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Original Article

Pathology Section

Pancytopenia: Clinical and Haematological Profile from a Tertiary Care Centre in Central India

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ABSTRACT

Introduction: Pancytopenia is a characterised by the decrease in number of red blood cells, white blood cells, and platelets. It is not a final diagnosis; instead, a manifestation of underlying haematological and other disorder. No study has been carried out to evaluate the cause of pancytopenia from this region. The majority of the Western world studies suggest aplastic anaemia as a significant cause of pancytopenia. However in India, the pancytopenia causes are not well defined and varied. Earlier studies from India show megaloblastic anemia being the primary cause of pancytopenia.

Aim: To investigate the clinical and haematological correlation of pancytopenia and to ascertain aetiopathological causes of pancytopenia in patients admitted to a tertiary care center.

Materials and Methods: This prospective cross-sectional study was conducted from August 2012 to August 2014 at RD Gardi Medical College, Ujjain, a total of 100 consecutive patients with two or all three of the following inclusion criteria were enrolled: Haemoglobin <10 gm/dL Total Leukocyte Count (TLC) <4000/µL and platelet count <1,00,000/µL. All patients underwent complete hemogram, peripheral smear, and reticulocyte count evaluation. Bone marrow aspiration was also performed in all patients, and in addition, a trephine biopsy was done in the same setting in 23 patients. Data were analysed using standard statistical methods. Various sign, symptoms of pancytopenia were recorded and analysed.

Results: Underlying cause of pancytopenia was ascertained with the help of blood picture of bone marrow aspiration and biopsy, fatigue was the most common symptom (54%) followed by fever (49%) and breathlessness (15%). Pallor was detected in 85% of patients, splenomegaly in 47%, followed by hepatomegaly, oedema, lymphadenopathy, icterus, and ascites. Megaloblastic anemia was found to be the most prevalent cause of pancytopenia, which was seen in 49% of patients and followed by hypersplenism (16%).

Conclusion: Pancytopenia is not an uncommon condition and should be suspected on clinical grounds when a patient presents with unexplained anaemia, fatigue and prolonged fever. Along with the clinical examination, the haematological study includes peripheral smear, bone marrow aspiration and bone marrow biopsy plays a critical role in the diagnosis.

Keywords: Aplastic anaemias, Blood diseases, Myelodysplastic-myeloproliferative

INTRODUCTION

Pancytopenia is a disorder, characterised by the decrease in count of three elements of blood (red blood cells, white blood cells, and platelets) below the normal values. It is not a diagnosis; instead, a manifestation of underlying general medical or primary hematological disorders; some of which are life threatening conditions such as bone marrow failure syndromes and malignancies [1,2]. Nutritional anemias and infections are among few benign conditions, which can be responsible for pancytopenia in some geography [3,4]. The prognosis and clinical management of pancytopenia is determined by its underlying cause and severity [5].

Diligent assessment of the blood elements should be the first step in evaluating the hematological changes of the pancytopenia. Physical examination and findings of peripheral blood smear plays a crucial role in workup of these patients' and also help in further investigations such as bone marrow biopsy [4,6].

Bone marrow examination is a most important investigation which, can confirm the diagnosis of pancytopenia. It may occasionally provide a previously unsuspected diagnosis [7]. Bone marrow aspiration and trephine biopsy remain essential in the diagnosis of aplastic anaemia and malignant disorders [8].

The majority of the Western world studies suggest aplastic anaemia as a significant cause of pancytopenia [3,9]. In India, the causes of pancytopenia are not well documented and there is paucity of literature. Earlier studies from our country revealed megaloblastic anemia as the major cause of pancytopenia [5,6].

The aim of present study were to investigate the clinical and haematological correlation of pancytopenia and to ascertain aetiopathological causes of pancytopenia in patients admitted to a tertiary care centre; study and correlate the peripheral blood smear, bone marrow aspirate and trephine biopsy findings.

MATERIALS AND METHODS

The present study was a cross-sectional study conducted in the Department of Pathology, RD Gardi Medical College and CRG hospital from August 2012 to August 2014.

Inclusion criteria: All consecutive patients with the following inclusion criteria were enrolled in the study. Presence of two or all three of the following: Haemoglobin <10 gm/dL; TLC <4000/µL; 3) Platelet count <1,00,000/µL.

Exclusion criteria: Patients who refused informed consent, refused to undergo the bone marrow aspiration, biopsy and those with an already established diagnosis of pancytopenia were excluded from the study.

