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Research Article

Pancytopenia: a clinico hematological study

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ABSTRACT

Background: Pancytopenia is very common consequence of many haematological diseases. It is the shortage of all types of blood cells. It happens in many serious and life-threatening illnesses, ranging from simple drug-induced bone marrow hypoplasia, megaloblastic anemia to fatal bone marrow aplasias and leukemias. It has different causes and severity based on which the treatment is directed and prognosis is implicated. Main objective of the study was to study the clinical presentations in pancytopenia due to various causes; and to evaluate hematological parameters, including bone marrow.
Methods: It was a prospective study, and 50 pancytopenic patients were evaluated clinically, along with hematological parameters and bone marrow aspiration in Hematology Unit, Department of Pathology, Hi-Tech Medical College and Hospital, Bhubaneswar, Orissa, India during the period of October 2013 to September 2015.
Results: Among 50 cases studied, age of patients ranged from 1 to 80 years with commonest age group being 41-50 years, and male predominance. Most of the patients presented with generalized weakness, pain abdomen and bleeding. Bone marrow aspiration was conclusive in all cases. The commonest marrow finding was hypocellularity followed by hypercellularity with megaloblastic erythropoiesis. The commonest cause for pancytopenia was aplastic anemia (44%), followed by mrgaloblastic anemia (20%).
Conclusions: The present study concludes that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of cytopenia. These are also helpful in planning further investigations and management.

Keywords: Bone marrow aspiration, Megaloblastic anemia, Pancytopenia, Aplastic anemia

INTRODUCTION

Pancytopenia is a disorder in which all the three formed elements of blood (red blood cells, white blood cells and platelets) are decreased than normal.[1] Pancytopenia is not a disease entity but a triad of findings that may result from number of disease processes [2].

It is not a diagnosis but a presentation of some underlying general medical or primary haematological disorder.[3] While bone marrow failure syndromes and malignancies are serious and life threatening causes, certain non-malignant conditions such as infection, and nutritional anemia are equally important.[4] The pattern of diseases leading to pancytopenia is expected to vary in different population groups with their difference in age pattern, nutritional status and prevalence of infective disorder.[5] The severity of pancytopenia and the underlying pathology determines the management and prognosis.[6] Pancytopenia is an important clinic-hematological entity encountered in our day-to-day clinical practice.[7] A detailed history, physical examination and review of the blood films remains fundamental to diagnosis.[8]

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.[9]

METHODS

The present study "Pancytopenia - A Clinico - hematological study" was carried out from October 2013 to September 2015 in the department of pathology, Hi Tech Medical College, Bhubaneshwar, Orissa, India. Cases from Hi Tech Medical Hospital formed the material for study.

Inclusion criteria

Cases showing the parameters as

- Hb< 13g/dl for adult male, Hb<12g/dl for adult female, Hb<10.7g/dl for children above 1year
- WBC count <4X10^9/L for male, female and children
- Platelet <150X10^9/L for male, female and children

Exclusion criteria

- Patients who have already been diagnosed with pancytopenia.
- Patients who have recently received blood transfusions.
- Patients who did not give consent for bone marrow aspiration and biopsy.

After obtaining informed consent and taking history and evaluating the patient clinically they are subjected to investigations. Following investigations carried out were hemoglobin; RBC count; WBC count; platelet count; reticulocyte count; hematocrit; red cell indices; bleeding-time and clotting time when required; peripheral smear study; bone marrow study.

Sample collection

Two ml of blood was collected by venepuncture under aseptic precaution in a dry tube containing ethylene di-amine tetra acetic acid (EDTA) anticoagulant.

Samples were processed by an automated autoanalyser (SYSMEX 800I), and complete blood counts with other details were obtained.

Peripheral smear study

Peripheral smears were prepared, the films were air dried, and stained with Leishman's stain:

Leishman's stain

- Smears were air dried.
- Slides placed on a slide stand and covered with Leishman stain for 5 min.
- Double the amount of distilled water added over the Leishman's stain and left for 10 min.
- Smears washed with distilled water and air dried.

