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# Pancytopenia: A multidisciplinary assessment of hemato-etiological and clinical spectrum in a tertiary care hospital

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## Abstract

**Background**: The causes of pancytopenia range from simple, completely treatable diseases to serious life-threatening conditions. A thorough evaluation of these cases is mandatory as it would benefit the patients to receive appropriate treatment. **Objectives:** Evaluation of etio-hematological and clinical spectrum of pancytopenia. **Settings and Design:** A prospective study of two years (Jan 2016 -December 2017) was conducted on pancytopenic patients, attending Navodaya Medical College, Hospital and Research Centre, Raichur, Karnataka. **Material and Methods**: Etio- hematological and clinical evaluation was done considering the relevant biochemical and serological investigations. **Results:** A total number of 1368 of cases were diagnosed as pancytopenia. The patients' age ranged from 19 to 68 years and M: F ratio was 2.1:1. Most frequent clinical symptom was generalized weakness (90%) and least was bony pain (2%). Peripheral smear examination revealed predominantly macrocytic blood picture (47.9%). Bone marrow aspiration was performed in 444 cases (32.4%), among which Megaloblastic anaemia (Exclusive and Combined with iron deficiency anemia) was the commonest (52.7%). Etiologies of pancytopenia in decreasing order of frequency included Megaloblastic anemia {935 cases (68.4%) – Exclusive type (713 cases; 52.2%) and Combined with iron deficiency anemia (222 cases;16.2%)z, followed by Dengue fever (141 cases;10.3%), Hypoplastic/Aplastic anemia [106 cases;7.8% (Drug induced - 4 cases; 0.2%)], Septicemia (60 cases;4.5%), Leukemia (46 cases;3.25%), Chronic malaria (46 cases ;3.25%) and Myelodysplastic syndrome (34 cases; 2.5%). **Conclusion**: Keeping in mind varied etiologies of pancytopenia, thorough diagnostic evaluation is required to achieve better clinical outcome.

**Keywords:** Clinical spectrum, Etio-hematological profile, Pancytopenia, Serological and Biochemical investigations.
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## Introduction

Pancytopenia is an important commonly encountered hematological condition characterized by a triad of findings that results from a number of disease processes - primarily or secondarily involving the bone marrow leading to decrease in all three lineages of blood cells [1]. The underlying mechanisms other than decrease in hematopoietic cell production are marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective hematopoiesis, defective stem cell formation, antibody mediated sequestration, destruction and trapping of cells in an overactive reticuloendothelial system [2,3]. Etiologies of this condition can be due to common diseases like nutritional anemias, drug induced myelosuppression and infections such as malaria, kala azar or dengue, to

life threatening conditions like aplasia, myelodysplasias and leukemias [4]. The prevalence and risk factors vary in different geographical areas depending on life style, nutritional status and exposure to chemical or biological myelotoxins. A wide range of clinical and hematological manifestations are exhibited due to broad spectrum of etiologies of pancytopenia.

An early detection of underlying pathology helps in timely diagnosis and therapeutic intervention favoring a better clinical outcome [5,6]. Hence, this study was thus undertaken to evaluate cases of pancytopenia in Raichur, Karnataka state.

## Objectives

1. Evaluation of hemato-etiological and
2. Clinical spectrum of cases of pancytopenia

## Materials and Methods

**Place and type of study-** This prospective study of 2 years (January 2016-December 2017) comprised of 1368 cases of pancytopenia who attended Navodaya Medical College, Hospital & Research Centre, Raichur, Karnataka. A detailed analysis of hematological, different etiologies and clinical findings were done.

**Sampling methods and sample collection-** A thorough clinical history was taken along with general and systemic examination of patients. Various hemato-logical and serological parameters were analyzed and are as follows:

i) Hematology- Using semi automated hematology analyzer Pentra ES 60, CBC (Hb%, red cell indices, total and differential leucocyte count, platelet count) along with grading of anemia, leucopenia and thrombocytopenia was done, while peripheral smear study by Leishman stained blood smears. Features observed in the latter were: RBC-Anisopoikilocytosis, nucleated RBCs and morphological type of anemia; WBC - Hypersegmented neutrophils, toxic granulation, relative lymphocytosis and immature cells/ blasts; Platelets- Normal, small & giant forms and Screening for hemoparasites. Reticulocyte count was estimated on New Methylene Blue stained smears. Bone marrow aspiration was performed wherever feasible after obtaining written consent from the patients. The procedure was done using Salah's needle, the aspirate obtained was spread on the glass slides which were subsequently stained by Leishman's & Giemsa stain

