Section: Pathology

Original Research Article

STUDY OF PANCYTOPENIA IN RURAL AREA

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ABSTRACT

Background: Pancytopenia is a relatively common hematological entity suggestive of many serious and life threatening illness ranging from simple viral infections to megaloblastic anemia. Drug induceed bone marrow hypoplasia to fatal aplasia and terminal phase of leukemias. The severity of pancytopenia determines management and prognosis sometimes cause cannot be determined. **Aim & objectives:** To evaluate various hematological parameters including bone marrow aspiration (where ever feasible) in pancytopenia of adult group.
Material and Methods: Fifty patients with a hematological diagnosis of pancytopenia were studied during the period august 2020 to august 2022, in the Department of Pathology, SVS Medical College and Hospital, Mahabubnagar.
Results: Out of 50 cases, 34 were males and 16 were females. Most of the patients were in the age group of 41-60 years (54%). Megaloblastic anemia was the most important cause of pancytopenia.
Conclusion: This study concluded that most common causes of pancytopenia is megaloblastic anemia followed by aplastic anaemia, hypersplenism and leukaemia. Nutritional anaemia is commonest cause for pancytopenia. This may be due to megaloblastic anaemia or deficiency of iron/vitamin B12/folate combined. Rare causes were infections, myeloproliferative disease and SLE. Bone marrow examination is a single useful investigation which reveals the underlying causes in patients with pancytopenia.
Keywords: Bone marrow aspiration; Pancytopenia.

INTRODUCTION

Pancytopenia is a common clinico-hematological entity encountered in day-to-day clinical practice. Pancytopenia refers to a disorder in which all three elements of the blood (RBCs, WBCs and Platelets) are lower in counts than normal. Thus, it is not a disease entity by itself, but rather a triad of findings. It is a primarily or secondarily affecting bone marrow manifesting and lead to various hematological derangements, which is reflected in the peripheral blood smear as pancytopenia. There are varying trends in its etiology, clinical pattern, treatment modalities, and outcome in different studies.[1-5]

Pancytopenia is defined as hemoglobin < 12 gm%, WBCs count < 4 × 109 /L and platelet count < 100 × 109./L. Anemia defined as mild (Hb 9–12 gm%), moderate (Hb 5-9 gm%), severe (Hb 3,000/ mm3), moderate (WBCs 1,000-3,000/mm3) and severe (WBCs 50,000/mm3), moderate (platelet count 20,000-50,000/ mm3) and severe as (platelet count < 20,000/mm3).

Most of the time pancytopenia is insidious in onset. The presenting symptoms are usually anemia and thrombocytopenia, Leukopenia is an uncommon cause of initial presentation. There are many factor encompassing geographic distribution and genetic disturbances which cause pancytopenia according to various studies.

To understand the etiology of pancytopenia bone marrow biopsy plays a significant role. In some other selected cases radiological, biochemical and microbiological investigations are useful. The severity of pancytopenia and underlying etiology determine management and prognosis. Thus identification of correct cause will help in treatment. This study is therefore aimed to identify the frequent causes of pancytopenia in patients presenting to a rural area with pancytopenia disturbances may cause

variation in the incidence of disorders causing pancytopenia. A few similar studies are available in literature.[6-8]

Although it is a common clinical pattern with an extensive differential diagnosis, there is little discussion of this abnormality in major textbooks of internal medicine and haematology. Since the underlying pathology of pancytopenia determines the management and prognosis of patients, there is a definite need to study about pancytopenia.

Aim and Objectives

To evaluate various hematological parameters including bone marrow aspiration (where ever feasible) in pancytopenia in adult groupsk for each category by follow-up histopathology.

MATERIAL AND METHODS

Inclusion Criteria: Patients between age group 18-60 with hematological evidence of pancytopenia.

Exclusion Criteria: patients with below 18 years and above 60 years with pancytopenia. Patients not ammendable for follow up are excluded.

RESULTS

Fifty patients with a hematological diagnosis of pancytopenia were studied during the period, august 2020 to august 2022, in the Department of Pathology, SVS Medical College and hospital, mahabubnagar.

