Original Research Article

Clinical and hematological profile of pancytopenia in a tertiary care hospital of Southern Odisha, India

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ABSTRACT

Background: Pancytopenia (anemia, thrombocytopenia and leukopenia) is a common haematological condition with various etiologies like ineffective haematopoiesis, bone marrow suppression, bone marrow infiltration and peripheral destruction of blood cells. The present study was done to see the clinical features and etiologies of pancytopenia in this geographical region.
Methods: About 150 patients above 15 years of age after fulfilling the inclusion criteria were included in the study. They were evaluated with appropriate laboratory tests including bone marrow study, if indicated to find out the underlying etiology.
Results: Common symptoms were generalized weakness (93.3%), fever (75.3%) and dyspnoea (54%). Common physical findings were pallor (100%), lymphadenopathy (43.6%) and hepatosplenomegaly (32%). Most common causes were aplastic anemia (28%), megaloblastic anemia (20%) followed by infections like malaria (13.3%), dengue (5.3%) and sepsis (1.3%). Bone marrow was hypocellular in 50 patients (41.7%), hypercellular in 45 patients (37.5%) and normocellular in 25 patients (20.8%).
Conclusions: There are some reversible causes of pancytopenia like megaloblastic anemia, malaria, dengue and sepsis. Conditions like disseminated TB, collagen vascular diseases also can be treated with specific treatment if diagnosed early to avoid further complications.

Keywords: Aplastic anemia, Dengue, Malaria, Megaloblastic anemia, Pancytopenia, Sepsis

INTRODUCTION

Pancytopenia is a quite common hematological problem encountered in medical practice. It refers to decrease in cell count in all three lineages in blood i.e., anemia (hemoglobin (Hb) <13 gm%), leukopenia (White blood cell (WBC) count <4000/cc) and thrombocytopenia (platelet count <1.5 lakh/cc).[1] Hematopoiesis (blood cell production) in the healthy adult takes place in the bone marrow, from which mature blood cells migrate into the circulation, spleen and other sites. The bone marrow is a dynamic organ and a hematopoietic reservoir that responds to ongoing needs for blood cell production. A balance between blood cell production, distribution in other organs, and ongoing cellular destruction (e.g., white blood cells fighting infections, platelet consumption in blood clots, cellular senescence) determines the levels of circulating blood cells.[2-5]

The likely causes of pancytopenia are influenced by geography, socioeconomic conditions, and endemic illnesses. As examples, the likelihood of infectious (e.g.,

malaria, tuberculosis, leishmaniasis) or nutritional causes (e.g., folate deficiency) of pancytopenia may be increased in some resource-constrained settings.[6,7] The vast majority of pancytopenia in adults is caused by acquired disorders. Rarely, a previously unrecognized inborn errors of metabolism may account for cytopenias that are first detected in adulthood.[8] This study was undertaken to know the different disorders resulting in pancytopenia in this part of the country, observe their clinical presentation and correlate the peripheral blood smear with bone marrow finding and to institute therapy in some cases and see their response.

METHODS

This was a cross sectional observational study where, 150 patients above 15 years of age coming to medicine department of MKCG Medical college hospital, Berhampur, Odisha, India were studied after approval from Institutional ethical committee. A detailed history was taken including recent drug intake. Then a thorough physical examination was done with special attention to lymph node enlargement, hepatosplenomegaly, sternal tenderness and gum hyperplasia. Relevant investigations like complete blood count (CBC) (done by automatic cell counter), comment of peripheral smear (CPS) (done by Leishmann stain), peripheral smear for malarial parasite, renal function test, liver function test, thyroid profile, serological tests for HIV, HbsAg and anti HCV, chest X-ray and ultrasonography of abdomen, were done for all patients. Other tests like dengue (NS1, IgM and IgG antibody), widal test, blood culture and sensitivity, ESR (erythrocyte sedimentation rate), CRP (C-reactive protein), RA factor (rheumatoid arthritis factor), ANA (anti-nuclear antibody) and anti-ds DNA (double stranded DNA) were done where it was necessary. Bone marrow examination was done for those who did not respond to initial special treatment (like with anti-malarial and antibiotics) under strict aseptic precautions after informed written consent from the patient.