Results

Cytoplasm was fund to be pink and nucleus was found to be blue. Smears were examined under microscope for following features

- RBC morphology- to assess morphological type of anemia, immature RBC's, any inclusions etc.
- WBC morphology- for differential count, morphology of each cell, immature cells.
- Platelet count and its morphology.
- Any parasite and any other abnormalities

Reticulocyte count

Two drops of new methylene blue filtrate and two drops of well-mixed blood specimen is transferred into a small test tube. Sample is mixed and tube left undisturbed for 30-45 minutes in the incubator at 37°C. After incubation, a thin smear was prepared, air dried and examined under microscope. Reticulocytes were identified by the fine, deep violet filaments arranged in a network and fine dot like structure. A small circular piece of black paper with 5 mm diameter hole was made and placed in the eye piece or Ehrlich's eye piece was used. Ten consecutive fields or 150-200 red cells including reticulocytes were counted and the percentage was calculated using the formula

$$\text{Reticulocyte count} = \frac{\text{Number of reticulocyte counted X 100}}{\text{Number of red cells counted}}$$

A detailed physical examination was done to look for the presence of hepatomegaly, splenomegaly, lymphadeno-pathy and sternal tenderness. Gum hypertrophy, evidence of hyperspleenism and primary malignancies were searched for when necessary. Further bone marrow evaluations were carried out in all cases.

Bone marrow aspiration

Bone marrow aspiration was performed in all the patients showing Pancytopenia in peripheral blood smear using Jamshidi needle after obtaining written consent for the procedure either from the patient or the guardian.

- The aspiration site:Mostly aspiration was done from the posterior iliac crest .
- All aseptic precaution was taken and under local anesthesia (2% lignocaine) aspiration was done.
- The aspirate was then transferred to a set of slides and films were prepared by crushing the marrow particles.
- The needle was withdrawn and the puncture site was sealed with tincture benzoin swab.

In cases of unsuccessful attempts of bone marrow aspiration, a repeat aspirate was done at the different site.

Slides were fixed in methanol for 15 minutes, dried and later stained with Leishman's stain and marrow aspiration smears were examined for cellularity; M:E ratio cells, lymphocytes, mast cells; erythropoiesis; myelopoiesis; megakaryopoiesis; others – plasma; parasites; abnormal cells. special stains like Prussian blue stain were done for all cases to assess iron stores, and grading was carried out.

Table 1: Bone marrow iron grading.[10]

Grade	Criteria	Iron content (ug/g)
0	No iron granules observed	42±23
1+	Small granules in reticulum cells (seen only in oil immersion)	130±50
2+	Few granules visible under high power field	123±75
3+	Numerous small granules in all marrow particles	406±131
4+	Large granules in small clumps	762±243
5+	Dense large clumps of granules	1618±464
6+	Very large deposits obscuring marrow detail	3681±1400

Other special stains were done wherever required. In haematological malignancy case, sample was sent for flow cytometry study.

Bone marrow biopsy

Bone marrow biopsy was done in all cases. Jamshidi needle was used for trephine biopsy. Site: Posterior iliac crest

Procedure

- Under all aseptic precautions and using local anesthesia (2% lignocaine), biopsy was performed.
- The needle, with stylet locked in place, is held with the palm and index finger and repositioned at insertion site. Once the needle touches the bone surface, the stylet is removed.
- Using firm pressure and with rotatory motion, an adequate bone marrow specimen measuring approximately 1.6-2.0cm in length was removed.
- Biopsy tissue removed from needle was taken on slide, imprint smears were prepared.

Processing of tissue

Decalcification was done using bouin's fluid. Then the tissue was processed as routine histological processing with routine hematoxyline and eosin stain. Slides were examined and reported as follows

- Adequacy of biopsy.
- Cellularity and topography.
- Any abnormality

Compiling clinical details, hematological parameters and bone marrow study, the cases were studied. The cause for pancytopenia, age and sex distribution and other relevant details were noted and analyzed.

RESULTS

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. There were 7 (14%) children in age group of 0-10 years.

Table 2: Distribution of patients according to symptoms.

