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Original Paper

CLINICO HAEMATOLOGICAL STUDY IN CASES OF PANCYTOPENIA

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Abstract:

Aims and Objectives: To study the various causes of pancytopenia in our region and assess the haematological and bone marrow findings in various cases of pancytopenia.

Materials and Methods: The study is of prospective and analytical type, conducted on patients attending outpatient and inpatient department of AVBRH, tertiary care centre. All the cases irrespective of age and sex with pancytopenia were included in this study. Peripheral smear was used for morphological classification and typing of anemia. Bone marrow aspiration was then carried out under all aseptic precautions and slides were stained with leishmans stain. Cytochemistry was done using Myeloperoxidase stain and Periodic Acid and Schiff reagent stain were performed where necessary. Significant parameters like aetiology, age, gender, clinical features, hematological parameters, peripheral blood film, bone marrow aspiration findings in different cases of pancytopenia were compared with various studies published in literature.

Results: A detailed peripheral blood smear examination was done on all patients. Megaloblastic anemia had 28 cases, 11 patients of acute leukemia immature cells, aplastic anemia had total 5 cases. The commonest bone marrow finding was megaloblastic anaemia 28(52.8%), followed by acute leukemia 11(20.8%) and normoblastic erythroid hyperplasia 6(11.3%), aplastic anaemia5(9.4%) other causes were mixed nutritional anaemia, multiple myeloma and Non hodkins lymphoma all had 1(1.9%) case each.

Conclusion: In our country main cause of pancytopenia being fortunately megaloblastic anaemia which responds very well to treatment if diagnosed correctly in time. The present study concludes that detailed haematological investigations along with bone marrow examination in cytopenic patients are not only helpful in understanding the disease process but also to diagnose or to rule out the causes of pancytopenia and planning further investigations and management of these patients.

Key words: Acute Leukemia, Aplastic Anemia, Megaloblastic Anemia, Mixed Nutritional Anemia, Pancytopenia.

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INTRODUCTION:

Pancytopenia was not a discrete hematological entity even as late as 1919. The term was used almost synonymously for aplastic anaemia, it being the major cause of pancytopenia in the western countries[1] . Aplastic anaemia (AA) is a lifethreatening bone marrow failure disorder, if untreated, is associated with very high mortality. The incidence of AA is higher in Asia than in the West. It appears to be 2 to 3-fold more common in Asia than in Europe[2]. The precise incidence of AA in India is not known due to lack of epidemiological study. However, in hospital based study, it is known that 20-40% of pancytopenic patients are diagnosed as AA in referral centres[3]. In an epidemiological study in children in and around Lucknow, UP, showed the annual incidence of aplastic anaemia is around 6.8 cases per million of population per year[4].

Peripheral cytopenia is defined as reduction in either of the cellular elements of the blood, i.e. red blood cells, white blood cells or platelets. Bicytopenia is the reduction of any of the two cell lines and pancytopenia is reduction of all the three (haemoglobin<10g/dl, absolute neutrophil count 1.5 x 109/l and platelet count <100 x 109/L)[5]. The etiology of bicytopenia and pancytopenia varies ranging from transient marrow viral suppression to marrow infiltration by life threatening malignancies. Pancytopenia can result from a failure of production of hematopoietic

progenitors, their destruction, or replacement of the bone marrow by tumor or fibrosis. Although selective cytopenias are important clinical entities, pancytopenia is a loss of all marrow elements. Pancytopenia can be constitutional, arising as a consequence of an inherited genetic defect affecting hematopoietic progenitors, or can be acquired as a consequence of either direct destruction of progenitors, immune mediated damage to either haematopoietic progenitors or their nurturing microenvironment, or suppression of or crowding out of progenitors by tumor cells or fibrosis.

Although Fanconi anemia is the best-recognized constitutional pancytopenia, a number of other infrequent genetic disorders have also been implicated. These genetic syndromes include various modes of inheritance and may be associated with a number of congenital abnormalities, especially of the bones, kidneys, and heart. Because the hematologic manifestations of the congenital pancytopenias may not become manifested until the first years to even decades of life, a genetic predisposition to bone marrow failure should be considered in all cases of aplastic anemia .These disorders can be autosomal recessive (e. g., Fanconi anemia, dyskeratosis congenita), X linked, or autosomal dominant (e. g., dyskeratosis congenita). Several of these genetic disorders may present initially with a single cytopenia and progress to pancytopenia (Swaschman- Diamond syndrome, amegakaryocytic thrombocytopenia, reticular dysgenesis). In addition, a number of inheritable familial marrow dysfunction syndromes have been associated with pancytopenia (which can also be autosomal recessive, autosomal dominant, or X linked), and aplastic anemia also occurs in association with other genetic disorders. Thus, pancytopenia can be either the primaiy disease manifestation or can emerge as a rare complication during the course of another illness. Because of the chromosomal fragility or defective repair mechanisms that may be associated, several of these disorders can also be complicated by cancer or other organ dysfunction(s)[6]

