RESEARCH ARTICLE

CLINICAL AND HEMATOLOGICAL PROFILE OF PANCYTOPENIA

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ABSTRACT

Background: *Pancytopenia is a disorder in which all three cellular elements of blood (red blood cells, white blood cells & platelets) are decreased and* **this** *leads to triad of findings which includes anemia, leucopenia and thrombocytopenia. It can be due to reduction in hematopoietic cell production in the bone marrow due to infections, chemotherapy, parasitic infestation etc. The severity of pancytopenia and the underlying pathology determines the management and prognosis of the patients. Thus, identification of correct cause will help in implementing appropriate therapy.*
Aims and Objectives: *i) To evaluate haematological parameters in pancytopenic cases. ii) To classify pancytopenic cases on etiological basis. iii) To study various clinical presentations in pancytopenic cases.*
Material and Methods: *70 pancytopenic patients were evaluated clinically, along with haematological parameters and bone marrow examination in the Department of Pathology, CSSH, Meerut, during the period of September 2011 to June 2013.*
Results and Conclusion: *Among 70 cases studied, all age group patients were included. Maximum number of patients were in the age group 11-20 yrs with female predominance. Most of the patients presented with fever and pain in legs. The commonest physical finding was pallor. In most of the patients Hemoglobin ranged between 5.1-8.0 g/dl, Total leucocyte count ranged between 1000-2500/cumm and Platelet count ranged between <5000-50,000/cumm. The commonest cause for pancytopenia was malaria (28.57%), followed by aplastic anemia (14.28%). In our study most common bone marrow finding (n= 23) was hypocellularity with aplastic anemia.*

Key words: Pancytopenia, White blood cell, Red blood cell, Platelets

INTRODUCTION

Pancytopenia is an important clinico-hematological entity encountered in our day to day practice. It is a disorder in which all three cellular elements of blood (red blood cells, white blood cells and platelets) are decreased and thus **leads** to triad of findings which includes anemia, leucopenia and thrombocytopenia.[1,2] Patient usually presents with fatigue and weakness due to anemia, increased susceptibility to infections due to leucopenia and bleeding tendencies because of thrombocytopenia. Pancytopenia may result from number of disease processes which effect bone marrow either primarily or secondarily.[1,2] It can be due to reduction in hematopoietic cell production in the bone marrow by means of infections, malignant cell infiltration or suppression, chemotherapy, radiotherapy and parasitic infestation.[3,4,6,9] The incidence of different **disorders** causing pancytopenia

is variable according to geographical distribution and genetic variation.[3,11,12,13] Physical findings and peripheral blood picture provide valuable information in the workup of pancytopenic patients and help in planning investigations on bone marrow samples.[4] Bone marrow evaluation is an invaluable diagnostic procedure which may confirm the diagnosis of suspected **cytopenias**.[15] The present study has been undertaken to evaluate the various causes of pancytopenia and to correlate the peripheral blood findings with bone marrow aspirate.

MATERIAL AND METHODS

The present study was conducted on the **patients** attending outpatient and inpatient department of Chattrapati Shivaji Subharti Medical College and Associated Hospital over a period of 22 months from September 2011 to June 2013. All cases irrespective of age and sex with all of the 3

following criteria were included in the study –Hemoglobin <10g/dl; Total leucocyte count (TLC) <3,500/cumm and Platelet count <100,000/cumm. Complete history was taken and physical examination was performed on all pancytopenic cases and further investigations were conducted to evaluate the cause of pancytopenia. For haematological study, blood samples were collected in Ethylene diamine tetra acetic acid (EDTA) anticoagulant for all the tests except for Erythrocyte sedimentation rate (ESR) & coagulation profile, Trisodium citrate anticoagulant was used. All the hematological tests were carried out by MS9-

3H & ABX-PENTRA (automatic cell counter) based on the principle of Impedance counting. ESR was estimated in all cases by Westergren's method. Peripheral smears were stained by Leishman stain for all the cases and examined in details. Bone marrow aspiration and biopsy was carried out under aseptic precautions after obtaining written consent from the patients or guardian.