After informed consent, the patients were interviewed using a pre-designed questionnaire which included clinical and treatment history. Physical examination was done for pallor, icterus,hepatomegaly,splenomegaly, lymphadenopathy etc.

Procedure

Sample collection and all the procedures, including peripheral blood smears, bone marrow aspiration and bone marrow biopsy, were done as per the method described in Dacie and Lewis's practical haematology [10].

After taking all aseptic precaution, around 3 mL of blood was withdrawn after venepuncture and collected in Ethylenediamine Tetra-Acetic Acid (EDTA) vial. The sample was analysed using auto analyser as well as by peripheral smear for complete blood count and morphology. Bone marrow aspiration study was done using Salah bone marrow needle. The posterior iliac crest was anaesthetized before the advancement of the needle and standard aseptic precautions were also taken.

The procedure was performed with patient in a prone position and the anatomic landmark; posterior superior iliac crest was identified with palpation. The puncture site and surrounding skin was cleaned with 10% povidone-iodine solution in a circular motion. Povidone-iodine was wiped from the puncture site was swipe with am isopropyl-soaked swab. A sterile drape was placed over the site to be sampled.

The 2% lignocaine, was injected before the aspiration in and around the target site to anaesthetized the skin and periosteum over the selected site. The Salah needle with the stylet in-situ was inserted into the center of the posterior iliac prominence and advanced gently with constant pressure and twisting motion. A sudden decreased in resistance to advancement; indicated penetration of cortex and entry of the needle into the marrow cavity. The needle was progressed further about 1 cm into the marrow cavity. The stylet was slowly removed and around 0.2 ml of marrow fluid was aspirated into a 10 ml syringe. A pressure bandage was applied over the site after removal of the needle.

Smears were prepared from the marrow aspirate, air-dried, and stained with Leishman's stain. The stained smears were examined for its cellularity. The megakaryocytes, and presence or absence of malignant cells were also noted. The area where cell population was well spread out was chosen and at least 500 marrow cells were counted under oil immersion. The stained marrow aspiration smears were examined for cellularity, erythropoiesis, myelopoiesis, myeloid: erythroid ratio, megakaryopoiesis, plasma cells, lymphocytes, mast cells, parasites, and granulomas. Special staining agents such as Perls' Prussian blue stain, myeloperoxidase, and periodic acid Schiff were used wherever required.

The bone marrow biopsy sample was obtained from the same site used for marrow aspiration; however, the angle of the biopsy needle was changed from the aspirate needle in order to acquire sample from a different area. The needle was held securely and the stylet locked in place. Once the needle got fixed in the bone, the stylet was slowly removed while keeping outer needle in its position. With steady pressure, the needle was slowly advanced into the marrow cavity with gentle rotatory push in an alternating clockwise, counterclockwise motion. A bone marrow specimen measuring approximately 1.5-2 cm in length was obtained. Firstly, core biopsy was used to make touch preparations before placing the specimen in fixating solution (10% formalin) overnight. To achieve the hemostasis firm pressure was applied for two minutes; followed by compression bandage. Biopsy specimens were stained with hematoxylin and eosin. Special stains, such as myeloperoxidase and iron stain, were used wherever required.

STATISTICAL ANALYSIS

Descriptive statistics were used for analyses of the data.

RESULTS

Complete haemogram, peripheral examination, reticulocyte count and bone marrow aspiration were performed biopsy was done in the same setting in 23 patients. The range of age was 3 to 85 years with male to female ratio of 2:1 [Table/Fig-1].

A majority of patients presented with fatigue (54%) followed by fever (49%) and breathlessness (15%). Other less common symptoms were bleeding manifestations, abdominal pain abdomen, swelling, bone pain, etc. On examination, pallor was detected in 85% of patients, splenomegaly in 47%, followed by hepatomegaly, oedema, lymphadenopathy, icterus, and ascites [Table/Fig-2,3].

Megaloblastic anaemia was the most common aetiology of pancytopenia followed by hypersplenism [Table/Fig-4].

Age group (Years)	Male	Female	Total
1-9	4	2	6 (6%)
10-19	2	6	8 (8%)
20-29	15	5	20 (20%)
30-39	23	4	27 (27%)
40-49	5	7	12 (12%)
50-59	11	3	14 (14%)
60-69	4	5	9 (9%)
>70	3	1	4 (4%)
Total	67	33	100 (100%)

[Table/Fig-1]: Age and sex distribution of the pancytopenia cases.