Most common non malignant cause of acquired pancytopenia is aplastic anemia followed by megaloblastic anemia. Among the malignant causes acute leukemia is most common. Pancytopenia caused by marrow replacement is seen to occur in leukemia. Pancytopenias can be caused by various drugs-chemotherapeutic agents, antiepileptics (hydantoin, carbamazepine) NSAIDS (phenylbutazone, ibuprofen, diclofenac. Prolonged cytopenias can occur after infection with many of the hepatitis viruses, Epstein Barr Virus, Cytomegalovirus. Pancytopenia may occur after a single high dose of radiation[7]. Non malignant conditions are Immune Thrombocytopenic Purpurc, megaloblastic anemia, marrow hypocellularity and visceral leishmaniasis. Commonest malignant condition associated with bicytopenia is leukaemia, acute lymphoblastic leukemia being commoner.

Pancytopenia usually presents with symptoms of bone marrow failure such as pallor, dyspnea, bleeding, bruising and increased tendency to infections[8]. The main presenting features swith pancytopenia are fever and pallor. Other common symptoms are petechial rash, bleeding and bone pains. Dyspnea on exertion, easy bruising, epistaxis, gingival bleeding and headache may be the presenting features[7]. Oral infections in the form of gingivitis, tonsillitis and pharyngitis may be found[9]. Pancytopenia results in increased risk of fatigue, cardiac failure and infection. On clinical examination hepatomegaly and splenomegaly may be found.

Careful examination of peripheral blood smear for RBC, leukocyte and platelet morphology is important. A reticulocyte count should be done to assess erythropoietic activity. Bone marrow examination should include bone marrow aspiration along with biopsy wherever indicated. Marrow should be carefully examined for morphology and cellularity. Bone marrow examination is a simple and safe invasive procedure, which causes a moderate discomfort and can be performed easily. Its greatest utility is for investigating and it is an important diagnostic modality for evaluating the causes of pancytopenia[10]. In pancytopenia, the marrow can be hypocellular or hypercellular. The hypoplastic marrow, which occurs in 2% of pediatric ALL patients, may be misdiagnosed as aplastic anemia. Studies done have shown leukemia to be the second most common cause of pancytopenia in pediatric patients, marginally behind aplastic anemia[11].

In India, the causes of pancytopenia are not well defined, so the present study has been undertaken to evaluate the various causes and to correlate the peripheral blood findings with bone marrow aspirate[12,13]. Thereby, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia. Treatment and prognosis of patients with pancytopenia are governed by the cause and severity of the underlying disease[12].

MATERIAL AND METHODS:

The present study was conducted in the haematology section of Department of Pathology of Jawaharlal Nehru Medical College, Sawangi (M). The duration of the study was two years from July 2014 to august 2016. It was a prospective analytical study. The study was conducted on total 53 patients attending outpatient and inpatient department of AVBRH, tertiary care centre. Informed consent was taken from all patients prior to enrollment in the study. All the cases irrespective of age and sex with pancytopenia were included in this study. Diagnostic criteria for Pancytopenia are, i) Haemoglobin less than 10 gm/dl. ii) Total leucocyte count <4000/cumm iii) Platelet count less than 1,50,000/cumm. Complete history was taken and physical examination was performed. For haematological study, blood samples were collected in EDTA anticoagulant. Complete blood count was carried out using Automated Haematology Analyser. It is an automated cell counter based on the principle of impedance. Hematological parameters considered in this study were haemoglobin, total leucocyte count, platelet count and red cell mass. Peripheral smear were stained using leishmans stain for all the cases and examined in details. Peripheral smear was used for morphological classification and typing of anemia. Bone marrow aspiration was then carried out under all aseptic precautions and slides were stained with leishmans stain. Cytochemistry was done using Myeloperoxidase stain and periodic acid and Schiff reagent stain were performed where necessary. Significant parameters like aetiology, age, gender, clinical features, hematological parameters, peripheral blood film, bone marrow aspiration findings in different cases of pancytopenia were compared with various studies published in literature. *Inclusion criteria:* Patients of all age groups and sex presenting with pancytopenia. *Exclusion criteria:* Pancytopenia due to the effect of chemotherapy, radiotherapy and immunosuppresants.

RESULTS:

The present study is an analytical type and prospective study conducted on 53 cases which were diagnosed as pancytopenia on peripheral smear and was confirmed on bone marrow aspiration was carried out in the Department of Pathology, Jawaharlal Nehru Medical College, Sawangi (Meghe) Wardha, Maharashtra. The duration of study period was from 1st august 2014 to 31st July 2016.

