

## **BONE MARROW EVALUATION OF PANCYTOPENIA PATIENTS, A STUDY IN TMC & DR BRAM TEACHING HOSPITAL**

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### **Abstract**

**Aim:** To evaluate bone marrow among pancytopenia patients.

**Material and Method:** A hospital based study was undertaken at Tripura Medical College & Dr BRAM Teaching Hospital from August 2017 to January 2021. During this period, 57 cases had the clinical presentation of pancytopenia. Relevant medical history and clinical details were collected from each patient. Bone marrow aspiration was done from posterior superior iliac spine using Salah bone marrow aspiration needle. Simultaneously, from same puncture site but from a different plane, bone marrow biopsy was done using Jamshidi needle taking all aseptic precautions and consent. Peripheral blood smear and bone marrow aspirate smear were stained by Leishman Stain and trephine biopsy were processed and stained by Haematoxylin and eosin stain. Special stain was applied whenever required.

**Results:** Majority of the patients (16/57) belonged to the age group of 51-60 years (28%). The commonest mode of presentation was pallor and generalised weakness, followed by fever and other. Splenomegaly was seen mostly in cases of megaloblastic anemia followed by sub/aleukemic leukemia. Lymphadenopathy was noted in all cases of sub/aleukemic leukemia lymphoblastic type. Commonest cause of pancytopenia was micronormoblastic erythroid hyperplasia.

**Conclusion:** This study concluded that most common cause of pancytopenia is Micronormoblastic erythroid hyperplasia followed by sub leukemic leukemia/aleukemic leukemia (acute leukemia), aplastic marrow and plasma cell dyscrasia. Thus, Bone marrow examination can diagnose most of the cases of pancytopenia and helps in planning further investigations and management.

**Keywords:** Bone Marrow, Pancytopenia, Blood smear.

**Introduction:** Pancytopenia is an important clinicohaematological entity encountered in our day to day clinical practice. Pancytopenia is a triad of findings characterised by reduction in all three major formed elements of blood erythrocytes, leucocytes, platelets below their reference values.<sup>1</sup>

It is not a diagnosis in itself but a presentation of some underlying general medical or primary haematological disorder.<sup>2</sup> The mechanism of development of pancytopenias varies from the decrease in haematopoietic cell production as in aplastic anemia, trapping of normal cells in hypertrophied and over reactive reticuloendothelial system as in hypersplenism, ineffective haematopoiesis as in megaloblastosis or replacement of normal bone marrow elements by abnormal or malignant cells.<sup>3</sup>

The chief complaints and clinical presentation in the patients having pancytopenia are pallor, fatigue, fever, infection, bleeding, weight loss, organomegaly.<sup>4</sup> With proper evaluation like proper clinical examination, hematological investigation as complete blood count, peripheral smear and bone marrow examination, early diagnosis for the cause of pancytopenia can be done. Bone marrow aspiration is extremely helpful in evaluating the cause of pancytopenia by cellularity and cytology in order to prevent grave complications and mortality as the underlying pathology determines the management and prognosis of the patients.<sup>5</sup>

Marrow cellularity and composition differ in relationship to the cause. The marrow is generally hypocellular in cases of pancytopenia caused by a primary production defects. Cytopenias resulting from ineffective hematopoiesis, increased peripheral utilization or destruction of cells and bone marrow invasive processes are usually associated with a normocellular or hypercellular marrow<sup>6</sup>. Marrow aspirate has been primarily utilized for cytological assessment. Trepine biopsy; on the other hand, allow for studies of the marrow's overall cellularity, detection of focal lesions, and extent of infiltration by various pathologic entities<sup>7</sup>. The present study was conducted with the following aim and objective:

**Aim:** Bone marrow evaluation of pancytopenia.

**Objectives:** To evaluate the etiology and various causes of pancytopenia by bone marrow examination.

**Material and method:** A hospital based study was undertaken at Tripura Medical College & Dr BRAM Teaching Hospital from August 2017 to January 2021. During this period, a total of 123 bone marrow smears were examined. Out of these, 57 cases had the clinical presentation of pancytopenia. The subjects were recruited according to the following inclusion and exclusion criteria:

**Inclusion criteria:** Subjects having Hb <10.5 gm/dl, TLC<4000/cu mm and Platelet <100000/cu mm were included in the study.