Symptoms	Number (%)
Fatigue	54 (54%)
Fever	49 (49%)
Breathlessness	15 (15%)
Bleeding	14 (14%)
Abdominal pain	10 (10%)
Swelling	08 (8%)
Bone pain	04 (4%)
Abdominal distention	03 (3%)
Vomiting	02 (2%)
Loose motion	02 (2%)

[Table/Fig-2]: Presenting complaints in the patients with pancytopenia.

Physical findings	Number (%)
Pallor	85 (85%)
Splenomegaly	47 (47%)
Hepatomegaly	22 (22%)
Oedema	8 (8%)
Lymphadenopathy	5 (5%)
Icterus	4 (4%)
Ascites	1 (1%)

[Table/Fig-3]: Physical findings in the patients of pancytopenia.

Aetiology	Number (%)
Megaloblastic anaemia	49 (49%)
Hypersplenism	16 (16%)
Aplastic anaemia	12 (12%)
Acute leukaemia	11 (11%)
Myelodysplastic syndrome	09 (09%)
Nutritional anaemia	03 (03%)

[Table/Fig-4]: Aetiological distribution of pancytopenia (N=100).

Haematological Data

Analysis of haematological data reveals majority of patients had haemoglobin (38%) 5.1-7 gm/dL, Total Leucocyte Count (TLC) (70%) 1100-3000 cells/cumm, platelet count (37%) of 51000-75000 cells/cumm and reticulocyte count (83%) of 0.1-2%. Macrocytic normochromic was the most predominant erythrocyte morphology observed (34%) [Table/Fig-5]. Hypercellular marrow was observed in 47% of patients, whereas 33% and 20% exhibited normocellular and hypocellular marrow.

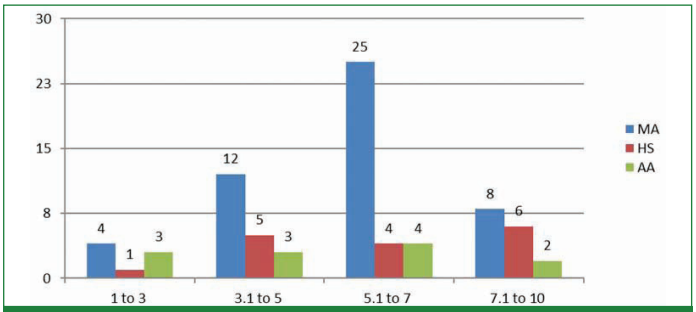
A. Pancytopenia with Megaloblastic Anaemia

A total of 49 patients were diagnosed with megaloblastic anaemia, aged 6-78 years. Fatigue (30%) was the commonest symptom

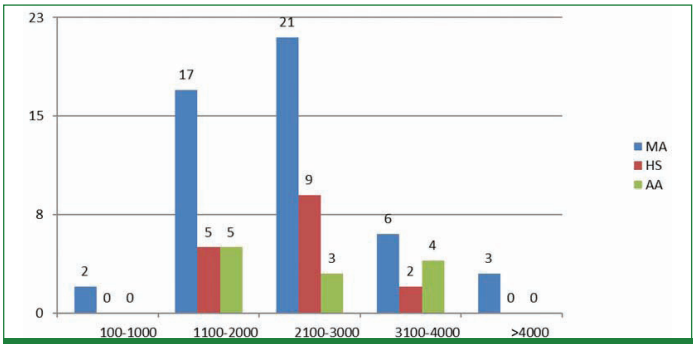
Red blood cell morphology	Number
Normocytic normochromic	29 (29%)
Normocytic hypochromic	04 (4%)
Dimorphic	20 (20%)
Macrocytic normochromic	34 (34%)
Microcytic hypochromic	13 (13%)
Total	100 (100%)

[Table/Fig-5]: Red blood cell morphology in patients with pancytopenia.

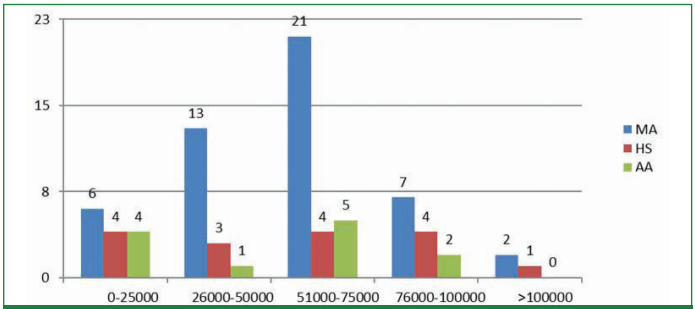
followed by fever (23%) and breathlessness (6%). Pallor was the most common sign (n=42), followed by splenomegaly. Haemoglobin value varied from 1.5-10 gm/dL though majority had values of 5.1-7 gm/dL [Table/Fig-6]. Other haematological parameters are presented in [Table/Fig-7-9].