RESULTS

A total of 70 cases who presented with pancytopenia were studied. The results are as per the tables below.

TABLE 1: INCIDENCE OF PANCYTOPENIA IN DIFFERENT AGE GROUPS

AGE GROUPS (yrs.)	NUMBER OF CASES	PERCENTAGE
1-10	08	11.43%
11-20	19	27.14%
21-30	09	12.86%
31-40	07	10.00%
41-50	12	17.14%
51-60	08	11.43%
61-70	06	8.57%
71-80	01	1.43%
TOTAL	**70**	**100**

Maximum number of patients were between 11-20 yrs (27.14%).

Table 2: Presenting Complaints among Pancytopenic Cases

S.NO.	SYMPTOMS	NUMBER OF PATIENTS	PERCENTAGE
1.	Fever	45	64.28%
2.	Pain in legs	29	41.42%
3.	Weakness	24	34.28%
4.	Bleeding tendencies	24	34.28%
5.	Abdominal pain	12	17.14%
6.	Resp. Symptoms	10	14.28%

The commonest mode of presentation was fever which was present in 64.28% of cases. The other main symptoms were pain in legs (41.42%), weakness (34.28%), bleeding tendencies (34.28%), abdominal pain (17.14%) and respiratory symptoms (14.28%). Pallor was noted in all cases.

Splenomegaly (22.85%) was seen most commonly in malaria patients. Hepatomegaly (18.57%) was also seen most commonly in malaria patients followed by CLD. Jaundice was seen in 10 cases (14.28%).

Table 3: Haematological Parameters in Cases of Pancytopenia

S.NO.	PARAMETER	RANGE	NUMBER OF CASES	PERCENTAGE
1.	HB (g/dl)	1.5 - 5.0	27	38.57%
		5.1 - 8.0	24	34.29%
		8.1 - 9.9	19	27.14%
	TOTAL		**70**	**100%**
2.	TLC (cumm)	490 – 1000	05	7.14%

		1000 – 2500	36	51.43%
		2500 – 3500	29	41.43%
	TOTAL		**70**	**100%**
3.	PLT (cumm)	< 5000 - 50,000	36	51.43%
		51,000 - 80,000	14	20.00%
		81,000 - 99,000	20	28.57%
	TOTAL		**70**	**100%**

Hemoglobin percentage varied from 1.5 – 9.9 g/dl. Most of the patients had haemoglobin percentage between 1.5 – 5.0 g/dl. Lowest value of 1.5 g/dl was seen in a case of Malaria. Total leucocyte count ranged from 490 – 3,500/cumm. Most of the patients had total leucocyte count in range of 1,000– 2,500/cumm. Lowest count of 490/cumm was found in a case of Aplastic anemia. Platelet count ranged from < 5,000 – 99,000/cumm. Most of the patients had platelet count between < 5,000 – 50,000/cumm. Lowest platelet count of <5,000/cumm was seen in a case of Malaria.

Table 4: Peripheral Blood Smear in Pancytopenic Patients

S.NO.	TYPE OF ANEMIA	NO. OF CASES	PERCENTAGE
1.	Dimorphic	25	35.71 %
2.	Normocytic hypochromic	20	28.57 %
3.	Microcytic hypochromic	20	28.57 %
4.	Normocytic normochromic	04	5.72 %
5.	Macrocytic	01	1.43 %
	TOTAL	**70**	**100 %**

The predominant blood picture was dimorphic anemia constituting 35.71%, followed by normocytic hypochromic (28.57%) and microcytic hypochromic anemia (28.57%).

Table 5: Cellularity Of Bone Marrow Examination

S.NO.	TYPE OF CELLULARITY	NO. OF CASES	PERCENTAGE
1.	Hypocellular	11	44%
2.	Hypercellular	07	28 %
3.	Normocellular	03	12 %
4.	Inadequate	04	16 %
	TOTAL	**25**	**100 %**

Out of 70 cases bone marrow examination was performed in 25 cases which showed three distinct types of cellularity – hypocellularity, hypercellularity and normocellularity. Hypocellular marrow was observed in 11 cases (44 %) followed by hypercellular marrow in 7 cases (28 %) and normocellular marrow in 3 cases (12 %). There were 4 cases (16%) which were reported as inadequate material.