RESULTS

In present study, out of 150 patients, 87 (58%) were male and 63 (42%) were female. Among these maximum patients were of age group 35-44 years (56.25%) and 45-54 years (43.75%) (Table 1).

Table 1: Age distribution.

Age in years	Male	Female	Number
15-24	15	15	30
25-34	6	6	12
35-44	27	21	48
45-54	24	9	33
55-64	3	9	12
≥65	12	3	15
Total	87 (58%)	63 (42%)	150

Common clinical features were generalized weakness and fatigue (140 patients, 93.3%), fever (113 patients, 75.3%), dyspnea (81 patients, 54%). Other clinical features were bleeding manifestations like purpuric spots (18%), weight loss (10.7%) and loss of appetite (10.7%). On physical examination, pallor was present in all cases. Other signs included lymphadenopathy (43.3%), hepatosplenomegaly (32%), icterus (26.3%) and sternal tenderness (12%) (Table 2).

Table 2: Symptoms and signs.

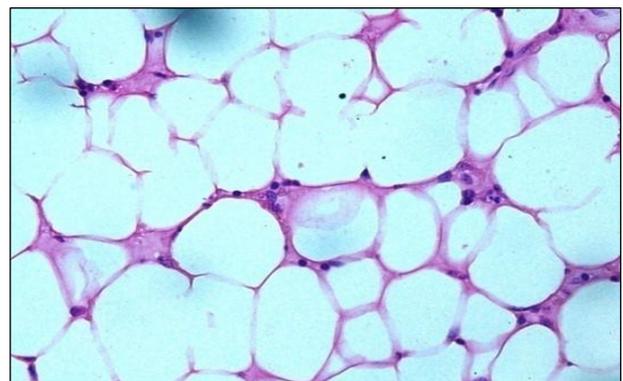| Clinical feature	Number	Percentage
Generalized weakness	140	93.3
Fever	113	75.3
Dyspnoea	81	54
Bleeding manifestation	27	18
Weight loss	16	10.7
Decreased appetite	16	10.7
Pallor	150	100
Icterus	42	26.3
Lymphadenopathy	65	43.3
Hepatosplenomegaly	48	32
Sternal tenderness	18	12

Figure 1: Bone marrow showing hypocellularity with increased fat-aplastic anemia (Leishman, ×100).
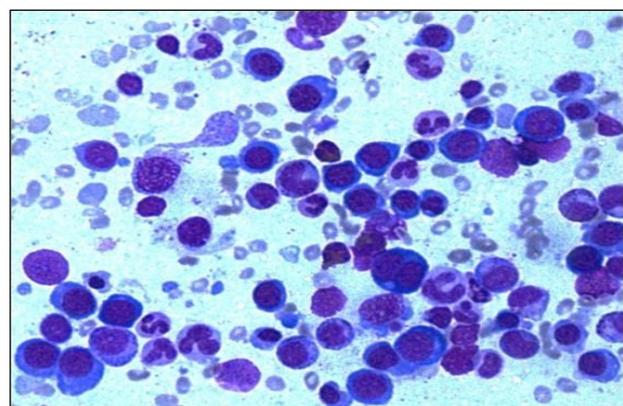