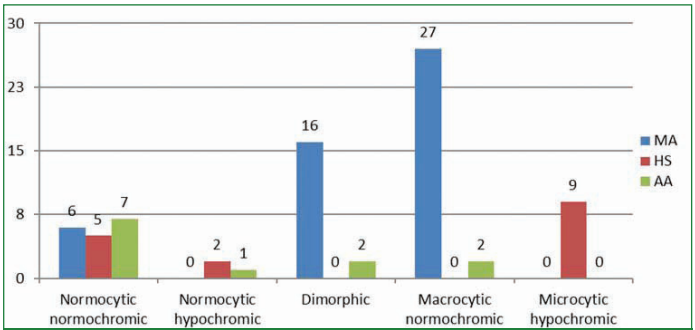
[Table/Fig-6]: Comparison of haemoglobin range between three major cause of pancytopenia. Megaloblastic anaemia (MA), Hypersplenism (HS) and Aplastic anaemia (AA).



[Table/Fig-7]: Comparison of TLC between three major cause of pancytopenia. Megaloblastic anaemia (MA), Hypersplenism (HS) and Aplastic anaemia (AA).

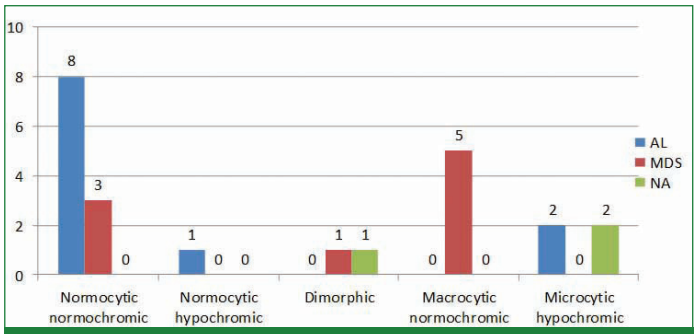


[Table/Fig-8]: Comparison of Platelet count between three major cause of pancytopenia Megaloblastic anaemia (MA), Hypersplenism (HS) and Aplastic anaemia (AA).



[Table/Fig-9]: Comparison of red cell morphology in cases of Megaloblastic anaemia (MA), Hypersplenism (HS) and Aplastic anaemia (AA).

Macrocytic normochromic red blood cells were the most predominant erythrocyte morphology observed in 55.1% of patients, followed by dimorphic Red Blood Cells (RBCs) (32.7%) [Table/Fig-9]. On peripheral smear, macroovalocytosis with a considerable degree of anisopoikilocytosis was the main feature. Mean corpuscular volume was more than 100 fL in 27 (55.1%) of patients. Hypersegmented neutrophils were seen in most of the patients. The bone marrow was hypercellular with a reduction in fat cells in a majority (67.3%) [Table/Fig-10]. Erythroid hyperplasia with megaloblastic maturation and reversal of M:E ratio was seen in all the patients.



[Table/Fig-10]: Bone marrow cellularity in different causes of pancytopenia. Megaloblastic anaemia (MA), Hypersplenism (HS) and Aplastic anaemia (AA), Acute leukaemia (AL), Myelodysplastic syndrome (MDS) and Nutritional anaemia (NA).

B. Pancytopenia Associated with Aplastic Anaemia

Out of 12 patients with aplastic anaemia 50% in age group of 20-29 years with significantly high male preponderance (83.3%). Contrary to the megaloblastic anaemia, Fever was the commonest symptom followed by fatigue (5%) and bleeding manifestations (3%). The haemoglobin value varied from 2-7.9 gm/dL [Table/Fig-6]. The TLC from 1100 or 1200-3700 cells/cumm. Other haematological parameters are illustrated in [Table/Fig-7-9]. The bone marrow was hypocellular, and the aspirate was mostly composed of fat cells [Table/Fig-10].