Table 6: Distribution of Various Causes of Pancytopenia

S. NO.	ETIOLOGY	NO. OF CASES	PERCENTAGE
1.	Malaria	21	30.00%
2.	Aplastic anemia	10	14.28 %
3.	Tuberculosis	09	12.86 %
4.	Drug induced	08	11.43 %
5.	CLD	07	10.0 %
6.	Nutritional def. anemia	05	7.14 %

7.	Megaloblastic anemia	01	1.43 %
8.	Myelodysplastic syndrome	01	1.43 %
9	Iron def. anemia	01	1.43 %
10.	Ineffective erythropoiesis	01	1.43 %
11.	Refractory anemia	01	1.43 %
12.	Acute leukemia	01	1.43 %
13.	Undiagnosed (Inadequate)	4	5.71%
14.	**TOTAL**	**70**	**100%**

Malaria is the most common cause of pancytopenia, accounts for 30% of cases. Aplastic anemia was the second most common cause accounts for 14.28% of cases followed by Tuberculosis in 12.86%, drug induced pancytopenia in 11.43%, Chronic liver disease in 10.00%, Nutritional deficiency anemia in 7.14% of cases. 1.43% cases each of Megaloblastic anemia, Myelodysplastic syndrome, Iron deficiency anemia, Ineffective erythropoiesis, Refractory anemia and Acute leukemia were observed.

DISCUSSION

70 cases of pancytopenia during the period of September 2011 till June 2013 were studied. Statistical data of age, sex, presenting complaints, various causes of pancytopenia, peripheral smear and bone marrow aspiration smears were studied, and compared with those published in the literature. In the present study, 11-30 years age group was most commonly affected. Common age group affected was 1 – 30 yrs in the studies done by Tilak et al, Kishore et al, Khunger et al, Jha et al..[5,7,11,13]

In our study 32 cases were male and 38 cases were female. There was a female preponderance (54.28%) with male to female ratio of 1:1.2. Kumar and Raghupati in their study on 48 cases also found female predominance with male to female ratio of 1: 1.8.[14] Although several other studies showed male predominance[1,7,11,13]. Common presenting symptoms in our study were fever (64.28%) followed by pain in legs (41.42%), weakness (34.28%) and bleeding tendencies (34.28%). This is comparable to a study by Khodke et al in which the common presenting symptoms were fever (40%) followed by weakness (30%) and bleeding

manifestation (20%).[7] In the present study pallor was present in all patients. 16 out of 70 patients had splenomegaly (22.85%) and 13 cases had hepatomegaly (18.57%). 10 patients (14.28%) had icterus either because of hemolysis or hepatocellular injury due to malaria. Khodke et al in their study also found pallor in all patients followed by splenomegaly (40%), hepatomegaly (38%), purpuric spots (28%) and lymphadenopathy (12%).[7] In the present study of 70 patients it was observed that malaria was the most common cause of pancytopenia. The incidence of malaria in our study was 30%. Our study is comparable to the study done by Tareen et al in which most common cause of pancytopenia was malaria in 29.44% patients.[3] Also Hamid et al in their study of 75 cases found malaria as the most common cause of pancytopenia with an incidence of 17.3%.[6] Arya and Prasad reported fatal pancytopenia in malaria.[15] Thakkar et al in their study found that malaria accounts for 19% of cases of pancytopenia.[16] Although literature shows that most common cause of pancytopenia is aplastic anemia worldwide and in **India** it is megaloblastic anemia, the high incidence of malaria in our study may be related to its endemic nature in this part of world and also due to lack of hygiene (sanitation) in the residential area.