Figure 2: Bone marrow showing megaloblasts with royal blue cytoplasm and sieve-like chromatin - megaloblastic anemia (Leishman, ×100).
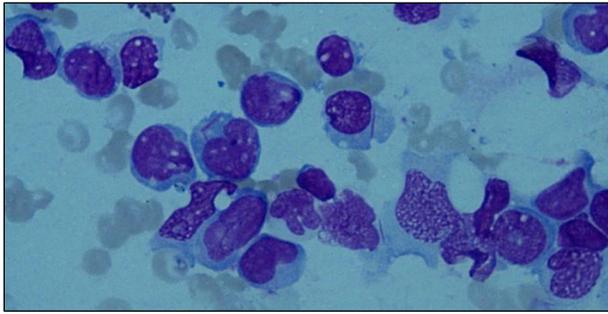
Figure 3: Bone marrow showing myeloblasts with Auer rods - AML (Leishman, x400).
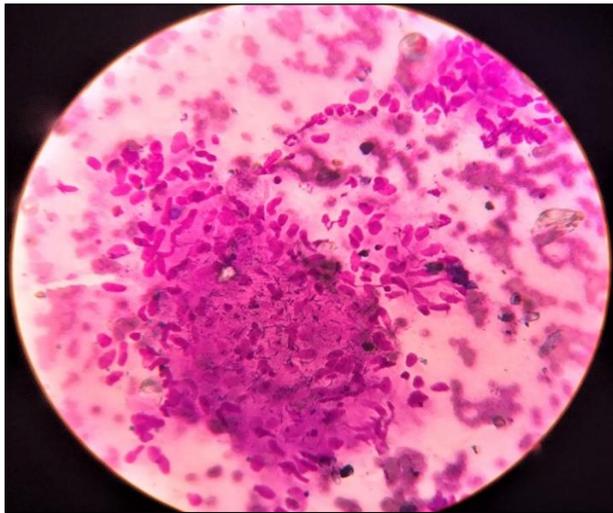

Figure 4: Bone marrow showing epithelioid cell clusters-tuberculosis (Leishman, x100).

Regarding the etiology of pancytopenia, most common causes were aplastic anemia (42 cases, 28%) (Figure 1), megaloblastic anemia (30 cases, 20%) (Figure 2) and malaria (20 cases, 13.3%). Other cases included acute myeloid leukemia (AML) (15 cases, 10%) (Figure 3), plasma cell dyscrasias (12 cases, 8 %), dengue (8 cases, 5.3%), myelodysplastic syndrome (MDS) (6 cases, 4%), systemic lupus erythematosis (SLE) (6 cases, 4%), myelofibrosis (3 cases, 2%), small lymphocytic lymphoma (SLL) (3 cases, 2%). Disseminated tuberculosis (TB) (3 cases, 2%) (Figure 4) and sepsis (2 cases, 1.34%) (Table 3).

Table 3: Causes of pancytopenia.

Diagnosis	No.	%
Aplastic anemia	42	28
Megaloblastic anemia	30	20
Plasma cell dyscrasia	12	8
Myelofibrosis	3	2
TB bone marrow	3	2
AML	15	10
Myelodysplastic syndrome	6	4
Small lymphocytic lymphoma	3	2
SLE	6	4
Malaria	20	13.3
Dengue	8	5.3
Sepsis	2	1.34
Total	150	100

Out of the 150 cases, those patients of malaria, dengue and sepsis recovered fully after 1-2 weeks of treatment. Rest of the patients were subjected to bone marrow study.

Bone marrow was hypocellular in 50 patients (41.7%), hypercellular in 45 patients (37.5%) and normocellular in 25 patients (16.6%) (Table 4).

Table 4: Bone marrow cellularity.

Cellularity	Number	Percentage
Hypocellular	50	41.7
Normocellular	25	20.8
Hypercellular	45	37.5
Total	120	100

Most common cause of hypocellular bone marrow was aplastic anemia (84%). Majority of hypercellular bone marrow were contributed by megaloblastic anemia (45%) and plasma cell dyscrasia (26.7%) (Table 5).

Table 5: Pancytopenia etiology vs bone marrow cellularity.

	Bone marrow cellularity		
Etiology	Hypocellular	Normocellular	Hypercellular
Aplastic anemia	42	0	0
Megaloblastic anemia	0	12	18
Plasma cell dyscrasia	0	0	12
Myelofibrosis	0	0	3
Disseminated TB	3	0	0
AML	0	6	9
Myelodysplastic syndrome	1	2	3
SLL	2	1	0
SLE	2	4	0
Total	50	25	45

DISCUSSION

A total of 150 cases of pancytopenia were studied, where male to female ratio was 1.4:1. Maximum patients were in the age group 35-44 years. In the study by Khunger JM et al, male to female ratio was 1.2:1 and the study by Kumar R et al, male to female ratio was 2.1:1 (Table 6).[9,10]

Table 6: Age, sex distribution compared to those in other studies of pancytopenia.