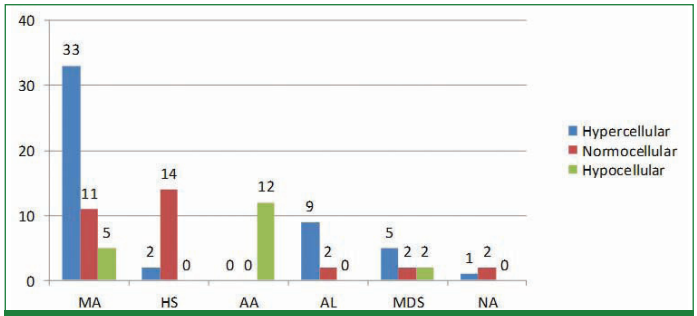
C. Pancytopenia with Hypersplenism

A total of 12 out of 16 patients with hypersplenism were in the 30-59 age group. Fatigue (7%) and fever (7%) were the common symptoms. Splenomegaly, pallor was detected in 11 patients. Haemoglobin value varied from 4-10 gm% [Table/Fig-6]. The TLC ranged from 1100-4000 cells/cumm [Table/Fig-7-9]. The reticulocyte count ranged from 0.6-6%. Microcytic hypochromic red blood cells were the predominant erythrocyte morphology, followed by normocytic normochromic RBCs (31.2%) [Table/Fig-9]. Majority had normocellular marrow. Erythroid hyperplasia was observed in 90% of patients.

D. Pancytopenia with Malignant Diseases

Acute Leukaemia

A total of 11 patients with acute leukaemia were detected. Like other causes, fatigue and fever were the two most common symptoms, and pallor was the most common sign. Like other causes of pancytopenia haemoglobin (2.8-7.1), TLC (1900-31000 cell/cumm) and platelet count (4000-77000) were reduced. Normocytic normochromic was the most predominant erythrocyte morphology observed in 72.7% of leukaemia patients, followed by microcytic hypochromic RBCs (18.2%) [Table/Fig-11]. The marrow was hypercellular in most (81.8%) of the cases. Typically these patients presented with peripheral pancytopenia or bicytopenia. The leukocyte count was decreased with the presence of immature cells. Myeloblasts with fine chromatin, 2-3 nucleoli, and occasional Auer rods were seen in Acute Myelogenous Leukemia (AML) and lymphoblast cases with chromatin coarser than myeloblast, and 1-2 nucleoli are seen in cases of Acute Lymphocytic Leukemia (ALL). Platelets were decreased. On bone marrow biopsy all cell lineage decreased, and more than 80% of blasts were seen in most patients.



[Table/Fig-11]: Comparison of red cell morphology in cases of Acute leukaemia (AL), Myelodysplastic syndrome (MDS), Nutritional anaemia (NA).

E. Pancytopenia with Myelodysplastic Syndromes

A total of nine patients were diagnosed with Myelodysplastic Syndrome (MDS) with 2:1 male to female ratio. Symptoms and signs were similar to leukaemia patients. All patients had reduced haemoglobin (1.9-8.1 gm/dL), TLC (2000-12000 cells/cumm) and platelet count (23,000-120,000 cells/cumm). Macrocytic normochromic red blood cells were the most predominant erythrocyte morphology observed in 55.6% of patients of MDS, followed by normocytic normochromic RBCs (33.3%) [Table/Fig-11]. Peripheral smear showed peripheral pancytopenia with a macrocytic type of anaemia in majority of patients. In most cases, bone marrow dysmyelopoiesis with hypogranular neutrophils and blasts were also observed [Table/Fig-10].

F. Pancytopenia with Nutritional Anaemia

Only three patients of pancytopenia had nutritional anaemia as the aetiology. Two were male and one female. All three had fatigue, and pallor. Their haemoglobin value (3.4-6), TLC (2000-3200 cells/cumm) and platelets count (43000-89,000 cells/cumm) were reduced as other causes of pancytopenia. Two patients had microcytic hypochromic erythrocyte morphology, and one had a dimorphic picture [Table/Fig-11]. Erythroid hyperplasia, megaloblastic and micronormoblastic maturation was observed in all three patients. Leucopoiesis was normal. Megakaryocytes were either normal or increased. Marrow was normocellular marrow in two and hypercellular in one. On peripheral smear, they had microcytic hypochromic anaemia.

DISCUSSION

The present study analysed the clinical, haematological and aetiological profile of pancytopenia patients in a tertiary care centre in central India. The age range (3 to 85 years), and male to female ratio (2:1) of this study were comparable to the age distribution observed in most studies in the Indian subcontinent [5-7,9,10]. Fatigue was the most common symptom (54%), followed by fever and breathlessness in 49% and 15% patients, respectively. These findings were comparable to other studies from the Indian subcontinent [9,11-13]. Similar to this study Santra G and Das BK, studied clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre and found fatigue the most frequent complaint in 74.77% of patients, followed by fever in 50.45% patients [11]. Santra G and Das BK also reported findings similar to the study by Gayathri BN and Rao KS [11,12]. Pallor was the most common sign observed as 85% of the patients had pallor. Splenomegaly was the second common (47%). Similar to the symptoms these findings were also comparable to other studies reported from the Indian subcontinent [5,6,7,14]. Several studies reported pallor as commonest and splenomegaly as the second common sign [5,6]. Hepatomegaly as the next common finding is reported by Indian study conducted in the year 1999 [6].