The following data was recorded and analysed.

Age and sex distribution of patients with pancytopenia.

Most of the patients were in the age group of 41-60 years (54%) and least occurrence was seen in the age group of 61-70 years (4%). The sex distribution of pancytopenia showed a male preponderance. The male to female ratio was 2.1:1. [Table 1]

Clinical features

Generalised weakness (88%) was the commonest symptom in pancytopenic patients, followed by fever (38%), bleeding manifestations (6%), pain abdomen (46%), abdominal distension (41%) and fever with rashes (10%). [Table 2]

Hematological Data

Hemoglobin percentage

The hemoglobin percentage varied from 1 gm% to 10 gm%. Majority (50%) of the patients had hemoglobin ranging from 5.1-7 g%. 10% of the patients had hemoglobin values between 1% and 3%. [Table 3]

Total leukocyte count

The total leukocytic count was in the range of 500-4000 cells/cumm. Most (44%) of the patients had values in the range of 3100-4000 cells/cumm. 6% of the patients had values in between 500 and 1000 cells/cumm. [Table 4]

Platelet count

The range of platelet count varied from 4000-1,50,000 cells/cumm. Most (40%) patients had platelet counts in the range of 51,000-75,000 cells/cumm. [Table 5]

Reticulocyte count

The reticulocyte count varied from 0.1-20%. Majority (82%) of the patients had reticulocyte count in the range of 0.1-2%, 4% of them had a value in between 8.1 and 20%. [Table 6]

Cellularity bone marrow

Bone marrow aspirate in the present study of pancytopenia showed the following types of cellularity. [Table 7]

a. Hypocellularity – 10%
b. Hypercellularity – 76%
c. Normocellular – 14%

PANCYTOPENIA ASSOCIATED WITH HYPOCELLULAR MARROW

In the present study, 5 out of 50 patients had hypocellular marrow.

Age and sex distribution

Aplastic anemia showed a peak incidence (60%) in the age group (41-50 years). The least incidence (20%) was seen in the age group of 31-40 years. Aplastic anemia was more common in males (60%). The male to female ratio of incidence was 1.5:1. [Table 8]

Hemoglobin percentage

The haemoglobin percentage varied from 3.1-10 gm%. Most patients (40%) had hemoglobin values in the range of 5.1-7 g%. 20% of patients were seen to have hemoglobin values in the range of 7.1-10 g%. [Table 9]

Total leukocyte count

The total leukocyte count ranged from 1100-4000 cells/cumm. Most patients (40%) had a value in the range of 1100-2000 cells/cumm and 3100-4000 cells/cumm. [Table 9]

Platelet count

The platelet count was in the range of 51,000-1,50,000 cells/cumm. Most of them (80%) had platelet values in the range of 51,000-1,00,000 cells/cumm. [Table 10]

Reticulocyte count

The reticulocyte count was in the range of 0.1-1.5%. Majority of the patients (80%) had values in the range of 0.1-1.0%.

Blood picture

Most of the patients (64.2%) had normocytic normochromic erythrocytes. Some (35.8%) showed macrocytosis. 42.8% of them had relative neutrophilia while the others had relative lymphocytosis. The erythrocyte sedimentation rate was increased in most of the patients and ranged from 28-140 mm/hr. [Table 11]

Bone marrow

The bone marrow was hypocellular and the aspirate was mostly composed of fat cells. Other precursors appeared normal. There was a relative increase in the number of plasma cells and lymphocytes.

PANCYTOPENIA WITH HYPERCELLULAR AND NORMOCELLULAR MARROW

Hypercellular bone marrow was observed in 38 patients and it was normo- cellular in 7 patients.

Most common etiology noted was megaloblastic anemia (48.9%), followed by nutritional anemia (22.2%), hypersplenism (13.3%), leukemia (6.7%), myelodysplastic syndromes (2.2%) and others (6.6%). Normocellular marrow was seen in (8%) megaloblastic anemia, (4%) hypersplenism and 2% in nutritional anemia. [Table 12]

PANCYTOPENIA WITH MEGALOBLASTIC ANEMIA

In the present study, 22 cases of megaloblastic anemia were seen. It constituted 47.4% of cases with hypercellular marrow, and 44% of all patients with pancytopenia.