The second most common cause of pancytopenia in our study was aplastic anemia (14.28%). It is the commonest cause of pancytopenia reported from various studies throughout the world.[5,17] The incidence of aplastic anemia varies from 10% to 52.7% as a cause of pancytopenia.[11,17] Some other studies showed that aplastic anaemia is the 2nd most common cause of pancytopenia.[11,13,18] Our incidence of aplastic anemia correlate with the studies done by Khodke et al and Khunger et al

whose incidence for the same was 14.0%.[7,13] A higher incidence of 29.5% was reported by Kumar et al.[17] The incidence of aplastic anemia quoted from west is much higher than observed by us. Their **increased** incidence may be related to environmental factors such as increase exposure to toxic chemicals.

Tuberculosis related pancytopenia is the third most common observation in our study. It was noted in 12.86% of our cases. Tareen et al in their study found that tuberculosis accounts for 17.22% cases of pancytopenia.[3] Pancytopenia was seen in 8% in a series of 38 patients with milliary T.B by Mert et al.[19] Basu et al, Yadav et al and Singh et al reported various causes of pancytopenia in disseminated T.B.[20,21,22]

In our study there were 8 cases (11.42%) of drug induced pancytopenia, 6 were due to intake of chloramphenicol, 1 due to administration of streptomycin and 1 was due to intake of methotrexate. The role of chloramphenicol as the causative agent of aplastic anemia has been investigated extensively.[23] Also there are few reports of development of pancytopenia secondary to intake of streptomycin.[24] I Gutierrez urena et al and Wluka et al reported development of pancytopenia in 1.4% cases and 2.8% cases respectively exposed to methotrexate.[25,26] Thakkar et al in their study showed drug induced pancytopenia in 3% of cases.[16] Tilak et al and Verma et al found 5.2% and 4.2% cases of drug induced pancytopenia respectively.[11,27]

In our study pancytopenia due to CLD were found in 10% of cases. Osama ishtiaq et al in their study showed that cirrhosis leading to hypersplenism accounts for 12% of cases of pancytopenia.[28] Megaloblastic anemia is the most common cause of pancytopenia with incidence ranging from 39% to 72% as shown in studies by Tilak et al, Khunger et al and Osama et al .[11,13,28] whereas, it was 2nd most common cause in studies done by Kumar et al and Memon et al.[17,29] This may be explained by nutritional deficiency and low socioeconomic condition in developing country. In our study megaloblastic anemia was uncommon constituting 1.42% patients only. This wide variation in the incidence of megaloblastic anemia is probably due to variation in the nutritional status of that particular region where the study was done. Nutritional anemia as a common etiological factor causing pancytopenia is well recognized and established. The nutritional deficiency of either B12 or folate results in megaloblastic anemia. Other causes include mixed nutritional deficiency anemia (microcytic and macrocytic). In the present study, mixed nutritional deficiency was seen in 7.14% cases. This is comparable to study by Memon et al in which mixed nutritional deficiency was seen in 8.69% cases.[29] Mobina et al in their study of 392 cases of pancytopenia found 11.2% cases of mixed nutritional deficiency anemia.[30] In the present study we had one case of MDS with pancytopenia. Pancytopenia with few abnormal cells as seen in MDS was also noted in 2% cases by Khunger et al.[13] Variation in the frequency of disorders causing pancytopenia has been ascribed to differences in methodology, stringency of diagnostic criteria, geographic area, period of observations, genetic differences, and varying exposure to cytotoxic agents.

CONCLUSION

Pancytopenia is not an uncommon haematological problem encountered in clinical practice and should be suspected on clinical grounds when a patients presents with unexplained anemia, prolonged fever and tendency to bleed. In the present study Malaria was the commonest cause of pancytopenia followed by Aplastic anemia, Tuberculosis, Drug induced. Chronic liver disease and Nutritional deficiency anemia.

The other rare causes were Megaloblastic anemia, Myelodysplastic syndrome, Iron deficiency anemia, Ineffective erythropoiesis, Refractory anemia and acute leukemia. Present study concludes that detailed primary haematological investigations along with bone marrow aspiration is helpful in identifying cause of pancytopenia

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