Age group of patients in the present study ranging from 1 year to 70 years with a Mean of 33.90. Highest number of patients i.e. 15 (28.30%) belong to the age group of 21-30 years followed by 10 patients (18.87%) in the age group of 31-40 years followed by 9 (16.98%) belong to the age group of 11-20 years, 8 (15.09%) belong to the age group of 41-50 years,5(9.43%) of age group of 61 -70 years ,4(7.55%) of age group of 51-60 years, lowest were 2(3.77%) patients of age group of 1-10 years.

In the present study, 25 were male patients (47.17%) and 28(52.83%) were females. In present study in females, pancytopenia was common in the 21-30 years age group (10 cases) followed by age groups 31-40 years and 41-50years (5 cases in both groups) 11-20 years(3 cases) 51-60 and 61-70(2 cases each) followed by1-10 years (1case). Pancytopenia was common in the age group of 11-20 years (6 cases) followed by the age groups 21-30 years(5 cases), 31-40 years (5cases) and 61- 70 years(3 cases) 51-60 years(2 cases)followed by 1-10 years(1 case). Male: Female ratio was 1:1.12 .Hence pancytopenia was more common in females in the present study.

In the present study most common presentation was of generalized weakness i.e 36 (67.9%) followed by fever 33(62.26%)followed by bleeding6(11.32%),and edema in 3(5.66%) cases. Pallor was the most common finding was present in all patients i.e 53(100%) followed by splenomegaly i.e in 32cases (60.4%) followed by hepatomegaly in 18 cases(33.96%)followed by lymphadenopathy i.e 12 cases (22.64%),the minimum patients presented with petechiae i.e 9 cases(16.98%).

Table no.1:-Total no. of diagnosed cases of pancytopenia:-

Diagnosis	**No of Cases (n=53)**	**Percentage%**
Megoloblastic Anemia	28	52.8%
Acute Leukemia(Aml)	11	20.8%
Normoblastic Erythroid Hyperplasia	06	11.32%
Aplastic Anemia	05	9.4%
Mixed Nutritional Anemia	01	1.9%
Multiple Myeloma	01	1.9%
Non Hodkin's Lymphoma	01	1.9%

The commonest finding in the present study was megaloblastic anaemia 28(52.8%).followed by acute leukemia 11(20.8%) and normoblastic erythroid hyperplasia 6(11.3%), aplastic anaemia 5(9.4%), other causes were mixed nutritional anaemia, multiple myeloma and Non hodkins lymphoma all had 1(1.9%) case each.

Table 2: Peripheral Blood findings In 53 cases of Pancytopenia:-

Peripheral Blood Findings	Diagnosis						
	Megaloblastic Anemia (n=28)	Acute Leukemia (n=11)	Normoblastic Erythroid Hyperplasia(n((n=6)	Aplastic Anemia (n=5)	Mixed Nutritional Anemia(n=1)	Multiple Myeloma (n((n=1)	Non Hodgkin's Lymphoma(n=1)
Anisocytosis	28(100%)	2(18.18%)	5(83.33%)	2(20%)	1(100%)	1(100%)	1(100%)
Hypersegmented Polymorphs	25(89.29%)	0(0%)	0(0%)	0(0%)	1(100%)	0(0%)	0(0%)
Circulating Erythroblast	4(14.29%)	5(45.45%)	3(50%)	0(0%)	1(100%)	0(0%)	0(0%)
Immature Cells	0(0%)	10(90.91%)	0(0%)	1(10%)	0(0%)	1(100%)	0(0%)
Lymphocytosis	16(57.14%)	2(18.18%)	2(33.33%)	5(100%)	1(100%)	0(0%)	1(100%)

A detailed peripheral blood smear examination was done on all patients. Megaloblastic anemia had 28 cases out of which anisocytosis was seen in all 28 (100%) patients, followed by hypersegmented polymorphs in 25(89.29%), followed by lymphocytosis in 16(57.14%). followed by circulating erythroblast in 4 (14.29%). There were 11 patients of acute leukemia immature cells were seen in 10(90.91%) cases, followed by erythroblast in 5(45.45%), followed by anisocytosis and lymphocytosis in 2 (18.18%), aplastic anemia had total 5 cases out of which lymphocytosis was present in all cases, i.e 5 (100%), followed by anisocytosis i.e 2(20%), followed by immature cells in 1(10%). In mixed nutritional anemia anisocytosis, hypersegmented polymorph, erythroblast and lymphocytosis was present in single case. Anisocytosis and immature (plasma) cells were seen in multiple myeloma. In Non hodgkins lymphoma anisocytosis and lymphocytosis was present in a single case.