Aetiologies of Pancytopenia

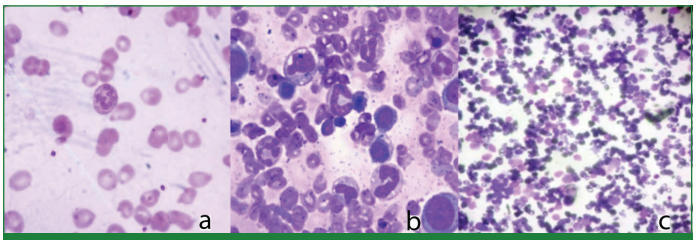
A wide variety of underlying conditions can manifest as peripheral pancytopenia [4]. The commonest cause of pancytopenia, reported in published studies from the western world, is aplastic anaemia. Conversely, most studies from Indian subcontinent revealed megaloblastic anemia as the dominant etiology [5,6,8,12,15-17]. However, few studies from the Indian subcontinent reported the similar findings as that of western literature and observed aplastic anemia as the most common underlying etiology of pancytopenia followed by the megaloblastic anemia [4,7,18]. Few studies from Indian subcontinent reveled hematological malignancies and hypersplenism as other common etiologies of pancytopenia [4,12]. Some studies reported hypersplenism as the second most common cause of pancytopenia [7]. Dodhy MA et al., found megaloblastic anaemia (35.9%) followed by hypersplenism (16.3%) as the common causes [19]. Occasional studies from Indian subcontinent reported myelodysplastic syndrome and nutritional anemia as the underlying cause of pancytopenia [4-6,8,9,20]. In the present study, megaloblastic anaemia was found to be the most common etiology 49% of pancytopenia patients, followed by hypersplenism (16%), aplastic anaemia (12%), acute leukaemia (11%), MDS (9%) and nutritional anaemia in 3% patients.

The incidence of megaloblastic anemia as an underlying cause of pancytopenia reported in the Western literature is quite variable ranges from 0.8% to 32.26% [6,18]. [Table/Fig-12] shows the comparison of this study from other studies [4-6,9,11,12,17,21-27]. In this study the incidence of megaloblastic anemia was much higher (49%) than the Western studies. This finding correlated well with the high incidence ranging from 44% to 74.04% reported by some studies from Indian subcontinent [5,6,12]. Peripheral smear

Author's name	Country	Year (of publication)	No. of cases	Most common cause	Second most common cause
Tilak V and Jain R [6]	India	1999	77	Megaloblastic anaemia (68%)	Aplastic anaemia (7.7%)
Savage DG et al., [21]	Zimbabwe	1999	134	Megaloblastic anaemia	Aplastic anaemia
Khodke K et al., [5]	India	2001	166	Hypoplastic anaemia (29.51%)	Megaloblastic anaemia (22.3%)
Naeem Khan M et al., [22]	Pakistan	2001	30	Aplastic anaemia (20%)	Megaloblastic anaemia (16.7%)
Kumar R et al., [4]	India	2001	166	Aplastic anaemia (29.5%)	Megaloblastic anaemia (22.3%)
Khunger JM et al., [27]	India	2002	100	Megaloblastic anaemia (72)	Aplastic anaemia (14)
Niazi M and Fazli-Raziq [23]	Pakistan	2004	89	Aplastic anaemia (38.3%)	Megaloblastic anaemia (27.7%)
Rahim F et al., [24]	Pakistan	2005	424	Megaloblastic anaemia (24.9%)	Aplastic anaemia (14.15%)
Memon S et al., [17]	Pakistan	2008	230	Aplastic anaemia (23.9%)	Megaloblastic anaemia (13.04%)
Jha A et al., [9]	Nepal	2008	148	Hypoplastic anaemia (29.5%)	Megaloblastic anaemia (23.64%)
Gupta V et al., [25]	India	2008	105	Aplastic anaemia (43%)	Acute leukaemia (25%)
Santra G and Das BK, [11]	India	2010	111	Aplastic anaemia (22.72%)	Hypersplenism (11.7%)
Gayathri BN and Rao KS, [12]	India	2011	104	Megaloblastic anaemia (74%)	Aplastic anaemia (18%)
Naseem S et al., [26]	India	2011	571	Aplastic anaemia (43%)	Megaloblastic anaemia (13.7%)
Present study	India	2020	100	Megaloblastic anaemia (49%)	Hypersplenism (16%)