Hemoglobin percentage

Hemoglobin percentage varied from 2-10 g%. Majority of the patients (68.2%) had values in the range of 5.1-7 gm%. [Table 13]

Total leukocyte count

The total leukocyte count ranged from 500-4000 cells/cumm. Majority of the patients (81.8%) had a leukocyte count in the range of 2100-4000 cells/cumm. 4.6% of patients had values ranging from 500-1000 cells/cumm. [Table 14]

Platelet count

The platelet count varied from 26,000-1,50,000 cells/cumm. Most of the patients (40.9%) had a platelet count in the range of 51,000-75,000 cells/cumm. 9.1% patients had values in the range of 26,000-50,000 cells/cumm. [Table 15]

The reticulocyte count varied from 0.1-6%. Most of them (77.3%) had reticulocyte count in the range of 0.1-2%. [Table 16]

Reticulocyte count

Platelet count

The platelet count was in the range of 26,000-1,40,000 cells/cumm. Majority (33.3%) of the patients had values in the range of 51,000-75,000 and 1,01,000- 1,50,000 cells/cumm. [Table 18]

Platelet count

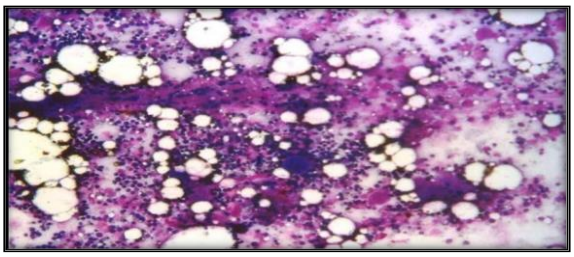

Figure 1: Normal bone marrow. (Leishman's stain 10x X 10x)

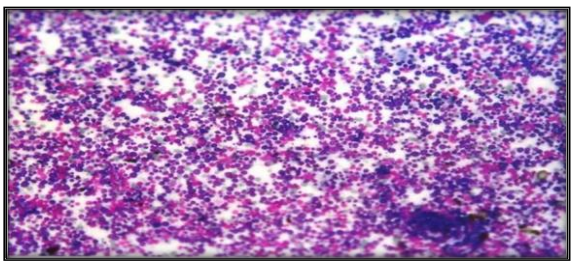

Figure 2: Bone marrow aspiration smear showing Erythroid Hyperplasia (Leishman's stain 10x X 10x)

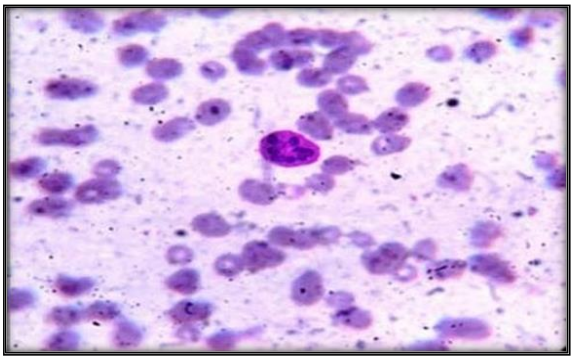

Figure 3: Megaloblastic anemia. Peripheral smear showing hypersegmented neutrophils and macroovalocytes. Leishman's stain – 10x X 100x

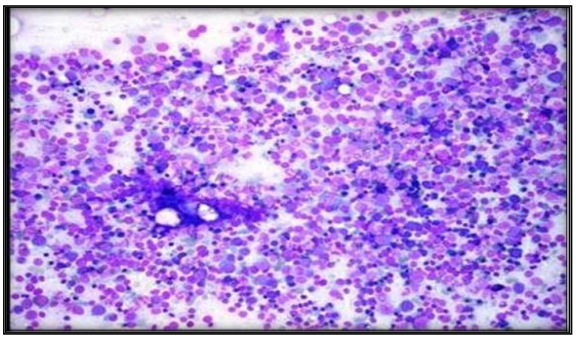

Figure 4: Megaloblastic anemia. Bone marrow aspiration smear showing hypercellular marrow. Leishman's stain – 10x X 10x