and observed for cellularity, myeloid: erythroid (M:E) ratio, erythropoiesis, myelopoiesis, megakaryopoiesis, lymphocytes, plasma cells, bacteria/parasites/ fungal elements, blast cells and other infiltrative disorders. Blasts were categorised as per WHO and FAB classification criteria. Special stains with Myelo-peroxidase (MPO) and Periodic acid Schiff reagent (PAS) were done on peripheral smears & bone marrow smears, wherever required.

ii) Relevant biochemical investigations included serum iron, ferritin, Vitamin B12 & folate studies and c-reactive protein (CRP).

iii) Serological tests with Rapid Card Malaria test and Dengue card test (NS1, IgM and IgG) were performed in suspected cases.

### Inclusion criteria

Patients between 18-70 years of age whose hemoglobin values recorded < 12 gm/dl (in males) and < 11 gm/dl (in females) respectively, total leucocyte count < 4000/mm$^3$ and platelet count < 1.5 lakh/mm$^3$ (As per WHO guidelines).

### Exclusion criteria

1. Patients <18 years and > 70 years of age.
2. Those cases who received whole blood or component therapy.
3. Patients on chemotherapy or radiotherapy.

## Results

A total number of 1368 of cases were diagnosed as pancytopenia. Age of cases ranged from 19 to 68 years, maximum (74%) were in 41-50 years age group, males (68%) outnumbered females (32%) and M: F ratio was 2.1:1.

Among clinical features, generalized weakness (1231 cases; 90%) was most common, while bony pain (27 cases; 2%) was least common (Refer table 1).

**Table-1: Overall distribution of clinical features in pancytopenic cases.**

| Clinical Features | No. of cases | Percentage (%) |
|---|---|---|
| Generalized weakness | 1231 | 90 |
| Pallor | 903 | 66 |
| Dyspnoea | 684 | 50 |
| Fever | 300 | 22 |
| Bleeding Manifestations | 82 | 6 |
| Jaundice | 68 | 5 |
| Splenomegaly | 287 | 21 |
| Hepatomegaly | 123 | 9 |
| Lymphadenopathy | 41 | 3 |
| Bony Pain | 27 | 2 |

Hematological findings: i) Hemoglobin values varied from 2.6 to 8.4 gm%, mean corpuscular volume (MCV) from 48.2 to 110.5 fl, mean corpuscular hemoglobin (MCH) from 14 to 35.2 pg/ml and mean corpuscular hemoglobin concentration (MCHC) from 0.5 to 46 gm/dl. Leucocyte count ranged from 500 to 3600/ mm$^3$, while platelet count from 12,000 to 1,20,000/mm$^3$. Range of blood cell parameters observed is illustrated in table 2.

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**Table-2: Distribution of hematological parameters.**

| Parameters | Range | Present study |
|---|---|---|
| Hemoglobin (gm %) | 1.5- 5 | 246 (18%) |
| | 5-8 | 958 (70%) |
| | >8 | 164 (12%) |
| Total leucocyte count (cells/mm3 ) | 500-1000 | 109 (8%) |
| | 1001-2500 | 533 (39%) |
| | 2501-3900 | 725 (53%) |
| Platelet count(cells/mm3) | 10k-50k | 259 (19%) |
| | 50k-1lakh | 656 (48%) |
| | 1lakh-1.5 lakh | 451 (33%) |

ii) On peripheral smear examination, varying degree of anisopoikilocytosis was observed, predominantly tear drop cells followed by target cells, schistocytes, microspherocytes and few cases (6.3%) showed nucleated RBCs. Morphologically, macrocytic anemia (656 cases; 47.9%) was commonest (Fig 1), followed by dimorphic (478 cases; 34.9%), microcytic hypochromic (179 cases;13.1%) and normocytic normochromic (55 cases; 4.1%) blood picture (Fig 2). Hypersegmented neutrophils were seen in 586 cases (42.8%), toxic granulation in 80 cases (5.8%) and relative lymphocytosis was noted in 309 cases (22.6%). Few patients (46 cases; 3.3%) showed blasts of either myeloid or lymphoid lineage. Ratio of platelet morphologies where, giant: small: normal was noted as 2.3:1:9.6. Hemoparasites were seen in 46 cases out of 1368 cases (2.7%), where Plasmodium falciparum (36 cases; 78.2%) was more frequent (Fig 4) compared to Plasmodium vivax (10 cases; 21.8%).