**Exclusion criteria:** Patient on chemotherapy/radiotherapy, follow up cases of leukemia, pregnant women, who had recently received blood transfusion and not giving consent were excluded from the study.

Relevant medical history and clinical details were collected from each patient. All relevant details and sample was collected after taking consent. Bone marrow aspiration was done from posterior superior iliac spine using Salah bone marrow aspiration needle. Simultaneously, from same puncture site but from a different plane, bone marrow biopsy was done using Jamshidi needle taking all aseptic precautions and consent. Peripheral blood smear and bone marrow aspirate smear were stained by Leishman Stain and trephine biopsy were processed and stained by Haematoxylin and eosin stain. Special stain was applied whenever required.



Figure 1a: Salah/Klima Needle



Figure 1b: Jamshidi Needle

**Statistical analysis:** Microsoft word 2013 and Microsoft office 2013 excel was used to generate tables and data was analysed with the help of frequency and proportion.

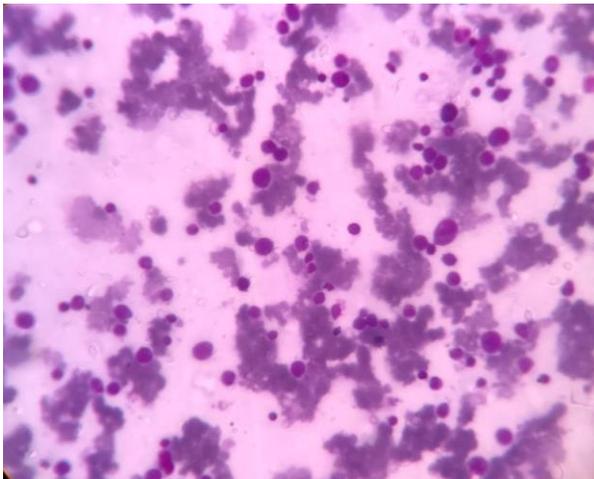


Figure 2a: Micronormoblastic erythroid hyperplasia

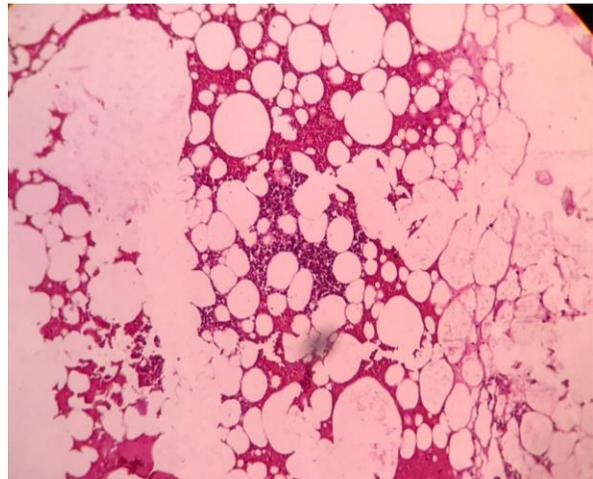
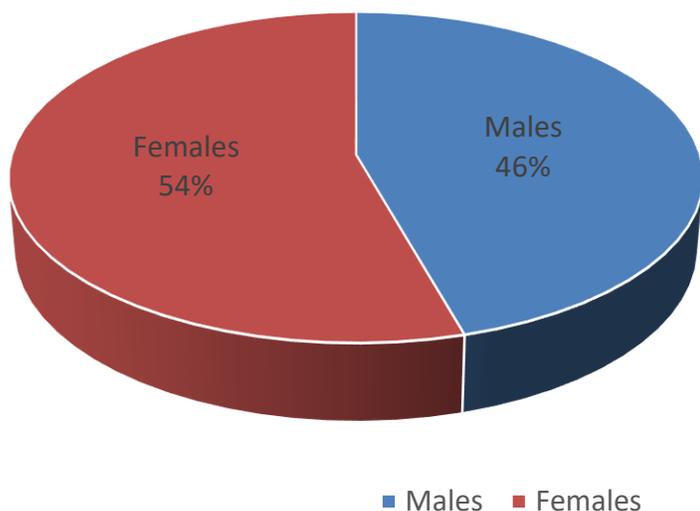