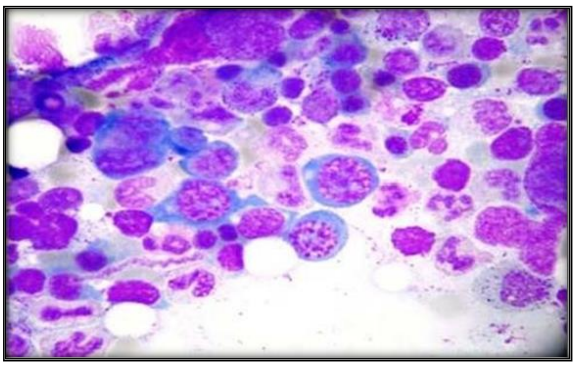

Figure 5: Megaloblastic anemia. Bone marrow aspiration smear showing megaloblasts with open chromatin. Leishman's stain – 10x X 100x

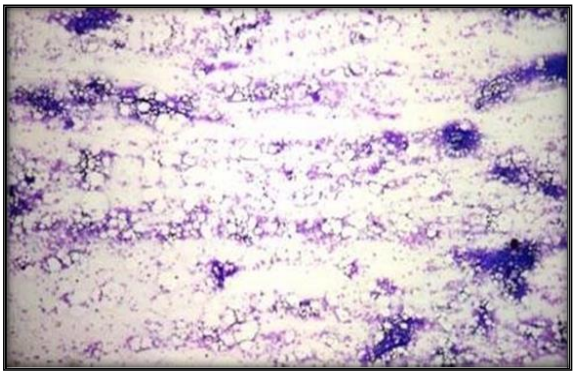

Figure 6: Aplastic anemia. Bone marrow aspiration smear showing increase in fat cells. Leishman's stain- 10x X 10x

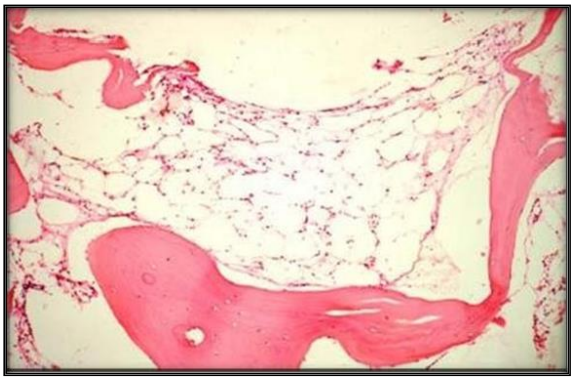

Figure 7: Aplastic anemia. Bone marrow trephine biopsy showing increase in fat cells. H & E Stain- 10x X 40x

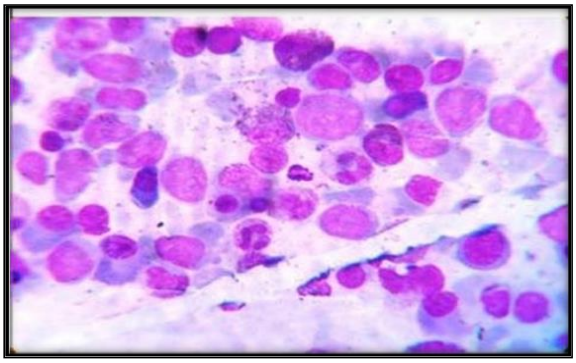

Figure 8: AML. Bone marrow aspiration smear showing myeloblasts.
Leishman's stain- 10x X 40x