Table no.3: Mean Peripheral Blood Indices

Diagnosis	Hb%(g/dl)	TLC*10^9	Platelets *10^9
	Mean	Mean	Mean
Megaloblastic Anemia	6.49±1.80	2432.14±771.26	47071.43±16197.68
Acute Leukemia	6.86±0.66	2570.90±205.44	27636.36±3500.64
Normoblastic Erythroid Hyperplasia	5.30±0.61	2483.33±213.69	24000.00±2449.49
Aplastic Anemia	5.04±1.62	2220.00±752.99	44600.00±7231.87
Mixed Nutritional Anemia	4.80±0	2000.00±0	32000.00±0
Multiple Myeloma	6.00±0	3200.00±0	49000.00±0
Non Hodgkin's Lymphoma	7.00±0	2210.00±0	55000.00±

The mean Hb was highest in Non Hodkins Lymphoma followed by acute leukemia, followed by megaloblastic anemia, followed by multiple myeloma, followed by normoblastic erythroid hyperplasia, followed by aplastic anemia and it was lowest in mixed nutritional anemia. The mean Tlc was highest in multiple myeloma i.e 3200, followed by Acute leukemia, followed by Normoblastic erythroid hyperplasia, followed by megaloblastic anaemia, followed by aplastic anaemia, lowest count was seen in mixed nutritional anaemia.

Mean platelet count was highest i.e 55000 in Non hodkins lymphoma followed by Multiple myeloma i.e 49000 followed by megaloblastic anaemia i.e 47071.43±16197.68, followed by Aplastic anaemia i.e 44600.00±7231.87. It was lowest in Mixed nutrition anaemia i.e 32000. Out of 53 cases, Hypercellular marrow was observed in 42 cases (79.24%) followed by normocellular 6(11.32%) and hypocellular marrow in 5 cases(9.43%) respectively.

Out of total 28 cases of megaloblastic anemia 32.08%(17/28) were females and 20.75%(11/28) were males. The second commonest presentation was of acute leukemia, out of 11 cases 15.09%(8/11) were males and 5.66%(3/11) were females, in Normoblastic erythroid hyperplasia total 6 cases were reported out of which 7.55%(4/6) were females and 3.77%(2/6)were males. out of 5 cases of aplastic anemia5.66%(3/5) were males and 3.77%(2/5) were females, a single case reported of mixed nutritional anemia which was a

male. Non hodkins lymphoma and multiple myeloma were found in female.

Table 4: Bone marrow diagnosis in 53 cases of Pancytopenia

Etiological Profile	No of Cases (n=53)	Percentage%
Megaloblastic Anemia	28	52.8%
Acute Leukemia(Aml)	11	20.8%
Normoblastic Erythroid Hyperplasia	06	11.32%
Aplastic Anemia	05	9.4%
Mixed Nutritional Anemia	01	1.9%
Multiple Myeloma	01	1.9%
Non Hodkin's Lymphoma	01	1.9%

The commonest finding in the present study was megaloblastic anaemia 28(52.8%).followed by acute leukemia 11(20.8%) and normoblastic erythroid hyperplasia 6(11.3%) ,aplastic anaemia5(9.4%),other causes were mixed nutritional anaemia, multiple myeloma and Non hodkins lymphoma all had 1(1.9%) case each.

Table 5: Bone Marrow Findings In Cases Of Pancytopenia.

Case No	Cellularity	M:E	Erythro	Myelocyte	Megakaryocyte	Blast				L and P Cells	Final diagnosis
						N:C ratio	Cytoplasm	Nucleoli	Chromatin		
1	↑↑	1.3:5	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
2	↑↑	1.5:1	Megalo	Giant MM,Stab forms	D	_	_	_	_	N	Megaloblastic Anaemia
3	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
4	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
5	↑↑	_	Normo	_	D	I	Moderate	Conspcious	Open		Acute Leukemia
6	↑↑	1:2	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
7	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
8	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Open	N	Acute Leukemia
9	↓	1:3	Normo	D	D	_	_	_	_	↑	Aplastic anaemia
10	↑↑	_	_	_	I	I	Scant	Conspcious	Clumped	↑	Multiple myeloma
11	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Open	N	Acute Leukemia
12	↑↑	1:1.5	Normo	N	N	_	_	_	_	N	Normoblastic erythroid hyperplasia
13	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia

14	↑↑	1:2	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
15	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Open	N	Acute Leukemia
16	↑↑	-	-	-	N	I	Scant	Indistinct	Coarse	↑	non hodkins lymphoma
17	↑↑	1:1.4	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
18	↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
19	↑↑	1:1.3	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
20	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
21	↑↑	1:1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
22	↑	1:1.5	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic Anaemia
23	↑↑	1:2	Normo	N	N	-	-	_	_	N	Normoblastic erythroid hyperplasia
24	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
25	↑	1:1	Normo	N	N	_	_	_	_	N	normoblastic erythroid hyperplasia
26	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic anaemia
27	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
28	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
29	↑↑	1:1.4	Megalo	Giant MM	D	_	_	_	_	N	megaloblastic anaemia
30	↑	1:1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
31	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	acute leukemia
32	↓	1:1	Normo	D	D	_	_	_	_	I	Aplastic anaemia
33	↑↑	1:3:5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
34	↑↑	1:1	Megalo	Giant MM	D	_	_	_	_	N	Megaloblastic anaemia
35	↑	1:1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
36	↑↑	1.5:1	Mixed	N	N	_	_	_	_	N	Normoblastic erythroid hyperplasia
37	↑↑	1:1	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
38	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
39	↑	1:1	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
40	↓	1.2 : 1	MNB	D	D	_	_	_	_	I	aplastic anaemia
41	↑↑	_	Normo	-	D	I	Moderate	Conspcious	Fine	N	Acute Leukemia
42	↑↑	1:1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
43	↑↑	1:1.4	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia

44	↑↑	1 : 1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
45	↑↑	1 : 1	Normo	N	N	_	_	_	_	N	normoblastic erythroid hyperplasia
46	↓	1:3	Normo	D	D	_	_	_	_	I	Aplastic anaemia
47	↑↑	1:1.4	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
48	↓	1:1	Normo	D	D	_	_	_	_	I	Aplastic anaemia
49	↑↑	1 : 1	Normo	N	N	_	_	_	_	N	Normoblastic erythroid hyperplasia
50	↑↑	2 :1	Megalo	Giant MM	N	-	-	-	-	N	Mixed nutritional anemia
51	↑↑	1 : 1	Megalo	Giant MM	N	_	_	_	_	N	megaloblastic anaemia
52	↑↑	1 : 1	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia
53	↑	1:1.5	Megalo	Giant MM	N	_	_	_	_	N	Megaloblastic Anaemia

All the 53 cases were subjected for bone marrow aspiration findings were :

Megaloblastic Anemia:- 28(52.8%)patients with pancytopenia were recognized. Cellularity was found to be increased. Erythropoiesis was hyperplastic and megaloblasts were seen. Early erythroid precursors were found to outnumber mature precursors. Dyserythropoiesis was also noted. Giant metamyelocytes and stab forms ranged from few to fair in number.

Aplastic Anemia: 11(20.8%) of the pancytopenic patients were found to have aplastic anemia. Aspirates were hypocellular with bone marrow fragments being composed largely of fat. M:E ratio ranged from normal to increased Megakaryocytes were found to be diminished. Lymphocytes, mast cells and plasma cells were found to be increased in all cases

Erythroid Hyperplasia :- 6(11.35%) of the patients presenting with pancytopenia were found to have erythroid hyperplasia. There was a predominance of erythroid series cells. The reaction varied from normoblastic to mixed reaction. Normoblasts and micronormoblasts were seen in some cases.

Acute Leukemia:- 11(20.8%) of the pancytopenic patients were recognized under this heading were of acute myeloid leukemia. The marrow smears were cellular. Blasts showed high N:C ratio, moderate amount of cytoplasm, open chromatin and 2-3 nucleoli. Reaction,was normoblastic , megakaryopoiesis was severely diminished in the cases.

***Multiple Myeloma*:- was established in one case of bone marrow aspirate. Bone marrow aspirate showed infiltration by typical and atypical plasma cells.**

Non hodgkins lymphoma:-bone marrow was hypercellular, with increased N:C ratio with blasts lymphoblast showing scant cytoplasm with indistinct nucleoli, with coarse chromatin with lymphocytosis.

DISCUSSION:

The study titled" Clinico Haematological study in cases of pancytopenia" was carried out in the department of pathology of Jawaharlal Nehru Medical College, Sawangi (M) from July 2014 to august 2016. Total 53 cases were subjected for clinical and haematological study. Patients selected were those who were diagnosed as pancytopenia on peripheral blood smear and were subjected for bone marrow aspiration. Examination of the bone marrow is a key element in diagnosing many haematological and non-haematological disorders. Patients having pancytopenia due to the effect of chemotherapy, radiotherapy and immunosuppressant were excluded.