[Table/Fig-12]: Comparison of the findings of this study with other studies [4-6, 9, 11, 17, 21-27].

of megaloblastic anemia from the present study is shown in [Table/Fig-13]. The increased incidence of megaloblastic anaemia in some Indian studies reflects the high prevalence of nutritional anaemia's in the Indian population [6]. India being a large country with varied geographical and economical status, the exact deficiency of folic acid and vitamin B12 is not identified as facilities for measuring folic acid and vitamin B12 levels are not routinely available in each and every part of country [4].



[Table/Fig-13]: Peripheral smear: (a) megaloblastic anaemia showing macrocytes, macro ovalocytes and hypersegmented neutrophil (Leishman's stain, 100x). Bone marrow aspiration smear; (b) showing hypercellular marrow (Leishman's stain 40x). Bone marrow; (c) shows preponderantly early megaloblasts with open chromatin. Intermediate and late megaloblast are fewer (Leishman's stain 100x).

Hypersplenism was the cause of pancytopenia in 16% of our cases with portal hypertension secondary to cirrhosis responsible for the hypersplenism in the majority of cases. This observation correlates well with the incidence of 11.4% incidence observed by an Indian study published in 2001, which also reported portal hypertension as the most common underlying cause [4].

The incidence of aplastic anaemia among pancytopenic patients ranges from 10% to 52.7%. Which is quite higher than reported from the Indian subcontinent (7.7% to 29.6%) [4,5,6,8,9,20]. The incidence of aplastic anemia in this study was 12%, which correlated well with the incidence observed by other studies reported from this part of world. Most of the cases of aplastic anaemia in the present study were idiopathic.

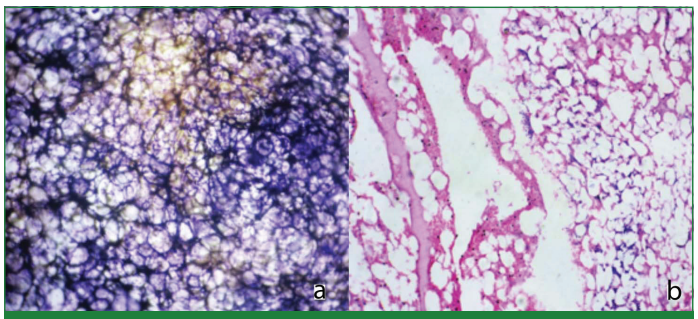
Acute leukaemia was responsible for pancytopenia in 11% of patients in this study, which is comparable to 12.04%, 19.6%, and 18.5% incidence of acute leukaemia reported by studies from India and Nepal [4,9]. In the present study, acute lymphoblastic leukaemia and acute myeloid leukaemia were the French-American-British (FAB) morphological type diagnosed in 63.6% and 36.4% of acute leukaemia patients, respectively. A study published by Bio Med Central (BMC) Haematology in 2013 shows that out of the seven cases in the leukaemia group, four were ALL, and three were AML [4,14,20,28]. In another study, done by Naseem S et al., pancytopenia was the most common cause of aplastic anaemia (33.8%) followed by acute leukaemia (26.6%) of which ALL is more common than AML [26].

MDS was the underlying cause of pancytopenia in 9% of patients in this study, which is comparable to the incidence observed by other studies. Jha A et al., revealed MDS as a cause of pancytopenia in 6.8% of patients, which is almost similar to our observation [9]. Hayat AS et al., also reported findings similar to Jha A et al. as they reported a 7% incidence of MDS as a cause of pancytopenia [3]. Similar to this study where iron deficiency was responsible for 3% of cases of pancytopenia, in their study Ishtiaq O et al., reported 5% of pancytopenia cases due to iron deficiency anaemia. Iron deficiency anaemia can be associated with pancytopenia [8]. Though iron deficiency is associated with a reactive thrombocytosis, increasing the severity of iron deficiency leads to normalisation and occasionally decrease platelet counts [29,27]. Haematological parameters and peripheral smear findings in different aetiology of pancytopenia.