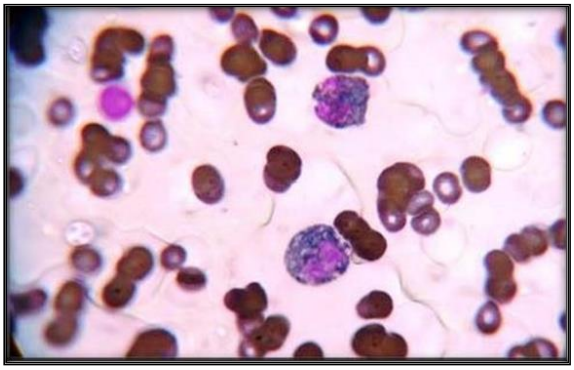

Figure 9: AML. Bone marrow aspiration smear showing myeloblasts positive for MPO.-10x X 100x

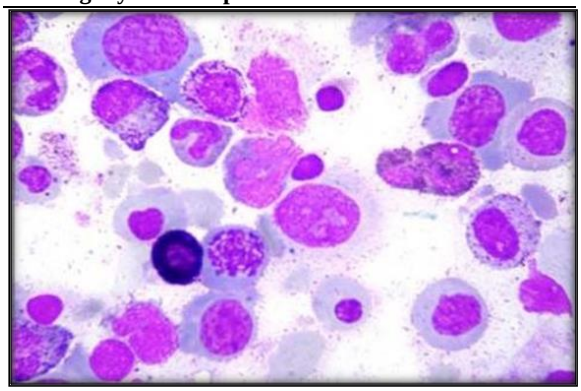

Figure 10: MDS. Bone marrow aspiration smear showing dyserythropoiesis and blasts. Leishman's stain- 10x X 100x

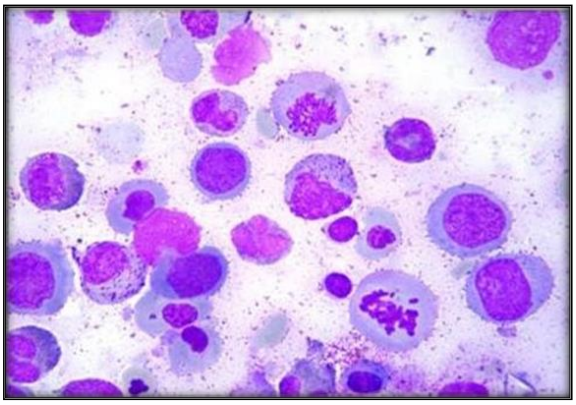

Figure 11: MDS. Bone marrow aspiration smear showing dyserythropoiesis and mitosis. Leishman's stain- 10x X 100x

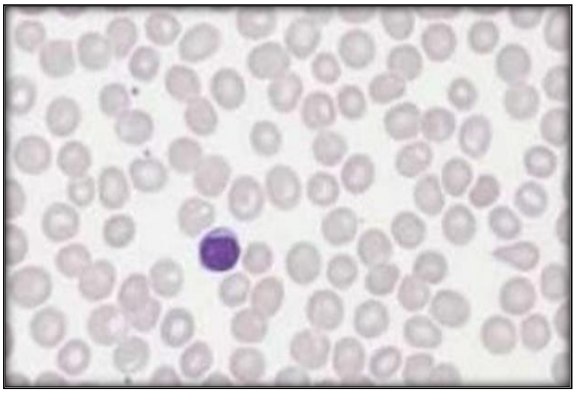

Figure 12: Macroovalocytes in megaloblastic anemia (H&E)

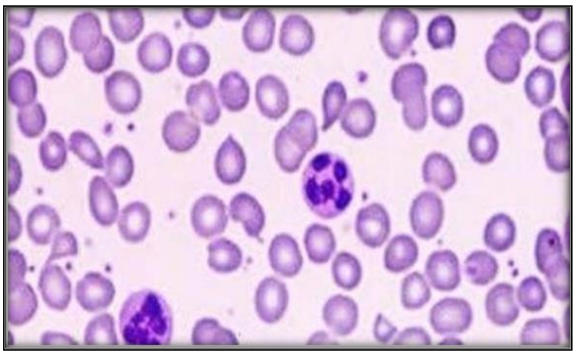

Figure 13: Hypersemented neutrophils in Megaloblastic anemia (Leishman stain 1000x)