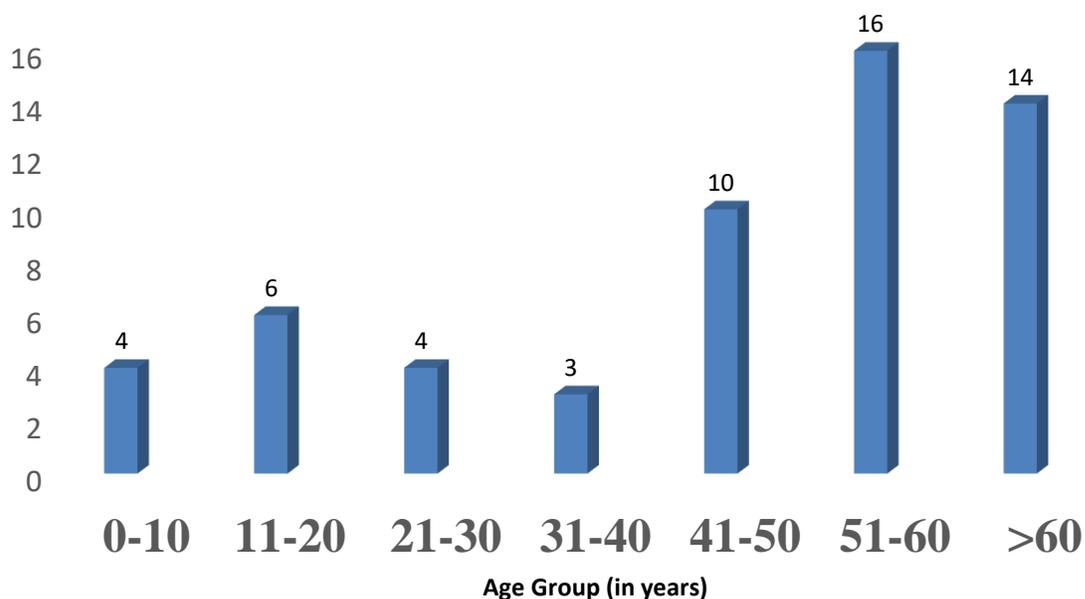
Figure 2b: Aplastic marrow (Bx)

**Results:** Out of 57 patients, 26 (46%) were males & 31 (54%) were females as shown in graph 1.

Majority of the patients (16/57) belonged to the age group of 51-60 years (28%) followed by 41-50 years (10 cases, 17.5%) as shown in graph 2.



Graph 1: Gender distribution among the study subjects



Graph 2: Age distribution of the study subjects

The commonest mode of presentation was pallor and generalised weakness, followed by fever and other. Splenomegaly was seen mostly in cases of megaloblastic anemia followed by sub/aleukemic leukemia. Lymphadenopathy was noted in all cases of sub/aleukemic leukemia lymphoblastic type (table 1).

Table 1: Presenting complaints in cases of Pancytopenia

Complaints	N	%
Generalised weakness	51	89.47

Fever	23	40.35
Bleeding Manifestations	9	15.79
Weight Loss	4	7.02
Pallor	57	100.00
Dyspnea	3	5.26
Jaundice	3	5.26
Splenomegaly	7	12.28
Hepatomegaly	1	1.75
Hepatosplenomegaly	6	10.53
Lymphadenopathy	9	15.79
Bony Pain	1	1.75
Other Pain (Body, Abdomen, chest)	13	22.81

Commonest cause of pancytopenia was micronormoblastic erythroid hyperplasia followed by acute leukemia aplastic/hypoplastic marrow and plasma cell dyscrasia. Dry tap was reported among 5.3% of the subjects. Myelodysplastic syndrome, ITP, Ewing sarcoma/PNET and NHL spill over was reported among 2, 2, 1 and 1 case respectively (table 2).

Table 2: Causes of Pancytopenia

Diagnosis	No. of cases	Percentage
Micronormoblastic erythroid hyperplasia	18	31.5%
Sub leukemic leukemia/Aleukemic leukemia (Acute leukemia)	14	24.5%
Aplastic/hypoplastic marrow	7	12.2%
Plasma cell dyscrasia	5	8.7%
Myelodysplastic syndrome	2	3.6%
ITP	2	3.6%
Ewing sarcoma/ PNET	1	1.8%
NHL spill over	1	1.8%
Normal marrow	4	7.0%
Dry tap	3	5.3%

**Discussion:** Pancytopenia is a common haematological finding with variable clinical presentations. It often creates diagnostic challenge to physician and the knowledge of accurate etiology of this condition is crucial in the management of the patient. 57 cases of pancytopenia were studied regarding age, gender wise distribution, presenting complaints, bone marrow examination findings and final various causes of pancytopenia were evaluated and the results were compared with previous similar studies done in India and abroad.