Symptoms	No. of cases	Percentage
Generalized weakness	44	88
Fever	19	38
Bleeding	32	65
Pain abdomen	23	46
Abdominal distension	9	18
Fever with rashes	5	10

Hematological data

1. *Hemoglobin percentage*

Table 3: Range of hemoglobin in patients with pancytopenia.

Hemoglobin percentage (gm%)	Female	Male	Children	No. of cases	Percentage
1 - 3	2	3	0	5	10
3.1 - 5	3	5	2	10	20
5.1 - 7	9	13	3	25	50
7.1 - 10	4	4	2	10	20
10.1 - 13	0	0	0	0	0
Total	18	25	7	50	100

2. *Total leukocyte count*

Table 4: Range of leukocyte count in patients with pancytopenia.

Leukocyte count (cells/mm3)	No. of cases	percentage
<500	0	0%
500-1000	7	14%
1100-2000	16	32%
2100-3000	16	32%
3100-4000	11	22%
Total	50	100

3. *Platelet count*

Table 5: Range of platelet count in patients with pancytopenia.

Platelet count (cellsmm3)	No. of cases	Percentage
<5000	0	0
5000-20000	11	22
21000-50000	10	20
51000-75000	15	30
76000-1,00,000	12	24
101000-1,50,000	2	4
Total	50	100

4. *Reticulocyte count*

Table 6: Range of reticulocyte count in patients with pancytopenia.

Reticulocyte count	No. of cases	Percentage
0.1-2	48	96
2.1-4	1	2
4.1-6	1	2
6.1-8	0	0
Total	50	100

Table 7: Aetiological distribution of cases with pancytopenia/mm^3.

Etiology	Total no. of cases	No. of cases (%)
Aplastic anemia	22	44
Megaloblastic anemia	10	20
Hypersplenism	6	12
Acute leukemia	6	12
Myelodysplastic syndrome	3	6
Dengue	2	4
Hemolytic anemia	1	2
Total	50	100

Vital hematological Parameters of patients with Aplastic anemia: hemoglobin percentage varied from 1-10 gm%. Majority of the patients (68.2%) had values in the range of 5.1-7 gm%. The total leukocyte count ranged from <500-4000 cells/mm^3. Majority of the patients (82%) had a leukocyte count in the range of 1100-3000 cells/mm^3. 9.1% of patients had values below 1000 cells. The platelet count varied from<5000-1,50,000 cells/mm^3.

Most of the patients (41%) had a platelet count in the range of 76,000-1,00,000 cells/mm^3. 13.7% patients had values in the range of 21,000-50,000 cells/mm^3. The reticulocyte count varied from 0.1-6%. Most of them (77.3%) had reticulocyte count in the range of 0.1-2%.

5. *Peripheral smear*

Most of the patients (64.2%) had normocytic normochromic erythrocytes. Some (35.8%) showed macrocytosis.42.8% of them had relative lymphocytosis and normoblastic anemia was not detected.

6. *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 megaloblastic anemia

Megaloblastic anemia was seen in the age group of 0-60 years. Majority of the patients (40%) were in the age group of 51-60 years.10% of them were in the age group of 11-20 years.

There was a male predominance and the male to female ration of incidence was 2.1:1. 40% of the cases were in age group 0-10 years. Vital haematological parameters of patients with megaloblastic anemia: that hemoglobin percentage varied from 1-7gm%. Majority of the patients (80%) had values in the range of 3.1-7 gm% The total leukocyte count ranged from <500-4000 cells/mm^3.

Most patients (60%) had a value in the range of 3100-4000 cells/mm^3. The platelet count was in the range of <5000-1,50,000 cells/mm^3. Most of them (40%) had platelet values in the range of 5000-50,000 cells/mm^3. The reticulocyte count was in the range of 0.1-8%. Majority of the patients (50%) had values in the range of 0.1-2.0%.

Peripheral smear

Macroovalocytosis with a considerable degree of anisopoikilocytosis were the main features. Mean corpuscular volume was more than 100 fl in 57.5% of patients. Dimorphic blood picture was seen in 10 patients (30%).

Basophilic stippling and cabot rings were present. Hypersegmented neutrophils were seen. Platelets were reduced in number in all the cases.