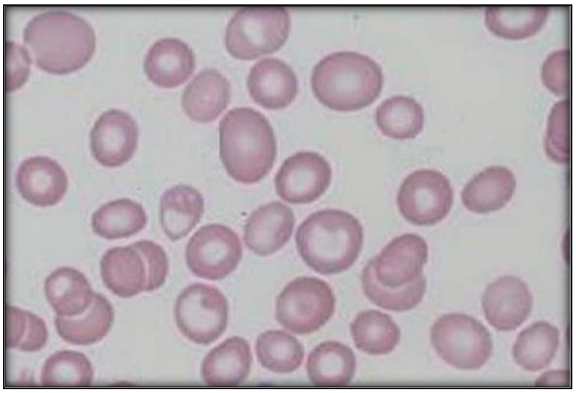

Figure 14: Dimorphic anemia. (Leishman Stain, 1000x)

Table 1: Age and sex distribution of patients with pancytopenia

Age group (years)	Female	Male	Total no. of cases	Percentage
18-20	1	3	4	6
21-30	2	3	5	14
31-40	4	7	11	22
41-50	3	12	15	28
51-60	5	8	13	26
61-70	1	1	2	4
Total	16	34	50	100

Table 2: Clinical features

Symptoms	No. of cases	Percentage	Chi-square andp-value
Generalised weakness	43	87	χ^2=16.867;p<.000
Fever	20	38	χ^2=1.451;p<.217
Bleeding	3	65	χ^2=24.008;p<.000
Pain abdomen	22	44	χ^2=0.150;p<.689
Abdominal distension	41	82	χ^2=11.408;p<.001
Fever with rashes	5	10	χ^2=19.048;p<.000

Table 3: Range of hemoglobin in patients with pancytopenia

Hemoglobin percentage	No. of cases	Percentage
1 to 3	5	10
3.1 to 5	10	20
5.1 to 7	25	50
7.1 to 10	10	20
Total	50	100

Table 4: Range of leukocyte count in patients with pancytopenia

Leukocyte count(cells/cumm)	No. of cases	Percentage
500-1000	3	6
1100-2000	11	22
2100-3000	14	28
3100-4000	22	44
Total	50	100

Table 5: Range of platelet count in patients with pancytopenia

Platelet count (cells/cumm)	No. of cases	Percentage
4000-25000	2	4
26000-50000	9	18
51000-75000	20	40
76000-1,00,000	12	24
101000-1,50,000	7	14
Total	50	100

Table 6: Range of reticulocyte count in patients with pancytopenia

Reticulocyte count	No. of cases	Percentage
0.1-2	41	82
2.1-4	5	10
4.1-6	2	4
6.1-8	0	0
8.1-20	2	4
Total	50	100

Table 7: Bone marrow cellularity in patients with pancytopenia

Type of cellularity	No. of cases	Percentage
Hypercellular	38	76
Hypocellular	5	10
Normocellular	7	14
Total	50	100

Table 8: Age and sex distribution of patients with aplastic anemia

Age (years)	Female	Male	Total no. ofcases	Percentage
18-20	0	0	0	0
21-30	0	0	0	0
31-40	0	1	1	20
41-50	1	2	3	60
51-60	1	0	1	20

61-70	0	0	0	0
Total	2	3	5	100

Table 9: Range of hemoglobin in patients with aplastic anemia

Hemoglobin percentage	No. of cases	Percentage
1-3	0	0
3.1-5	2	40
5.1-7	2	40
7.1-10	1	20
Total	5	100

Table 9: Range of leukocyte count in patients with aplastic anemia

Leukocyte count (cells/cumm)	No. of cases	Percentage
500-1000	0	0
1100-2000	2	40
2100-3000	1	20
3100-4000	2	40
Total	5	100