Pancytopenia can result from a failure of production of hematopoietic progenitors, their destruction, or replacement of the bone marrow by tumor or fibrosis. Although selective cytopenias are important clinical entities, pancytopenia is a loss of all marrow elements. Careful examination of peripheral blood smear for RBC, leukocyte and platelet morphology are important. Bone marrow examination is a simple and safe invasive procedure, which causes a moderate discomfort and can be performed easily. Its greatest utility is for investigating and it is an important

diagnostic modality for evaluating the causes of pancytopenia.[10]

In the present study male to female ratio was 1:1.12 and there was a female preponderance (54.28%). Present study correlated well with the finding of Kumar and Raghupati et *al(2012)*[28], tariq ajij et al(2010)[29] they also found females to be commonly affected in their study.

PANCYTOPENIA IN DIFFERENT AGE GROUPS:-

In the present study highest number of patients i.e. 15 (28.30%) belong to the age group of 21-30 years, followed by 10 patients (18.87%) in the age group of 31-40 years. Present study has similar findings and it is in close proximity with the studies done by **Tariq Ajij et al(2010)[29], Pathak Jha et al (2012)[27]**

Table 6: Bone marrow diagnosis in various studies on pancytopenia

Bone Marrow Findings	Megaloblastic Anemia	Acute Leukemia	Normoblastic Erythroid Hyperplasia	Aplastic Anemia	Mixed Nutritional Anemia	Multiple Myeloma	Non Hodkin's Lymphoma	total
Bhatnagar et al (2005)[28]	31(28.4%)	23(20%)	11(10%)	30(21%)	-	-	-	109
Jha et al (2008)[30]	35(23.6%)	32(21%)	29(19%)	43(29%)	-	-	-	148
Gayatri et al (2011)[32]	77(74%)	04(4%)	-	19(18%)	-	-	-	104
Kirpal das et al(2013)[33]	26(41.9%)	17(27.4%)	7(11.3%)	12(19%)				62
Present Study	28(52.8%)	11(20.8%)	6(11.3%)	5(9.4%)	1(1.9%)	1(1.9%)	1(1.9%)	53

In our study isolated megaloblastic anemia was the most common cause. Megaloblastic anemia is a group of disorder characterized by the presence of distinctive morphologic appearances of the developing red cell in the bone marrow. The commonest cause of megaloblastic anemia is folate and cobalamine deficiency and rarely by genetic or acquired abnormalities affecting the metabolism of the vitamin or because of defect in DNA synthesis not related to cobalamine or folate. Diagnosis of megaloblastosis in this study was established by bone marrow findings and further estimation of folic acid and vitamin B12 levels was not performed. The exact cause of deficiency of these vitamins was also not detected, although it was in sharp contrast with the study of Jha et al (2008)[30] who found aplastic anemia to be the commonest cause this could be because the reported incidence of aplastic anemia varies considerably between countries e.g. from 0.7 to 4.1 per million per year in one study. Incidence is lower in Europe and North America than in various other parts of the world e.g. Asia. 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.

Table 7: Compsarison according to physical findings in patients presenting with pancytopenia

Study	Total no of cases	Pallor	Splenomegaly	Hepatomegaly	Petechiae	Lymphadenopathy
Kishor khodke et al(2001)[31]	**50**	**100%**	**40%**	**38%**	**28%**	**20.75%**
Soma yadav et al 2017[34]	**60**	**100%**	**22.7%**	**22.5%**	**-**	**11.7%**
Present study	**53**	**100%**	**56.60%**	**35.85%**	**18.87%**	**20.75%**

In the present study, Pallor was seen in 100% followed by splenomegaly (56.60%) andhepatomegaly (35.85%,lymphadenopathy in 20.75%, petechial haemorrhage were present in 18.87%. The **present study** was in concordance with the findings of **Kishor Khodke et al (2001)[31] and Soma Yadav et al 2017[34**

Table 8: Cellularity of bone marrow in cases of pancytopenia:-

Type of cellularity	Hypocellular percentage	Hypercellular percentage	Normocellular percentage
Kalpana Chandra et[36]	16.86%	68.67%	14.45%
Rangaswamy M et al.[35]	14%	75%	11%
Present Study	9.43%	79.24%	11.32%

In the present study Out of 53 cases, Hypercellular marrow was observed in 42 cases (79.24%) followed by normocellular 6 (11.32%) and hypocellular marrow in 5 cases(9.43%) respectively. The present study is in concordance with the findings of **Kalpana Chandra et al[36], and Rangaswamy et al.[35]**

CONCLUSION

In conclusion, pancytopenia is a common entity. However, it has received an inadequate attention in the Indian subcontinent. A study of pancytopenia using easily available diagnostic techniques is therefore important for early diagnosis and timely management of patients. Megaloblastic anemia was the commonest cause of pancytopenia in the present study followed by acute leukemia, normoblastic erythroid hyperplasia and aplastic anemia among the non-malignant disorders. Acute leukemia constitutes the most common malignant haematological disorder causing pancytopenia. A comprehensive clinical, haematological workup and bone marrow study of patients usually help in evaluating the aetiology of pancytopenia. In addition attempt should be made for an early recognition of underlying aetiology so that treatable causes are identified without delay and prognosis can be improved. 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 after analysing the observations noted in the present study.

