manifestation was the presenting complaint in only 9%. Most common physical finding identified in our study group was pallor (96%), splenomegaly (21%), hepatomegaly

(11%), lymphadenopathy and purpura (7%) each, pedal oedema(4%) and icterus(3%). Hb among the patients in the present study varied from 1.8-9.9 gm/dl. 53% of patients had Hb in the range 6-9gm/dl and 39% of patients in the range of 3-6gm/dl. The lowest value of 1.9 gm/dl was seen in a case of aplastic anemia. TLC ranged from 500-4000 cells/cmm. Most of patients had TLC in range of 3000-4000cells/cmm (56%). Lowest count of 500cells/cmm was seen in a case of aplastic anemia. TPC ranged from 0.04-1.5 lakh/cmm. Most of patients had 0.5-1.0lakh/cmm (37%) followed by 35% in the range of 0-0.5lakh/cmm. Lowest TPC was 4000/cmm in a case of aplastic anemia. Peripheral blood picture was mostly macrocytic (68%), normocytic normochromic (24%), dimorphic (6%) and microcytic hypochromic (2%).

The commonest BM aspiration finding in pancytopenia patients in our study was hypercellular marrow (70%), followed by normocellular marrow (18%) and hypocellular marrow (12%). There was male predominance in the age-sex distribution of megaloblastic anemia in all the cases of pancytopenia in the present study except for the 31-40 age group. [Figure 2]

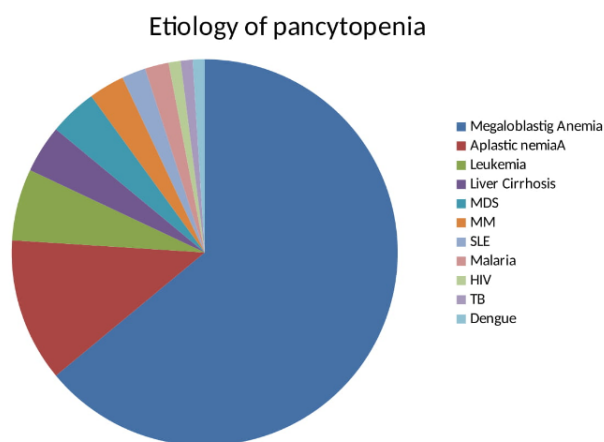


Fig. 1: Etiology of Case of pancytopenia in present study

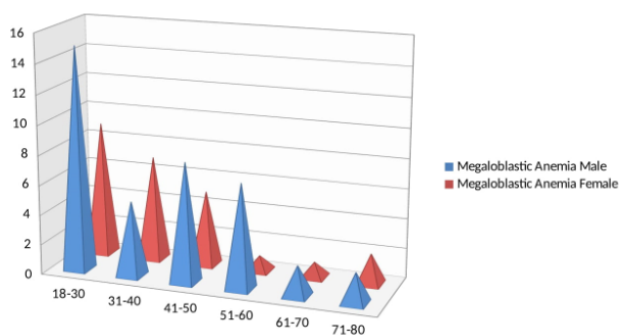


Fig. 2: Age-sex distribution of Megaloblastic anemia in cases of pancytopenia in present study.

4. Discussion

In clinical practice pancytopenia is commonly encountered and should be suspected on clinical grounds with presentation of unexplained anemia, prolonged fever and bleeding tendency in a patient. The physical findings and peripheral blood picture provides sufficient clue to the diagnosis of pancytopenic patients. BM aspiration is an important diagnostic tool in hematology which helps to evaluate various cases of cytopenias. It provides accurate, reproducible, rapidly available information at an economical cost and with minimal discomfort to the patient and to make a provisional diagnosis in cases of nutritional anemias and initial diagnosis of leukemia.

Pancytopenia is a striking feature of many serious and life-threatening illnesses and is caused by various different disorders.⁹ A total 100 cases of pancytopenia were studied. Age, gender wise incidence, presenting complaints, physical findings, peripheral blood picture, BM study and various causes of pancytopenia were studied in all cases and the observation were compared with studies published in the literature.

In our study, the commonest cause of pancytopenia was noted to be megaloblastic anemia [Table-1]. Similar kind of observation was noted in various studies conducted in India. [Table 2]. However the findings of the various reported studies outside India showed the commonest cause of pancytopenia, to be aplastic anemia [Table-3].

Various studies showed the overall incidence of megaloblastic anaemia varying from 22.3 to 72% in all pancytopenic patients. Our study found the incidence of megaloblastic anaemia to be 64%. Khunger JM et al⁷ reported the incidence of 72%, Tilak V et al³ of 64.9% and Khodke K et al¹⁰ found it to be 44%. [Table 1]

Incidence of aplastic anaemia varied from 7.8 to 29.5% among pancytopenic patients as reported in several studies conducted so far. The incidence of aplastic anemia was 12% in our study, which is comparable with the studies done by Khodke K et al¹⁰ and Khunger JM et al⁷ as the reported incidence in these studies for the same was 14%. Most of the cases of aplastic anemia were idiopathic. Western studies have shown much higher incidence of aplastic anaemia than that observed by us. This may be correlated to environmental factors such as increased exposure to toxic chemicals. Malaria presenting with pancytopenia was observed in 2% cases compared to Khunger JM et al⁷ who has reported an incidence of 1%, Tilak V et al³ reported 3.9% and Kumar R et al¹⁰ reported 3%. We encountered 4% cases of MDS with pancytopenia in our observation as compared to Khunger JM et al⁷ who have reported an incidence of 2% and Kumar R et al⁹ reported 3.6%. In contrast to other studies, our study encountered cirrhosis of liver in 4% cases which may be correlated with lower socioeconomic status and history of alcoholism in our region. From our study, we observed that the most common

Table 1: Various causes of pancytopenia compared to other studies.