Table 10: Range of platelet count in patients with aplastic anemia

Platelet count(cells/cumm)	No. of cases	Percentage
4000-25000	0	0
26000-50000	0	0
51000-75000	2	40
76000-1,00,000	2	40
101000-1,50,000	1	20
Total	5	100

Table 11: Range of reticulocyte count in patients with aplastic anemia

Reticulocyte count	No. of cases	Percentage
0.1-0.5	2	40
0.6-1.0	2	40
1.1-1.5	1	20
1.6-2	0	0
Total	5	100

Table 12: Pancytopenia with hypercellular and normocellular marrow

Etiology	Total no. ofcases		Hypercellular		Normocellular	
	No.	%	No.	%	No.	%
Megaloblastic anemia	22	100	18	81.8	4	18.2
Nutritional anemia	10	100	9	90	1	10
Hypersplenism	6	100	4	66.7	2	33.3
Leukemia	3	100	3	100	0	0
Myelodysplastic syndrome	1	100	1	100	0	0
Dengue	2	100	2	100	0	0
Hemolytic anemia	1	100	1	100	0	0

Table 13: Range of hemoglobin in patients with megaloblastic anemia

Hemoglobin percentage	No. of cases	Percentage
1-3	2	9.1
3.1-5	2	9.1
5.1-7	15	68.2
7.1-10	3	13.6
Total	22	100

Table 14: Range of leukocyte count in patients with megaloblastic anemia

Leukocyte count(cells/cumm)	No. of cases	Percentage
500-1000	1	4.6
1100-2000	3	13.6
2100-3000	9	40.9
3100-4000	9	40.9
Total	22	100

Table 15: Range of platelet count in patients with megaloblastic anemia

Platelet count(cells/cumm)	No. of cases	Percentage
4000-25000	0	0
260000-50000	2	9.1
51000-75000	9	40.9
76000-1,00,000	8	36.4

101000-1,50,000	3	13.6
Total	22	100

Table 16: Range of reticulocyte count in patients with megaloblastic anemia

Reticulocyte count	No. of cases	Percentage
0.1-2	17	77.3
2.1-4	4	18.2
4.1-6	1	4.5
6.1-8	0	0
8.1-20	0	0
Total	22	100

Table 17: Range of reticulocyte count in patients with nutritional anemia

Reticulocyte count	No. of cases	Percentage
0.1-2	5	50
2.1-4	2	20
4.1-6	2	20
6.1-8	1	10
8.1-20	0	0
Total	10	100

Table 18: Range of platelet count in patients with hypersplenism

Platelet count(cells/cumm)	No. of cases	Percentage
4000-25000	0	0
26000-50000	1	16.7
51000-75000	2	33.3
76000-1,00,000	1	16.7
101000-1,50,000	2	33.3
Total	6	100

Table 19: Range of platelet count in patients with leukemia

Platelet count(cells/cumm)	No. of cases	Percentage
4000-25000	0	0
26000-50000	1	33.3
51000-75000	1	33.3
76000-1,00,000	1	33.4
101000-1,50,000	0	0
Total	3	100

DISCUSSION

In the present study, megaloblastic anemia (44%) was the commonest cause of pancytopenia, followed by nutritional anemia (20%), hypersplenism (12%), aplastic anemia (10%), malignant diseases (6%), myelodysplastic syndromes (2%) and others (6%). Others included uncommon causes like Dengue fever (4%) and Hemolytic anemia (2%).

Verma N, Dash S,[8] (1992) found aplastic anemia in 40.6% and megaloblastic anemia in 23.26% of patients. Tilak V, Jain R,[9] (1998) found megaloblastic anemia (68%) to be the commonest cause of pancytopenia followed by aplastic anaemia (7.7%). Savage DG et al,[10] (1999) found megaloblastic anemia to be the commonest cause followed by aplastic anemia. Kumar et al,[11] (1999) found hypoplastic anemia (29.5%) to be the commonest cause followed by megaloblastic anemia.

