



Original Article

## Etiological Spectrum of Pancytopenia: Experience from North-Eastern Part of India

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### ABSTRACT

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**Background:** Pancytopenia i.e, reduction in all three cell lines of the blood is a commonly encountered abnormality in routine haematological practice. A wide spectrum of diseases can present with pancytopenia so an extensive work-up is required to approach the hematological abnormality. The incidence of various diseases causing pancytopenia varies depending on the geographical areas and genetic diversity.

**Methods:** The present study was a hospital based cross-sectional study to establish and to evaluate the causes of pancytopenia at a tertiary centre in upper-Assam. A total of 50 patients of pancytopenia were evaluated with detailed clinical and laboratory investigations along with bone marrow examination and ancillary methods in the Department of Pathology, AMCH, Dibrugarh for a period of two years.

**Result:** Out of the 50 cases of pancytopenia that were studied the most common age group ranged from 21-30 years with a male predominance. Majority of the patients presented with generalized weakness and fever. The commonest physical finding was pallor, followed by splenomegaly and hepatomegaly. Bone marrow examination, including biopsy was diagnostic in all the cases. The commonest cause of pancytopenia in this part of the country was megaloblastic anaemia (42%) followed by aplastic/hypoplastic anaemia (22%).

**Conclusion:** The etiological spectrum of pancytopenia is diverse. A detailed physical and peripheral blood examination including bone marrow examination supported by ancillary methods is required to establish and evaluate the underlying cause of pancytopenia.

**Keywords:** Pancytopenia, bone marrow, splenomegaly, megaloblastic anaemia.

### INTRODUCTION

The term pancytopenia denotes simultaneous reduction in all the three formed elements of the blood, i.e., erythrocytes, leukocytes, and platelets. Pancytopenia is a commonly encountered haematological abnormality in routine clinical practice. Pancytopenia is not a disease entity but a triad of findings that may arise from a number of disease processes.[1] Pancytopenia can be due to decrease in the hemopoietic cell production in bone marrow, e.g., by infections, toxins, malignant cell infiltration or suppression, or can have normocellular or even hypercellular marrow without any abnormal cells, e.g., in ineffective hematopoiesis and dysplasia, maturation arrest of all cell lines, and peripheral sequestration of blood cells.[2–4] The incidence of pancytopenia differs in various age groups and gender and depends on geographical distribution and genetic make-up of the population. The various disorders which cause pancytopenia being so diverse, the appropriate approach to diagnose pancytopenia needs to be emphasized. A detailed history, physical examination, and bone marrow examination along with ancillary procedures such as cytochemistry, flow cytometry, and bone marrow

cultures are required to establish the diagnosis. The present study was conducted in upper Assam, North-eastern region of India, to evaluate the etiological spectrum of pancytopenia and their relative frequencies.

## MATERIALS AND METHODS

The study conducted was a cross-sectional, hospital based single centre (Assam Medical College and Hospital, Dibrugarh) study for a period of two years on 50 cases of pancytopenia. Patients of all age groups and both sexes were taken. Pancytopenia was diagnosed in the presence of anemia (hemoglobin <11 g/dl), leucopenia (total leukocyte count <4,000/mm<sup>3</sup>), and thrombocytopenia (platelet count <150,000/mm<sup>3</sup>).<sup>[5]</sup> In all patients, a detailed relevant history including the treatment history, history of drug intake, radiation exposure was taken and thorough clinical examination of every patient was done. After history and examination basic investigations were performed for each patient including complete blood count and red blood cell indices. After obtaining full informed consent, and under all aseptic and sterile condition, the bone marrow aspiration was done from the posterior superior iliac spine by a Salah's needle and biopsy along with imprint smear wherever required by a Jamshidi needle of size 10G or 11G size with a length of 4.5 inches and a bore diameter of 3mm or 3.5mm respectively. The bone marrow aspiration and imprint smears were stained by May Grunwald Giemsa stain. Special stains, techniques and bio-chemical studies were done wherever required. The tissue core biopsy was fixed in buffered formalin, decalcified in di-sodium EDTA for 10 to 12 hours, and then the routine processing was done. Sections were stained by hematoxylin and eosin stain. IEC permission was taken for the study.