iii) Reticulocyte count was normal in 48%, increased in 32% and decreased in 20% of cases.

iv) Bone marrow aspiration was performed in 444 cases ; those with hypercellularity (316 cases; 71.2%) was most common, followed by hypocellular (105 cases; 23.6%) and normocellular marrow (23 cases; 5.2%).
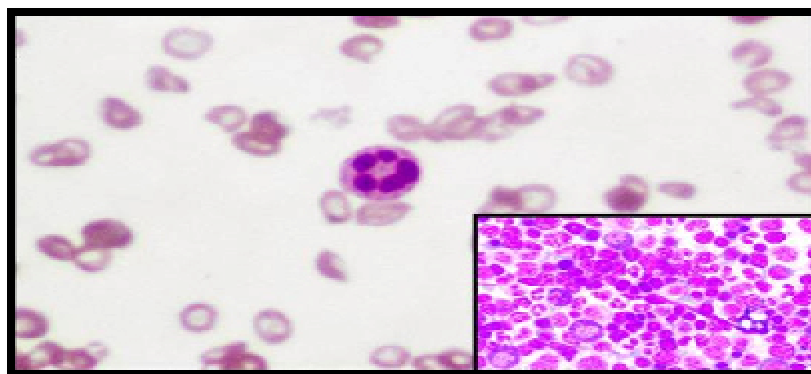


**Fig-1:** Peripheral smear showing macrocytic blood picture with segmented neutrophil (5 lobes) (Leishman's stain x400), with inset of bone marrow aspiration showing megaloblastic erythropoiesis (Leishman's stain x400).
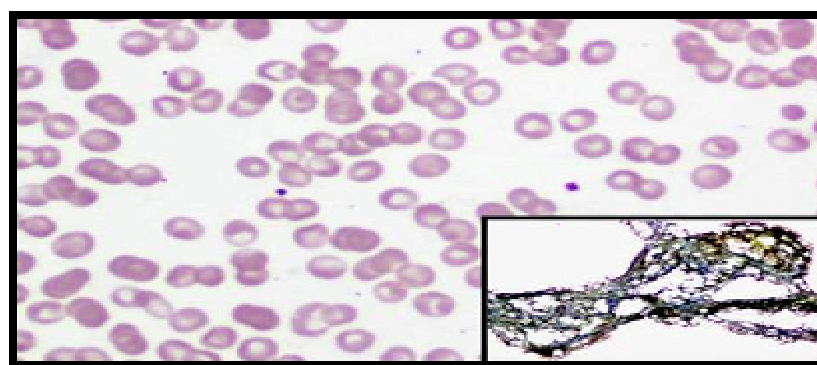


**Fig-2:** Peripheral smear showing normocytic normochromic blood picture ( Leishman's stain x400) with inset of bone marrow aspiration showing aplastic marrow with increased fat (Leishman's stain x400).

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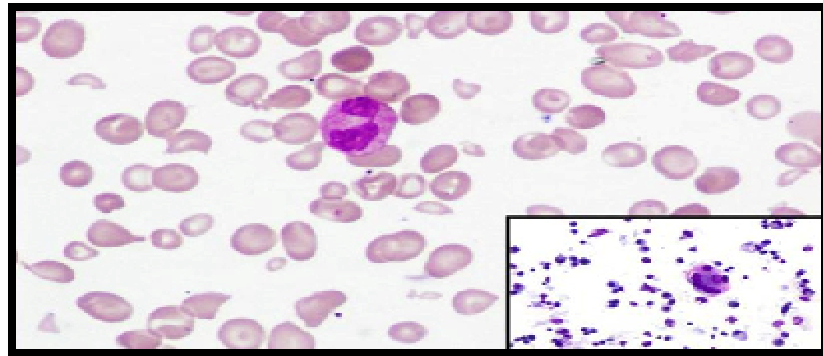


**Fig-3:** Peripheral smear showing Pelger Huet anomaly (Leishman's stain x 400),
with inset of bone marrow aspiration showing dysmyelopoiesis (Leishman's stain x400).