Bone marrow

The bone marrow was hypercellular with a reduction of fat cells in most of the patients (81.8%).Four patients (18.2%) had normocellular marrow. Erythroid hyperplasia with megaloblastic maturation and reversal of M;E ratio was seen in all the patients. Megakaryopoiesis was normal in 63.6%, decreased in 18.2% and increased in 18.2% of patients. No evidence of dyserythropoiesis, dysgranulopoiesis and dysmegakaryopoiesis seen.

Hypersplenism was seen to occur in the age group ranging from 41-70 years. Majority of them were in the age group of 51-60 years. There was a male preponderance and male to female ratio of incidence was 2:1.

Leukemia (acute myeloblastic leukemia)

1. *Age and sex distribution*

Table 8: Age and sex distribution of patients with leukemia (Acute myeloblastic leukemia).

Age (years)	Female	Male	Total no. of cases	Percentage
0	0	0	0	0
18-20	0	0	0	0
21-30	0	1	1	16.7
31-40	1	1	2	33.4
41-50	1	0	1	16.7
51-60	0	1	1	16.7
61-70	0	1	1	16.7
71-80	0	0	0	0
Total	2	4	6	100

Vital hematological parameters of patients with acute leukemia: hemoglobin percentage ranged from 1-10 gm%. Majority of patients (66.6%) had values in the range of 3.1-7 gm%. The total leukocyte count varied from <500-4000 cells/mm^3. 33.3% of the patients had values in between 3100-4000 cells/mm^3. Platelet count ranged from <5000-150,000 cells/mm^3. 33.3% of the patients had values in between 76,000 and 1,00,000 cells/mm^3. The reticulocyte count ranged from 0.1-6. 50% of the patients had a value ranging from 0.1-2

Peripheral blood

These patients presented with peripheral pancytopenia. In four cases of AML-M2 erythrocytes were normocytic normochromic. The leukocyte count was decreased with a presence of immature cells.

Myeloblasts with fine chromatin, 2-3 nucleoli and occasional Auer rods were seen. In two cases of AML-M3, erythrocytes were microcytic hypochromic. The leucocyte count was decreased. Myeloblasts with1-2 nucleoli and plenty of Auer rods were seen. Platelets were decreased Bone marrow. Bone marrow was hypercellular in 100% of the patients. Erythroid series were decreased in two of the patients and normal in four patients. Myeloid hyperplasia was observed with more than 20% blasts in all of them.

Myelodysplastic syndromes

Three cases of myelodysplastic syndrome were observed in the present study of peripheral pancytopenia in the age group of 64-75 years. Two cases of refractory anemia show hypercellularity of aspirate.Features as Megaloblastic erythroblasts, nuclear budding and hyperlobulation were present. Dysmyelopoiesis with hypogranular neutrophils and blasts were also observed. One case of refractory cytopenia with unilineage dysplasia showed erythroid hyperplasia and features of dyserythropoiesis were seen. Large hypolobulated magakaryocytes were seen.

Dengue fever

Two cases of dengue fever in a 18 year old male and a 22 year old female presented with pancytopenia. The total leukocyte count was 800 cells/mm^3 and platelet count was 28,000 cells/mm^3. Bone marrow was hypercellular with erythroid hyperplasia and a reversal of M:E ratio.

Hemolytic anemia

One case of hemolytic anemia having sickle cell disease with aplastic crisis presented with pancytopenia. The patient was a 21 year old female.

The peripheral blood showed features of hemolysis. Erythrocytes showed moderate degree of anisopoikilocytosis. The reticulocyte count was markedly decreased. Occasional irreversible sickled cells were seen. The bone marrow was hypocellular.

DISCUSSION

The present study was conducted to analyze the clinico hematological features of pancytopenia. The statistical data hence obtained were compared with previous published literatures.

Age distribution

In the present study the age ranged from 0-80 years. Majority of the patients were in the age group of 31-50 years. Similar age groups were included by Tilak et al, Kumar et al, Khunger et al.[3,9,11] Comparing present study with other studies showed that most of the patients of pancytopenia come in the age group of 31-50 years.