## RESULT

Out of the total 50 cases evaluated, the mean age group was 21–30 years and the mean age was 25.5 years with a male to female ratio of 1.78: 1. The commonest presenting symptoms were generalized weakness (52.0%) and fever (34.0%). Pallor was noted in all 50 cases (100%), followed by splenomegaly (22.0%) and hepatomegaly (20.0%) as the common physical signs. The clinical features of patients with pancytopenia are listed in [Table 1, Fig 5]. The marrow was hypercellular in 35 cases (70%) out of which megaloblastic anaemia was seen in 21 cases (42.0%). [Fig:1] Aplastic/hypoplastic anaemia was noted in 11 cases (22.0%). [Fig:2] Three cases each of tuberculosis (6.0%) and myelodysplastic syndrome (6.0%), two cases of myelofibrosis (4.0%). [Fig: 3] and subleukaemic leukaemia (4.0%), and one case each of hypersplenism (2.0%) and SLE (2.0%) were also noted. Non-specific changes were noted in six cases (12.0%). Serum Vitamin B12 estimation was done in cases presenting with megaloblastic anaemia. The majority of the patients diagnosed as having megaloblastic anaemia had MCV values < 100 fl which could be due to co-existent iron deficiency. The results of the study are listed in [Table 2].

Pleural fluid analysis was done in one of the cases of tuberculosis presenting with pleural effusion. Though AFB could not be demonstrated but the total count was high with predominance of lymphocytes and the pleural fluid Adenosine Deaminase (ADA) value was significantly raised.<sup>[6]</sup> Acid Fast stain was positive in the other two cases of tuberculosis in the bone marrow aspiration. In another case a young lady was seen to have anti-nuclear antibodies (ANA) in her serum and presented with megaloblastoid changes in the bone marrow examination. LE cell could be demonstrated in the buffy coat preparation from the peripheral blood of the patient. In the two cases of subleukaemic leukaemia, buffy-coat preparation from the peripheral blood and the bone marrow imprints prepared from the biopsy section was diagnostic. LD bodies were noted in the bone marrow examination of a patient from the north-India, presenting with hypersplenism leading to a diagnosis of Kala-azar. [Fig: 4]

## FIGURES:

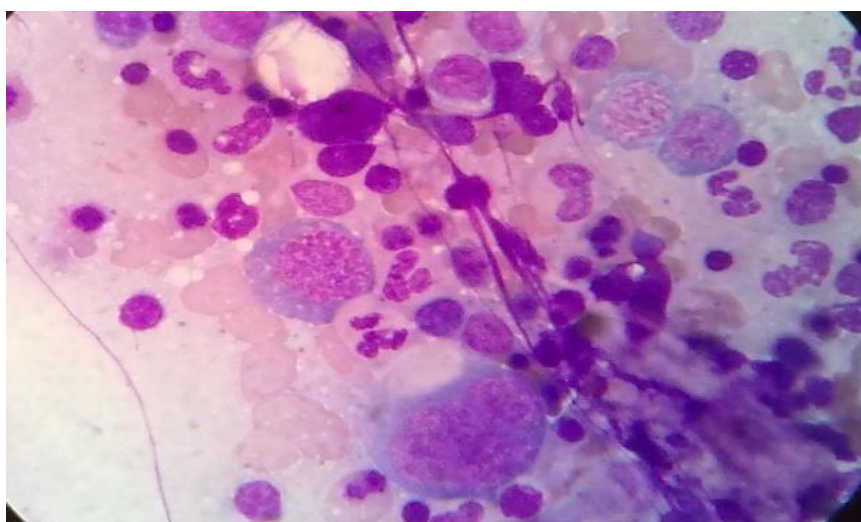


Fig 1: Photomicrograph of bone marrow imprint showing characteristic megaloblasts (MGG,40x)