**Fig-4:** Peripheral smear showing gametocyte form of Plasmodium falciparum
(Leishman's stain x400) with inset showing schizont forms of Plasmodium vivax (Leishman's stain x400).

Among the morphological categories of marrow, exclusive megaloblastic erythropoiesis (152 cases; 34.2%) was most frequent (Fig 1), followed by aplasia (105 cases; 23.6%) (Fig 2), combined megaloblastic and micronormoblastic erythroid hyperplasia (82 cases; 18.5%), leukemia (46 cases; 10.4%), myelodysplasia (35 cases; 7.9%) (Fig 3) and normoblastic erythropoiesis (24 cases; 5.4%). No hemoparasites/ granulomas /parasites /fungal elements were noted. The most common etiology was megaloblastic anemia [935 cases; 68.4% - exclusive (713 cases; 52.2%) and combined with iron deficiency anemia (222 cases; 16.2%)], while the least common cause was myelodysplastic syndrome (MDS- 34 cases; 2.5%) (Refer table 3).

**Table-3: Distribution of spectrum of etiologies of pancytopenic cases.**

| Etiologies | No of cases | Percentage (%) |
|---|---|---|
| Megaloblastic anaemia (with and without micronormoblastic erythroid hyperplasia) | 935 | 68.4 |
| Dengue fever | 141 | 10.3 |
| Hypoplastic/Aplastic anaemia | 106 | 7.8 |
| Leukemia | 46 | 3.2 |
| Myelodysplastic syndrome | 34 | 2.5 |
| Septicemia | 60 | 4.5 |
| Malaria | 46 | 3.2 |
| Others | - | - |

Four cases were drug induced where two patients diagnosed as rheumatoid arthritis were on gold treatment, one with bronchial asthma and one with SLE were on steroid therapy. Out of total leukemic cases, 38 were AML M2 (82.6%) and 8 were ALL L1 (17.4%). All etiological categories presented with symptoms like generalised weakness, pallor, dyspnoea and fever, while petechiae was noted in cases with dengue and leukemia. Patients with malaria, dengue and drug induced

aplastic anemia presented with jaundice; whereas two cases of leukemia (AML M2) had bony tenderness. Clinically, splenomegaly was observed in 425 cases (45.5%) of megaloblastic anemia, 30 cases of malaria (65.2%), 24 cases of leukemia (52.2%) and 20 cases of MDS (58.8%); whereas hepatomegaly was more predominant in leukemia (26.1%), followed by MDS (23.5%) and megaloblastic anemia (22.2%). Lymphadenopathy was present in 56 cases (5.9%) of megaloblastic anemia, all the 28 cases (100%) of aplastic anemia and 10 cases (21.7%) of leukemia respectively.

Hematological variations in different etiological groups:

i) CBC: Majority of cases showed moderate anemia (70%), followed by severe (18%) and mild degree (12%). Cases with high MCV values were more common (60%) in this study and belonged to nutritional anemia category, followed by low values (22%) which were observed in malaria and septicemia; while normal range was noted in rest of the cases (18%). MCH and MCHC were variably low among all cases. Majority of cases had mild leucopenia (53%), followed by moderate (39%) and severe (8%). Patients with moderate thrombocytopenia (48%) were more common followed by mild (33%) and severe degree (19%).

ii) Peripheral smear: Anisopoikilocytosis was most commonly seen in cases of megaloblastic anemia (76%) compared to aplastic anemia (10%), leukemia (4%) and MDS (2%). Microcytes, schistocytes and target cells were observed mainly in cases of septicemia (5%) and rarely in patients with malaria and MDS (2% each). Presence of nucleated RBCs was mostly observed in MDS (20%), followed by malaria (11%), megaloblastic anemia combined with iron deficiency anemia (8%) and leukemia [AML M2 (1%)].