Sex distribution

In the present study male to female ratio was 2.1:1.Similar results were obtained by Tilak et al, Kishore Khodke et al and Khunger et al.[3,5,9] Comparing our study with other studies showed that there is male preponderance with respect to female for pancytopenia.

Clinical features

In the present study, most common clinical manifestation was generalized weakness (88%) followed by bleeding (65%). Similar features were noted in studies by Kumar et al and Jha et al.[4,11] Other clinical manifestations included pain abdomen and fever. In the present study, pancytopenia was due to the following causes: aplastic anaemia; megaloblastic anaemia; hypersplenism; malignant disease – acute leukemia; myelodysplastic syndromes; others were dengue fever and hemolytic anaemia.

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

Table 9: Causes of pancytopenia in various studies.[12]

Study	Country	year	No. of cases	Commonest cause	Second most common cause
Retief FP et al[14]	South Africa	1976	195	Bone marrow failure (67.7%)	Severeinfection (9.7%)
International agranulocytosis and aplastic anemia study	Europe	1987	389	Aplastic anemia (52.7%)	MDS (10.5%)
Lmbeit Metai.	Europe	1989	213	Malignant myeloid disorders (42%)	Malignant, lymphoid disorders (18%)
K.eisn M et al.	Sweden	1990	100	Neoplastic disease (32%)	Aplastic anemia (16%)
Hossain M et al.	Bangladesh	1992	50	Aplastic anemia	Chronic malaria and kataazar
Varma N, Dash S	India	1992	202	Aplastic anemia (40.6%)	MegaloblasticAnemia (23:26%)
Tilak V et al[9]	India	1998	77	Megaloblastic anemia (68%)	Aplastic anemia (7.7%)
lavage DO et al.	Zimbabwe	1999	134	Megaloblastic anemia	Aplastic anemia
Kbodke et al.	India	2000	*166*	Hypoplastic anemia (29.51%)	Megaloblastic anemia (22.3%)
Khan NM et al[21]	Pakistan	2001	**30**	Aplastic anemia(20%)	Megaloblastic anemia (16.7%)
Kumar R et al.	India	2001	166	Aplastic anemia (29.5%)	Megaloblastic; anemia (22.3%)
Osama I et al[12]	Pakistan	2002	100	Megaloblastic anemia (39%)	Hypersplenism (19%)
MussafratNiazietal.	Pakistan	2004	89	Aplastic anemia (38.3%)	Megaloblastic anemia (27.7%)
Jha et al[6]	Nepal	2008	448	Hypoplastic anemia 29.5%	Megaloblastic anaemia 23.64%
Shanonaseem et al	Pakistan	2011	990	Malignant myeloid disorder 46%	Aplastic anemia 54%
Kirpal das makheja et al	India	2013	62	Megaloblastic anemia 41.9%	Acute myeloid leukemia 27.4%
Present study	India	2015	50	Aplastic anemia 44%	Megaloblastic anaemia 20%

Jhaet al and Kumar et al showed similar results as aplastic anemia being the commonest cause of pancytopenia.[6,11] Tilak et al and Osama et al have shown megaloblastic anemia as the commonest cause.[6,7] In present study megaloblastic anemia is the second most common cause of pancytopenia. The variation in the frequency of

various diagnostic entities causing pancytopenia has been attributed to difference in methodology and stringency of diagnostic criteria, geographic area, period of observation, genetic differences and various exposure to myelotoxic agents etc.[2,5,9]

Aplastic anemia associated with pancytopenia

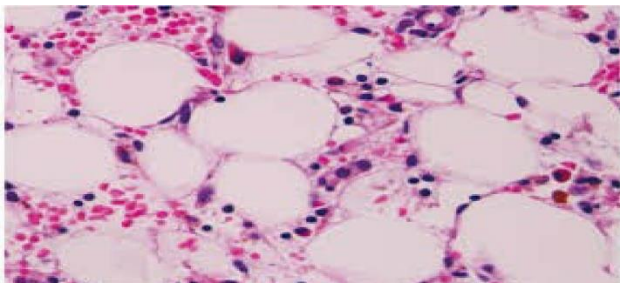

Figure 1: Aplastic anemia: BM biopsy 1000x.