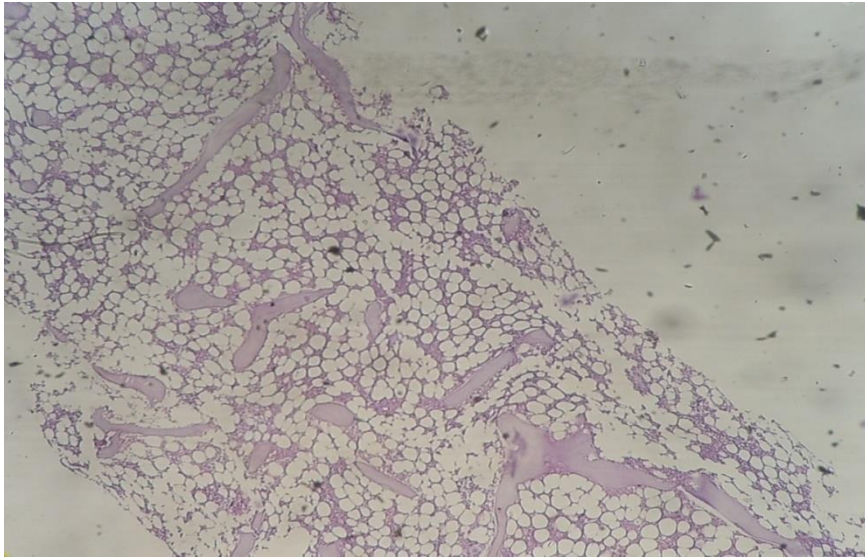


Fig 2: Photomicrograph of bone marrow biopsy in a case of aplastic anaemia (H&E,4X)

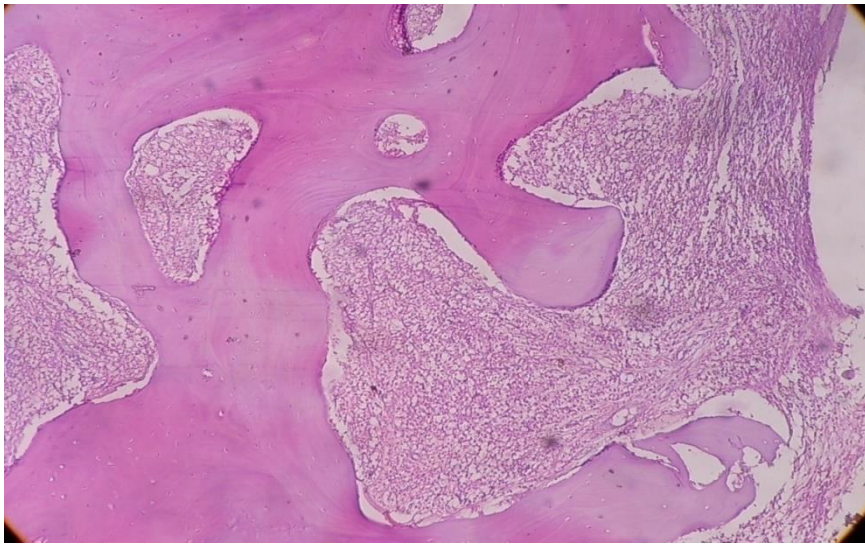


Fig 3: Photomicrograph of bone marrow biopsy in a case of fibrosis of the marrow (H&E,4X)