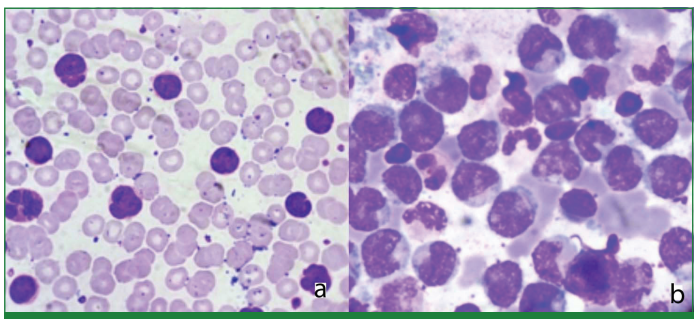
In this study, the overall haemoglobin percentage ranged from 1.5 gm to 10 gm, total leucocyte count ranged from 300-31000 cells/cumm, and platelet count ranged from 0-1,80,000 cells/cumm. In the major causes of pancytopenia, haematological parameters show overlap without any clue to the diagnosis. Similar results have been reported by other studies from the Indian subcontinent [4,9,12].

Bone Marrow Examination

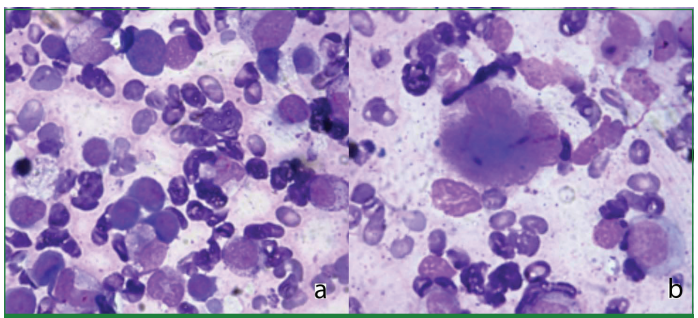
In megaloblastic anaemia, bone marrow was hypercellular in a majority with predominantly megaloblastic erythropoiesis. In patients with hypersplenism marrow was normocellular in over 80% of patients [Table/Fig-13]. In aplastic anaemia cellularity of bone marrow is significantly reduced. It may be hypocellular or acellular. Lymphocytes and plasma cells are prominent [Table/Fig-14]. Daniel NM and Byrd S, 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 [30]. In this 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 the replacement of marrow by fat cells. In acute leukaemia, bone marrow was hypercellular in most (81.7) of the patients. All cell lineage was decreased, and more than 80% blasts were seen in most of the patients [Table/Fig-15]. In most MDS cases, aspirate was hypercellular with erythroid hyperplasia, similar results were seen in studies by Juneja SK et al., and Kini J et al., [Table/Fig-16] [31,32].



[Table/Fig-14]: Aplastic anaemia: Bone marrow aspiration smear: (a) showing increase in fat cells with marked reduction in haemopoietic cells. (Leishman's stain- 10x). The biopsy of the marrow; (b) shows focal areas of cellu-larity. (H&E stain- 10x).



[Table/Fig-15]: Acute myeloid leukaemia: (a) Peripheral smear shows high leucocyte count with increased number of blast cells; (b) Bone marrow aspirate shows blasts with aure rods (arrow) and accompanying cells with maturation.



[Table/Fig-16]: Myelodysplastic syndrome: (a) Bone marrow aspirate smears show erythroid hyperplasia with features of dyserythropoiesis like cytoplasmic bridging and dysmyelopoiesis like bizarre shaped nuclei of band forms and myelocytes; (b) Bone marrow smear shows dysmegakaryopoiesis like multinucleate megakaryocyte.

Limitation(s)

Small sample size and single centre study might not represent true spectrum of pancytopenia. A multi-institutional study with large sample size is needed for more comprehensive analysis as certain aetiological factors such as nutritional anaemia might be common in certain geography.

CONCLUSION(S)

Pancytopenia is a commonly seen condition in clinical practice. The aetiological spectrum of pancytopenia is diverse. Majority of the studies from western countries as well as from Indian subcontinent; reported megaloblastic anemia, hypersplenism and aplastic anemia as causes of pancytopenia. The physical findings and peripheral blood examination are the usual first step in the evaluation of pancytopenia patients. However, peripheral blood picture shows considerable overlap in the common causes of pancytopenia, hence specific tests are needed to arrive at a confirmative diagnosis. Bone marrow aspiration is usually sufficient to make a diagnosis in cases of nutritional anaemias and initial diagnosis of leukaemia. However, aspiration is often unsuccessful and may yield a dry tap in patients with aplastic anaemia or myelofibrosis. Bone marrow trephine biopsy is essential for diagnosis in such conditions or when the aspiration is inconclusive.

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