This study emphasized that in developing countries like India majority of the patients had reversible etiology and patients can be put on a trial of hematinics and close haematological follow up. Causes of pancytopenia varies widely according to various geographic regions. It can range from transient marrow suppression to malignancy. Bone marrow examination is an important tool in the diagnosis and early initiation of treatment in vulnerable pancytopenic patients. Bone marrow aspiration coupled with trephine biopsy can diagnose majority but not all the cases of pancytopenia. Hypoplastic anemia, hematological malignancies and megaloblastic anemia are the commonest causes of pancytopenia. Maximum diagnostic yield can be achieved by correlation with clinical findings, peripheral blood findings and with other laboratory and radiological parameters. Bone marrow aspiration is fairly safe procedure with minimal discomfort to the patient. Bone marrow aspiration is useful in the differential diagnosis of cytopenias. In leukaemia, bone marrow aspiation gives an assessment of marrow cellularity, presence of fibrosis.

In our country main cause of pancytopenia being fortunately megaloblastic anaemia which responds very well to treatment if diagnosed correctly in time. The present study concludes that detailed haematological investigations along with bone marrow examination in cytopenic patients are not only helpful in understanding the disease process but also to diagnose or to rule out the causes of pancytopenia and planning further investigations and management of these patients.

REFERENCES

1. Varma A, Lokwin P, Malukani K, Gupta S, Maheshwari P. Study of haematological profile of adults presenting with pancytopenia in a tertiary care hospital of central India. Med J DY Patil Vidyapeeth 2018;11:512-8
2. Williams MD. Wintrobe's Clinical Haematology. In: Lee RG, Foerster J. Lukens J, Paraskevas F, Greer JP, Rodgers GM, editors. Pancytopenia, aplastic anaemia and pure red cell aplasia. 10th ed. Williams and Wilkins; 1997:1449-476.
3. Pancytopenia: aplastic Anemia. deGruchy's Clinical Hematology in Medical Practice. Wiley India edition. (6th Edition).2013; Chapter 6: 106-1192
4. Ahmed M, Anand M, Kumar A, Siddiqui MKJ. Childhood aplastic anaemia in Lucknow, India: Incidence,

organochlorines in the blood and review of case reports following exposure to pesticides. Clinical Biochemistry 2006;39:762-766

5. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico- haematological profiles of pancytopenia in children. Trop Doct 2008; 38:241-3

6. Nelsons Textbook of Paediatrics, Nineteenth edition, Pages 1642-1645

7. John Greer, John Foester, George M Rodgers, F'lxos Paraskevas, Wintrobes Clinical Haematology, 2009; Pages 1188-1189

8. Hayat, A.S., Khan, A.H., Baloch, G.H. and Shaikh, N. (2014) Pancytopenia: Study for Clinical Features and Etiologi- cal Pattern of at Tertiary Care Settings in Abbottabad. The Professional Medical Journal, 21, 060-065.

9. Kumar, abbas, Fausto and Aster; Pathological bases of disease- Eighteen Edition - Pages 744.

10. Desalphine, M., Bagga, P.K., Gupta, P.K. and Kataria, A.S. (2014) To Evaluate the Role of Bone Marrow Aspiration and Bone Marrow Biopsy in Pancytopenia. Journal of Clinical and Diagnostic Research, 8, FC11-FC15. http://dx.doi.org/10.7860/jcdr/2014/9042.5169].

11. Raja, S., Suman, F.R., Scott, J.X., Latha, M.S., Rajenderan, A. and Ethican, A. (2015) Pancytopenia: An Obstacle in the Diagnosis and Outcome of Pediatric Acute Lymphoblastic Leukemia. South Asian Journal of Cancer, 4, 68-71.

12. Tilak V, Jain R. Pancytopenia-A Clinco-hematologic analysis of 77 cases. Indian J Pathol Microbiol. 1999;42:399–404.

13. Kumar R, Kalra SP, Kumar H, Anand AC, Madan M. Pancytopenia-A six year study. J Assoc Physicians India. 2001;49:1079–81.