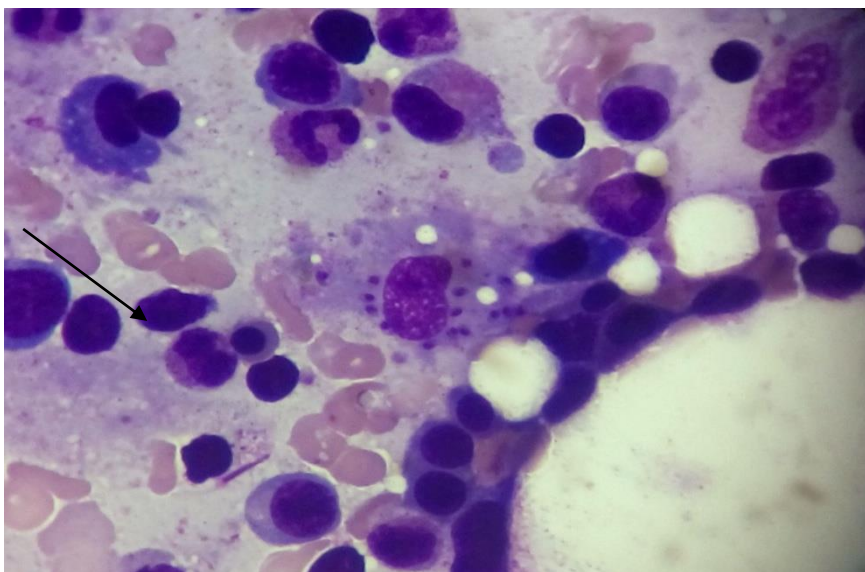


Fig 4: Photomicrograph of bone marrow aspiration showing intracellular LD bodies (arrow, MGG,40x)

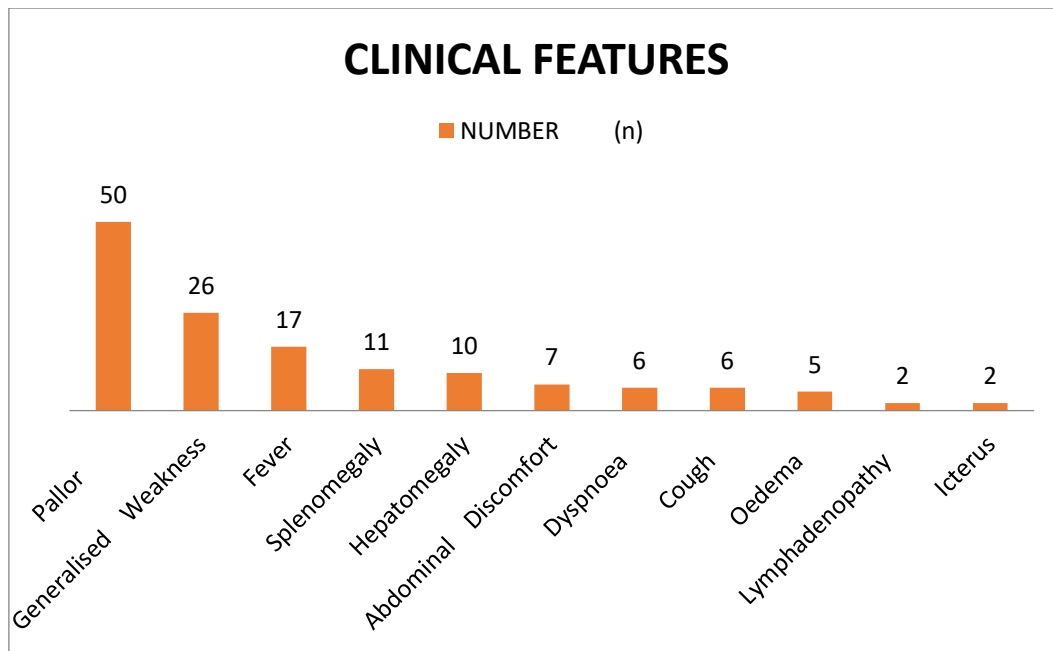


Fig 5: Clinical features of patients with pancytopenia

**TABLES:**

**Table 1: Clinical features of patients with pancytopenia**

CLINICAL FEATURES	NUMBER (n)	PERCENTAGE (%)
Pallor	50	100.0
Generalised Weakness	26	52.0
Fever	17	34.0
Splenomegaly	11	22.0
Hepatomegaly	10	20.0
Abdominal Discomfort	7	14.0
Dyspnoea	6	12.0
Cough	6	12.0
Oedema	5	10.0
Lymphadenopathy	2	4.0
Icterus	2	4.0