Age and sex distribution

In the present study, the age ranged from 0-80 years. Majority of the patients were in the age group of 31-50 years. Aplastic anemia was more common in males. The male to female ratio was 1.5:1.

In the study by Kumar et al.[11] the age ranged from 12-63 years. There was a male preponderance and male to female ratio was 1.4:1. In the study by Jhaet al the age ranged from 1.5-70 years.[6] There was a male preponderance with male to female ratio of 1.3:1.

Hematological parameters

The hematological parameters in aplastic anemia by various studies are compared with the present study.

- Peripheral smears

In the present study, 64.2% had normocytic normochromic erythrocytes.35.8% of the patients had macrocytic anemia and 56.3% of them had relatively mphocytosis.

In the study by Kishore Khodke, 3 out of 7 patients showed anisocytosis and 1 out of 7 patients showed relative lymphocytosis.[5] In the study by Tilak et al, 2 out of 6 patients had anisocytosis and 3 out of 6 patients had relative lymphocytosis.[9] The study by DanielNM et al found normocytic normochromic erythrocytes in 64% of the patients, macrocytic normochromic blood picture in 20% of the patients.[13]

Bone 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.

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.

Megaloblastic anemia associated with pancytopenia

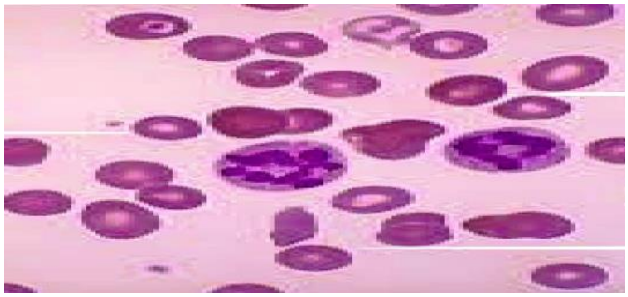

Figure 2: Megaloblastic anemia: BM aspirate.

Age and sex distribution

In the present study, age ranged from 11-60 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. Megaloblastic anemia is common in India. This seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

In the study of pancytopenia cases by Jha et al, the age range was 10-79 years.[6] There was a male preponderance and male to female ratio was 1.5:1. In the study by Kumar et al.[11]the age ranged from 14-73 years. There was a female preponderance and the male to female ratio was 1:2.

Table 10: Comparison of hematological parameters.

Hematological parameters	Jha et al[6]	Kumar et al[11]	Present study
Hb% (gm/dl)	2.3-9.8	2.4-7	1-10
TLC (cells/mm^3)	1200-3900	700-3600	500-4000
Platelet (C/mm^3)	2000-1.37 000	10,000-1.30 000	5000-1,50,000

Peripheral smear

In the present study, macroovalocytes with considerable degree of anisopoikilocytosis were the main features in all the cases. MCV was more than 100 fl in 57.5% of cases and dimorphic blood picture was seen in 30% of cases (10 patients). Hypersegmented neutrophils were seen in most of the patients

The principal hematologic manifestations are, varying degrees of anemia, leucopenia, thrombocytopenia, anisopoikilocytosis, macroovalocytosis and hyper-segmented neutrophils. In the study by Kishore Khodkeet al.[5] 20 out of 22cases showed anisocytosis, 10 out of 22 cases showed dimorphic blood picture and 20 out of 22 cases showed hypersegmented neutrophils. In the study by Tilaket al.[9] 51 out of 53cases showed anisocytosis, 45 out of 53 cases showed hypersegmented neutrophils, 13 out of 53 showed circulating erythroblasts. Reticulocytes were seen in 5 out of 53 and relative lymphocytosis was seen in 7 out of 53 cases.

Bone marrow

In the present study, the bone marrow was hypercellular with reduction of fat cells in most of the patients (81.8%). Four patients (18.2%) had normocellular marrow. Erythroid hyperplasia with megaloblastic maturation was seen in all the patients. Bone marrow is usually hypercellular with predominantly megaloblastic erythropoiesis. Giant band forms, metamyelocytes and giant megakaryocytes are also seen.