14. Hematology: Basic Principles and Practice, Expert Consult Premium Edition ...By Ronald Hoffman, Edward J. Benz Jr., Leslie E. Silberstein, Helen Heslop, Jeffrey Weitz, John

15. Incidence of Aplastic Anemia: The Relevance of Diagnostic Criteria 1718 Blood, Vol 70, No6 (December), 1987: pp 1718-1721 By the International Agranulocytosis and Aplastic Anemia Study

16. De Gruchys Clinical Haematology in Medical Practice (English) 6th Edition (DE GRUCHY;S CLINICAL HAEMATOLOGY IN MEDICAL PRACTICE, Renu Saxena, Colin Chesterman, Hara Prasad Pati, Manoranjan Mahapatra, Frank Firkin, David Penington, Bryan Rush

17. Pathak R1, Jha A1, Sayami G11 Department of Pathology, Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

18. Aseem S, Varma N, Das R, Ahluwalia J, Sachdeva Mu, Marwaha Rk. Pediatric Patients With Bicytopenia/Pancytopenia: Review Of Etiologies And Clinico-Hematoiogical Profile At A Tertiary Center. Indian J Pathol Microbiol 2011; 54: 75-80

19. Park GT, Jean DW, Roh KH et al. A case of pancytopeniasecondary to low – dose pulse methotrexate therapy in a patient with rheumatoid arthritis and renal insufficiancy. Korean Journal of Internal Medicine 1999; 14 (1): 85-7.

20. Craig JIO, McClelland DBL, Ludman CA. Blood disorders.In:BoonN, Colledge N, Walker B,Hunter J,editors. Davidsons Principles and Practice of Medicine.2^{0th}.ChurchillLivingstone; 2010.p-1019.synopsis Bangalore

21. Young NS, Barrett AJ. The treatment of severe acquired aplastic anaemia. J Am Soc of Hematol1995; 85: 3367-77.

22. Williams MD. Pancytopenia, aplastic anemia and pure red cell aplasia. In: Lee RG, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, (eds). Wintrobe's

Clinical Haematology 10th edn. Williams and Wilkins;1997. pp1449-76. pathak sayami nepal

23. Mckenna RW, Kroft SH. Disorders of bone marrow. Mills SE, Carter D, Greenson JK, Reuters VE, Stoler MH, (eds). In: Sternberg's Diagnostic Surgical pathology. 5th edn. Kluwer Lippincott; Wiliams and Wilkins; 2010. pp611-4.pathak sayami Nepaltol1995; 85: 3367-77.

24. Camitta BM, Storb R, Thomas ED. Aplastic anemia :pathogenesis, diagnosis, treatment and prognosis. Engl J Med s1982; 306: 645-52,

25. Trivette, E.T., Hoedebecke, K., Berry-Cabán, C.S. and Jacobs, B.R. (2013) Megaloblastic Hematopoiesis in a 20-Year- Old Pregnant Female. American Journal of Case Reports, 14, 10-12. http://dx.doi.org/10.12659/AJCR.883734

26. Rannelli, L., Watterson, R., Pandya, R. and Leung, A.A. (2014) Vitamin B12 Deficiency with Combined Hematologi-cal and Neuropsychiatric Derangements: A Case Report. Journal of Medical Case Reports, 8, 277..

27. Kumar, D.B. and Raghupathi, A.R. (2012), Clinicohematologic analysis of pancytopenia: Study in a tertiary care centre. Basic and Applied Pathology, 5: 19-21.

28. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: Etiological profi le. J Trop Pediatr 2005;51:236-9.

29. Aziz T, Ali L, Ansari T, Liaquat HB, Shah S, Ara J. Pancytopenia: Megaloblastic anemia is still the commonest cause. Pak J Med Sci 2010;26(1):132-136

30. Jha et al. Bone Marrow Examination in Cases of Pancytopenia, J Nepal Med Assoc 2008;47(169):12-7

31. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone Marrow Examination in Cases of Pancytopenia. JIACM 2001;2:55-59.

32. Gayathri BN, Rao KS. Pancytopenia: A clinico hematological study. J Lab Physicians 2011;3:15-20.

33. Makheja KD, Maheshwari BK, Arain S, Kumar S, Kumari S, Vikash. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. Pak J Med Sci 2013;29(5):1108-1111.

34. Yadav A, Nigam R K, Malik R. A study of clinico-hematological profile of pancytopenic patients in Central India. Int J Med Res Rev 2017;5(05):484-491.

35. Rangaswamy M, Prabhu, Nandin NM, Manjunath GV. Bone marrow examination in pancytopenia. J Indian Med Assoc 2012;110:560-2

36. Chandra, Kalpana, and Praveen Kumar. "MORPHOLOGICAL SPECTRUM OF BONE MARROW IN PANCYTOPENIA--A RETROSPECTIVE STUDY IN A TERTIARY CARE CENTRE." *Journal of Evolution of Medical and Dental Sciences*, vol. 3, no. 4, 27 Jan. 2014, pp.