**Table 2: Causes of pancytopenia**

DISEASES	FREQUENCY (n)	PERCENTAGE (%)
Aplastic Anaemia/Hypoplastic Marrow	11	22.0
Megaloblastic Anaemia	21	42.0
Hypersplenism (Kala-Azar)	1	2.0
MDS	3	6.0
Tuberculosis	3	6.0
Subleukaemic Leukaemia	2	4.0
SLE	1	2.0
Non-Specific Changes	6	12.0
Myelofibrosis	2	4.0

**Table 3: Bone marrow changes noted in cases of pancytopenia**

PARAMETERS	FINDINGS	NUMBER (n)	PERCENTAGE (%)
Cellularity	Hypocellular/Hypercellular/Normocellular	12/35/01	24.0/70.0/2.0
Bony Trabeculae	Normal/ Thick / Thin	48/01/01	96.0/2.0/2.0
Erythroid Series	Normal/Hypoplastic/Hyperplastic	1/13/34	2.0/26.0/68.0
Myeloid Series	Normal/Hypoplastic/Hyperplastic	1/12/35	2.0/24.0/70.0

Lymphocytes & Plasma Cells	Normal/Increased/decreased	28/12/08	56.0/24.0/16.0
Sinusoids	Normal/Dilated	49/01	98.0/2.0
Fibrosis etc.		2	4.0

## DISCUSSION

Pancytopenia is a common hematological problem encountered in clinical practice. There are varying trends in its clinical pattern, treatment modalities and, outcome. The present study was a hospital based prospective study of 50 cases of pancytopenia, the ages of the patients ranged from 14 to 75 years and the majority were in the age group of 21–30 years. Khodke K et al. (2001) reported the highest incidence in 12–30 years of age group. Sarode R et al. (1989), also reported highest incidence in second and third decade.<sup>[7,8]</sup> Male to female ratio was 1.78:1. Gayathri BN et al. (2011) noted that pancytopenia was more common in males with a ratio of 1.2:1. Jalbani A et al. (2010), reported the highest incidence in males (72.5%).<sup>[9,10]</sup>

In the present study it was observed that the most common cause of pancytopenia in this part of the country was megaloblastic anaemia seen in 21 cases (42.0%) followed by aplastic/hypoplastic anaemia in 11 cases (22.0%). The results correlated with the studies of Gayathri BN et al. (2011) and Khunger JM et al. (2002) which showed the incidence of megaloblastic anaemia to be 74.04% and 72% respectively.<sup>9,11</sup> Khodke K et al. (2001) and Tilak V et al. (1999) had an almost similar finding to that of the present study with megaloblastic anaemia as the major cause of pancytopenia in 68% and 44% cases respectively.<sup>[7,12]</sup>

The majority of the patients diagnosed as having megaloblastic anaemia had MCV values < 100 fl which could be due to co-existent iron deficiency.<sup>[13]</sup> This is a common problem in developing countries which could be due to malabsorption or due to poor nutrition. Steroid therapy, insecticides, herbal medicine and antiepileptic drugs were also seen to be associated with pancytopenia. Chemotherapy with Imatinib mesylate in chronic myeloid leukaemia patients lead to the development of pancytopenia.<sup>[14,15]</sup> The commonest presenting symptoms were generalized weakness and fever. Pallor was noted in all 50 cases, followed by splenomegaly and hepatomegaly as the common physical signs. Bone marrow examination preferably aspiration is an important diagnostic tool required for establishing the diagnosis in patients with pancytopenia. Biopsy is mandatory for confirming the diagnosis of aplastic anaemia and when aspirate is not obtained (dry aspirate or dry tap).<sup>[16]</sup> The bone marrow examination in our study was diagnostic in all the cases. The changes noted in the bone marrow are summarized in Table 3 .

## CONCLUSION

Pancytopenia is a relatively common hematological abnormality with an extensive differential diagnosis. The diagnostic work-up to establish the diagnosis and to evaluate the etiological spectrum depends upon proper physical and blood examination which gives important clues to the diagnosis of underlying cause of pancytopenia. These along with detailed bone marrow examination and ancillary procedures are an important tool to diagnosis and to evaluate the causes of pancytopenia.

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**COMPETING INTERESTS:** No competing interest for this study

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