Hypersplenism

Age and sex distribution

In the present study, hypersplenism was the cause of pancytopenia in 12% of cases. Age ranged from 41-70 years. There was a male preponderance with the male to female ratio being 2:1.

Hypersplenism is known to cause pancytopenia by sequestration of blood cells. In a study of 195 patients, Retief HP[14] found hypersplenism to be the cause of pancytopenia in 7.7% of the patients. ShaziaMemonet al.[15] in their study of 230 cases found hypersplenism in 10 patients (4.34%). Kumar et al reported an incidence of hypersplenism in 19 out of 166cases in which age ranged from 14-49 years.[11] There was a male preponderance with the male to female ratio being 2:1.

Table 11: Comparison of hematological parameters.

Hematological parameters	Jha et al[6]	Kumar et al[11]	Present study
Hb% (gm/dl)	2.9-7	3.5-8.6	3.1-10
TLC(cells/mm^3)	900-3800	1100-3600	500-4000
Platelet (c/mm^3)	1000-150000	40000-125000	5000-150000

Peripheral smear

Most of the patients (60%) had normocytic normochromic anemia. 40% of them had hemolytic anemia: In the study by Osama et al.[16]macrocytosis was seen in 63.1% cases and microcytosis in 36.8% cases.

Bone marrow

66.7% had hypercellular marrow while the rest had normocellular. Barbec V et al found hypercellular marrow in majority.[17]

Leukemia associated with pancytopenia

Age and sex distribution

In the present study leukemia accounted for 12% of pancytopenia cases. Majority (66.7%) of the pancytopenia cases were due to acute myeloid leukemia. The age varied from 21-70 years. There was a male preponderance with male to female ratio being 2:1.

In the study by Jha et al.,[4] acute leukemia alone constituted 90.62% of all the hematological malignancies. It accounted for 19.59% of total cases of pancytopenia. Age ranged from 2-75 years with a male to female ratio of 1.9:1. Khodkeet al.[5] and Tilaket al.[9] reported one case of AML causing pancytopenia.

Hematological parameters

Peripheral blood picture

In the present study, all the patients had normocytic normochromic anemia. Leukocyte count was reduced and circulating immature cells were seen. Platelet count was also reduced. In the study by Tilak Jain et al.[9] one case of acute myeloid leukemia with anisocytosis, circulating erythroblasts and immature cells was reported. KishoreKhodkeet al[5] found one case of acute myeloid leukemia with immature cells in the peripheral blood.

Bone marrow

Bone marrow was hypercellular in all the cases. Myeloid hyperplasia with immature cells was seen in all the cases. Erythropoiesis and megakaryopoiesis were reduced.

Myelodysplastic syndrome (MDS)

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 pancytopenia was found in 15% of the patients.[18] In a study of 31 patients of MDS by Kini J et al bicytopenia was the commonest finding.[19] The present study of three patients with MDS having pancytopenia were done.

Age and sex distribution

In the present study, three cases presented with pancytopenia in age group of 64-75 years. In a study of 118 patients with MDS by Juneja SK et al.[20] the age ranged from 48-95 years. In a study of 31 patients by

Kini J et al.[19] the patients were in the age group of 4-7 year.

Dengue fever

In the present study, 2 cases in 18 years (male) and 22 years (female) with dengue fever presented with pancytopenia. Total leukocyte count was 800 cells/cumm and platelet count was 28,000 cells/cumm. Bone marrow was hypercellular showing erythroid hyperplasia with reversal of M:Eratio. Naeem Khan et al studied 30 cases of pancytopenia and found 1 case of dengue fever.[21]

Hemolytic anemia

In the present study, one patient of hemolytic anemia presented with pancytopenia. Peripheral blood showed features of hemolysis. Occasional irreversible sickled cells were seen. Erythrocytes showed moderate degree of anisopoikilocytosis and an increase in number of polychromatophilic RBCs.

Reticulocyte count was markedly decreased. Bone marrow was hypocellular. Fazlur Rahim et al in their study found three cases of pancytopenia with hemolytic anemia.[16] Osama et al in their study found two cases of pancytopenia with hemolytic anemia.[12]

CONCLUSION

The present study concludes that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of cytopenia. These are also helpful in planning further investigations and management.

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