Authors	No. of cases	Male: female
Khunger JM et al[9]	200	1.2:1
Kumar R et al[10]	166	2.1:1
Knodke K et al[11]	50	1.3.1
Present study	150	1.4:1

The common presenting problem in present study were generalized weakness (93.3%), fever (75.3%) and dyspnea (54%).

Table 7: Comparison of physical findings with previous study.

Finding	Gayathri BN et al[12]	Present study
Pallor	100%	100%
Icterus	3.82%	26.3%
Hepatosplenomegaly	26.92%	32%
Lymphadenopathy	0.96%	43.3%
Sternal tenderness	0.96%	12%

In the study by Gayathri BN et al, generalized weakness was present in all cases and dyspnea in 48.25% cases.[12] Physical findings like pallor, icterus, hepatomegaly, splenomegaly and lymphadenopathy were comparable with the study by Gayathri BN et al (Table 7).[12]

Regarding various causes of pancytopenia, aplastic anemia (28%) was the commonest cause in present study, probably due to unnecessary usage of drugs especially indigenous drugs and intake of water contaminated with toxins and chemicals which might cause bone marrow suppression. This is supported by the study by Kumar R et al.[10] In the study by Khunger JM et al, megaloblastic anemia was the commonest cause of pancytopenia.[9] In present study, megaloblastic anemia (20%) was the second most common cause. Like other Indian studies, high incidence of megaloblastic anemia is probably due to deficiency of vitamin B12 and folic acid. Although estimation of vitamin B12 and folic acid was not available in this setup, author treated all patients of megaloblastic anemia with vitamin B12 and folic acid (Table 8).

Incidence of AML presenting as pancytopenia is 10%, compared to study by Savith A et al, where the incidence of was 8% and study by Abdullah Mir et al, where it was 6.8%.[13,14]

Plasma cell dyscrasias leading to pancytopenia was seen in 8% cases, whereas study by Savith A et al, showed that the incidence of multiple myeloma was 20%.[13] In the study by Mir A et al, it was 3.7%.[14] Myelofibrosis was found in 2% cases. Study by Kumar R et al, had 2.1% cases of myelofibrosis.[10]

Tubercular infiltration of bone marrow causing pancytopenia authors found in 2% of cases. Similar observation was made by Kumar R et al, while the study by Abdullah Mir et al, had 4% cases of disseminated tuberculosis.[10,14]

Table 8: Number of various causes of pancytopenia compared to those in other studies.

Causes	Khunjer JM et al[9]	Kumar R et al[10]	Abdullah Mir et al[14]	Present study
Aplastic anemia	28	49	4	42
Megaloblastic anemia	144	37	96	30
Malaria	2	5	-	20
Disseminated TB	1	1	4	3
Myelofibrosis	2	2	-	3
Multiple myeloma	2	-	7	12
MDS	4	6	4	6
Plasma cell dyscracias	3	-	-	12
AML	-	13	3	15

Myelodysplastic syndrome presenting with pancytopenia authors got in 4% of cases similar to the study by Abdullah Mir et al.[14] Small lymphocytic lymphoma was found in 2% cases. Abdullah Mir et al, study showed the incidence to be 3.7%.[14] Author got 4% cases of SLE presenting as pancytopenia. Study by Savith et al, showed

6% cases of SLE and 2% cases of rheumatoid arthritis.[13] Study by Yadav BS et al, showed 5.6% cases of rheumatoid arthritis.[15]

Regarding infectious etiologies, author got significant number of cases of malaria with pancytopenia (13.3%), dengue (5.3%) and sepsis (1.34%). Study by Savith et al, had 8% cases of malaria, 4% of dengue and 2% of sepsis cases.[13]

Limitations of this study was small sample size, estimation of different nutrients like vitamin B12 and folic acid and different trace elements could not be done.

CONCLUSION

Etiology of pancytopenia varies from one geographical area to other. There are some reversible causes of pancytopenia like megaloblastic anemia, malaria, dengue and sepsis. Conditions like disseminated TB, collagen vascular diseases also can be treated with specific treatment if diagnosed early to avoid further complications. Studies taking large number of patients in different geographical areas are required to detect different causes of anemia especially reversible rare causes.

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