In the present study, megaloblastic anemia (44%) was the commonest cause of pancytopenia followed by nutritional anemia (20%). The commonest cause of pancytopenia, reported from various studies throughout the world has been aplastic anemia. Megaloblastic anemia is common in India. This seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

Age and sex distribution

In the study of pancytopenia cases by Jha et al., the age range was 10-79 years (31 years). There was a male preponderance and male to female ratio was 1.5:1. In the study by Kumar et al,[11] the ages ranged from 14-73 years (39.5%). There was a female preponderance and the male to female ratio was 2:1. In the present study, age ranged from 18-70 years. Majority of the patients were in the age group of 31-50 years (62%). There was a male preponderance and the male to female ratio was 2.4:1.

Peripheral Smear

The principal hematologic manifestations are, varying degrees of anemia, leucopenia, thrombocytopenia, anisopoikilocytosis, macroovalocytosis and hyper- segmented neutrophils.

In the study by Kishore Khodke et al,[2] 20/22 cases showed anisocytosis, 10/22 cases showed dimorphic blood picture and 20/22 cases showed hypersegmented neutrophils. In the study by Tilak et al,[10] 51/53 cases showed anisocytosis, 45/53.

In the present study, mixed deficiency was seen in 20% of patients. This percentage is much lower than

expected because 60-80% of world population is affected by iron deficiency anemia which is the most common preventable nutritional deficiency in the world. The possible explanation is that, majority of the cases present with anemia rather than pancytopenia and are diagnosed on smear examination and treated as outpatients.

In the present study, 64.2% had normocytic normochromic erythrocytes. 35.8% of the patients had macrocytic anemia and 56.3% of them had relative lymphocytosis. Bone marrow

Cellularity of bone marrow in aplastic anemia is very much reduced. It may be hypocellular or acellular. Lymphocytes and plasma cells are prominent. Daniel NM in their analysis of 50 cases reported 74% of patients with hypocellular marrow, 16% of patients with normocellular marrow which later became hypocellular and 10% with acellular marrow.

In the present study, bone marrow was mostly hypocellular and the aspirate was composed of fat cells in all the patients. There was a relative increase in plasma cells and lymphocytes. Bone marrow trephine biopsy revealed replacement of marrow by fat cells.

In the present study, hypersplenism was the cause of pancytopenia in 10% of cases. Ages ranged from 41-70 years. There was a male preponderance with the male to female ratio being 2:1.

In the present study leukemia accounted for 6% of pancytopenia cases. Majority (66.7%) of the pancytopenia cases were due to acute leukemia. The ages varied from 21-40 years. There was a male preponderance with male to female ratio being 2:1.

Pancytopenia is known to occur in MDS. It is the least common finding encountered in patients with MDS as compared to mono and bicytopenia.

In a study of 816 patients with MDS by Greenberg et al,[12] pancytopenia was found in 15% of the patients. In a study of 31 patients of MDS by Kini J et al.13 bicytopenia was the commonest finding.

Age and sex distribution. In a study of 118 patients with MDS by Juneja SK et al,[14] the age ranged from 48-95 years. In a study of 31 patients by Kini J et al,[13] the patients were in the age group of 4-7 years.

In the present study, one case presented with pancytopenia in a female patient aged 55 years.

CONCLUSION

Pancytopenia is a common entity. However, it has received inadequate attention in the Indian subcontinent. A study of pancytopenia using easily available diagnostic techniques is therefore important. Age and sex distribution of patients with pancytopenia in this study was consistent with the findings in other studies. Megaloblastic anemia was the commonest cause of pancytopenia in the present study. Most other studies have reported aplastic anemia as the commonest cause. This seems to reflect higher prevalence of nutritional anaemia in the Indian subjects. The haematological parameters and bone marrow morphological features in patients with megaloblastic anaemia, aplastic anaemia and malignant diseases including MDS in the present study were comparable to the findings by other authors. Uncommon etiological factors like dengue fever and hemolytic anemia were identified in this study. A comprehensive clinical, haematological and bone marrow study of patients with pancytopenia usually helps in identification of the underlying cause. However, in view of a wide array of etiological factors, pancytopenia continues to be a challenge for hematologists.

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