In our study, there were 26 (46%) were males & 31 (54%) were females. Similarly Aziz et al found the same more in females<sup>8</sup>. Neeru Singhal et al<sup>9</sup> in their study shows a definite male

preponderance with male to female ratio 1.14:1 which is comparable with Gayateri and Rao et al<sup>10</sup> (1.2:1), Naniwal P et al<sup>11</sup> (1.15:1).

In our study; majority of the patients (16/57) belonged to the age group of 51-60 years (28%) followed by 41-50 years (10 cases, 17.5%). Similarly Meena Mittal et al<sup>12</sup> revealed that most cases were seen in the age group of 31-60 years. Neeru Singhal et al<sup>9</sup> in their study showed that most of the patients were in age group 11-30 years (36.67%) which is comparable to Desalpin M et al<sup>13</sup>, Bahal D et al<sup>14</sup>, Naniwal P et al<sup>11</sup>, Shah P et al<sup>15</sup>. The difference in the gender and age distribution might be due to the difference in the study area.

In this study, the commonest physical findings were pallor followed by generalised weakness, fever, splenomegaly and lymphadenopathy. Similar clinical findings have been reported in other studies, although their frequency varies<sup>9</sup>. The differences in the frequency of clinical features can be attributed to geographic variations, genetic make up of the patients and the haematological parameter being predominantly affected in pancytopenia cases.

In the present study; commonest cause of pancytopenia was micronormoblastic erythroid hyperplasia followed by acute leukemia aplastic/hypoplastic marrow and plasma cell dyscrasia. Dry tap was reported among 5.3% of the subjects. Myelodysplastic syndrome, ITP, Ewing sarcoma/PNET and NHL spill over was reported among 2, 2, 1 and 1 case respectively. The higher incidence of sub/aleukemic leukemia and multiple myeloma in this study can be attributed to the inclusion of referred and high risk cases in the study, as the study center is a tertiary care hospital with well established cancer hospital and laboratory.

In a study by Pathak R et al<sup>16</sup>, out of 102 cases of pancytopenia, 20% of BMA showed erythroid hyperplasia, however, after correlation with biopsy, it reduced to 16.6%. Erythroid hyperplasia by itself is not the cause of pancytopenia. Relationship of erythroid hyperplasia to pancytopenia is uncertain. Some of these cases may represent one phase in the evolution of hypoplasia, while some may be case of refractory anemia.

Mittal M et al<sup>12</sup> reported that second major cause of pancytopenia was aplastic/hypoplastic anemia in present study (19.05%). Tilak et al<sup>17</sup> and Khodke et al<sup>18</sup> also found the same results. However Pathak et al<sup>16</sup> and Jha et al<sup>8</sup> have aplastic anemia as common cause of pancytopenia. This may be due to the reason that Aplastic anemia is caused due to environmental factors or exposure to pesticides, drugs and toxic chemicals.

Hence most studies conducted in India have also reported megaloblastic anemia as a major cause of pancytopenia similar to this study. Higher incidence of megaloblastic anemia in Indian subcontinent can be attributed to low socioeconomic status, poor hygiene, inadequate nutrition and some cultural taboos.

The wide variation in incidence of causes of pancytopenia in different studies published from India as well as other countries can be attributed to the differences in methodology, selection of diagnostic criteria, nutritional status, prevalence of infective disorders and genetic differences in the population as well as varying exposure to myelotoxic agents. Although, the haematological parameters were usually nonspecific in many cases and show a considerable overlap, they do give a diagnostic clues for the evaluation of cases of pancytopenia.

**Conclusion:** This study concluded that most common cause of pancytopenia is Micronormoblastic erythroid hyperplasia followed by sub leukemic leukemia/aleukemic leukemia (acute leukemia), aplastic marrow and plasma cell dyscrasia. Thus, Bone marrow examination can diagnose most of the cases of pancytopenia and helps in planning further investigations and management. Clinical finding, peripheral smear examination and Bone

marrow examination should go hand in hand to work-up of the patient of pancytopenia to reach to a concrete diagnosis.

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