Causes	Khunger JM et al ⁷ (2002)	Kumar R et al ⁹ (2001)	Khodke et al ¹⁰ (2001)	Tilak V et al ³ (1999)	Present Study
Aplastic anemia	28(14%)	49(29.5%)	7(14%)	6(7.8%)	12(12%)
Megaloblastic anemia	144(72%)	37(22.3%)	22(44%)	53(64.9)	64(64%)
Subleukemic leukemia	10(5%)	20(12.1%)	1(2%)	1(1.3%)	6(6%)
Lymphoma	2(1%)	10(6.2%)	-	2(2.6%)	-
Myelodysplastic syndrome	4(2%)	6(3.6%)	1(2%)	-	4(4%)
Marrow metastasis	-	2(1.2%)	-	-	-
Myelofibrosis	2(1%)	2(1.2%)	-	1(2%)	-
Malaria	2(1%)	5(3%)	-	3(3.9%)	2(2%)
Enteric fever	-	2(1.2%)	-	-	-
Malignant histiocytosis	-	1(0.6%)	-	-	-
Disseminated Tuberculosis	1(0.5%)	1(0.6%)	1(2%)	1(2%)	1(1%)
Multiple myeloma	2(1%)	-	2(4%)	1(2%)	3(3%)
Waldenstrom's macroglobulinemia	1(0.5%)	-	-	1(2%)	-
Acquired immuno-deficiency syndrome(AIDS)	-	-	1(2%)	-	1(1%)
Dengue	-	-	-	-	1(1%)
Cirrhosis of liver	-	-	-	-	4(4%)
Total	200	166	50	77	100

Table 2: Frequency of most common causes of pancytopenia in different studies in India

Study	Country	Year	No. of Cases	Most Common Cause	Second Most Common Cause
Tilak et al ³	India	1998	77	Megaloblastic Anemia (68%)	Aplastic Anemia (7.7%)
Khodke et al ¹⁰	India	2000	166	Aplastic Anemia (29.5%)	Megaloblastic; Anemia (22.3%)
Khunger et al ⁷	India	2002	200	Megaloblastic Anemia (72%)	Aplastic Anemia (28%)
Gayathriand Rao et al ¹¹	India	2011	104	Megaloblastic Anemia (74%)	Aplastic Anemia (18.3%)
Jain and Naniwadekar et al ¹²	India	2013	250	Hypersplenism (29.2%)	Infection (25.6%)
Sweta et al ¹³	India	2014	100	Megaloblastic Anemia (66%)	Aplastic Anemia (18%)
Present study	India	2019	100	Megaloblastic Anemia (64%)	Aplastic Anemia (12%)

Table 3: Frequency of most common causes of pancytopenia in different studies outside India

Author	Location	Year of study	No of cases	Megaloblastic Anemia	Aplastic Anemia
Imbert et al ¹⁴	France	1989	213	7.5%	10%
Savage et al ¹⁵	Zimbabwe	1999	134	40%	22%
Jha A et al ¹⁶	Nepal	2008	148	21.6%	29%
Elizabeth et al ¹⁷	USA	2012	250	2%	22%
Present study	India	2019	100	64%	12%

presenting complaint of patients was easy fatigability (95%) cases followed by fever in (28%) cases, breathing difficulty in (20%) cases. This is in comparison to a study by Thakkar BB et al,¹⁸ where the most common symptom was generalized weakness in (97%) cases, followed by fever in (70%) cases and dyspnoea in (32%) cases. Kumar R et al¹⁰ in their study showed generalized weakness being the most common symptom in (70.8%) cases, followed by fever in (6.25%) cases.

The high prevalence of nutritional anemia in our region is attributed to megaloblastic anaemia being the commonest cause. The other common causes were aplastic anemia and cirrhosis of liver. Bone marrow aspiration following a detailed hematological workup in pancytopenic patients is necessary for assessing the disease process. It is also helpful in diagnosis and segregating other etiological cause of pancytopenia, further supporting the investigative evaluation and accurate management of cytopenic patients.

Deficiency of vitamin B12/folate leading to megaloblastic anaemia seems to reflect the higher prevalence of pancytopenia in Indian subjects, with the second position being occupied by aplastic anemia, which is the leading cause for pancytopenia in the Western countries.

5. Conclusion

With appropriate treatment megaloblastic anemia can be a reversible cause of pancytopenia. In the context of Indian settings, megaloblastic anemia should be sorted during the investigative work up and depending upon the cause and severity, an early and prompt therapeutic intervention can result in a better prognosis.

6. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

7. Source of Funding

None.

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