The toxic granulation in neutrophils and shift to left in myeloid series were noted in septicemia cases (65%), and hypersegmented neutrophils were observed in cases with megaloblastic anemia (62%). Presence of blasts was predominant in leukemia (46 cases; 57.5%) compared to MDS (34 cases; 42.5%). Immature lymphoid cells were most commonly found in cases of aplastic anemia (95%), followed by megaloblastic anemia (22%) and MDS (12%). Peripheral smear study showed classical features of blasts of respective leukemia and were confirmed using special stains. Giant forms of platelets were mostly seen in patients with nutritional anemia (25%), compared to septicemia (8%) and dengue cases (6%), while smaller forms were observed in aplastic anemia and rest other cases showed normal platelets.

iii) Reticulocyte count: Increased count was observed in malaria, nutritional anemia and septicemic cases, whereas those with aplastic anemia and MDS showed reduced reticulocyte count.

iv) Bone marrow study: Varying degrees of dysmyelopoiesis was observed and was most predominant in MDS (98%) followed by megaloblastic anemia (86%).

## Discussion

The demographic pattern of pancytopenia varies all over the world possibly due to the differences in methodology, stringent diagnostic criteria, duration of study, geographic distribution, genetic differences, age distribution, nutritional status, infections and exposure to myelotoxic agents [7].

In present study, maximum cases of pancytopenia (74%) were observed in 41-50 years age group, which corroborated with the study of Shane et al (30 -55 years; 70%), while Anita Javalgi et al documented higher proportion in 15-25 years (39.6%) [6,8]. M:F ratio of this study (2.1:1) was in accordance with Lakey et al (2.6:1), while there was decline in the ratio in the studies conducted by Gayatri et al (1.2:1) and Anita Javalgi et al (1.35:1) [4,6,9]. Majority of the cases presented with weakness/ fatigue (90%) followed by pallor (66%) and dyspnoea (50%), while a small proportion of patients had bleeding manifestations (6%). Symptoms attributable to anemia or thrombocytopenia were more common in this study than those due to leucopenia. Similar observation was documented by Anita Javalgi et al [6]. Presentation of organomegaly {splenomegaly (21%), hepatomegaly (9%) and lymphadenopathy (3%)} and bony tenderness (2%) was comparable to those of Gayatri et al, Khunger et al, Khodke et al and Anita et al [4,5,6,10].

### Hematology

i) CBC- The variations in hemoglobin value, leucocyte count and platelet count in this study were comparable to other authors' studies (Refer table 4).

**Table-4: Comparison of blood cell parameters.**

| Parameters | Range | Anita Javalgi et al [6] (2013) | GPK Reddy et al [11] (2016) | Present study |
|---|---|---|---|---|
| Hemoglobin (gm %) | 1.5- 5 | 32(30.18%) | 17(40.5%) | 246 (18%) |
| | 5-8 | 58(54.71%) | 14(38.1%) | 958 (70%) |
| | >8 | 16(15.09%) | 9 (21.4%) | 164 (12%) |
| Total leucocyte count (cells/mm3) | 500-1000 | 5(4.71%) | 3(7.1%) | 109 (8%) |
| | 1001-2500 | 23(21.69%) | 22(52.4%) | 533 (39%) |
| | 2501-3900 | 78(7.58%) | 17(40.5%) | 725 ( 53%) |
| Platelet count (cells/mm3) | 10k-50k | 27(25.47%) | 22(52.4%) | 259 (19%) |
| | 50k-1lac | 35(33.08%) | 9(21.4%) | 656 (48%) |
| | 1lac-1.5 lac | 44(41.50%) | 11(26.2%) | 451 (33%) |

The variations in the red cell indices (MCV, MCH and MCHC) were in accordance with the study of Nazish Shinwari et al [12].

ii) Peripheal smear findings: Anisopoikilocytosis was observed commonly in cases of megaloblastic anemia (76%), followed by hypoplastic/aplastic anemia (10%), leukemia (5%) and MDS (1%). Similar findings were noted by Gayatri et al and Khunger et al [4, 10] (Refer table 5). Among the peripheral smear findings, macrocytic (48%) was the commonest which was in accordance with Sweta et al (49%), whereas Gayatri et al reported dimorphic anemia (37.5%) as predominant type [4,13]. The least common blood picture was normocytic normochromic (4%) in this study, while Sweta et al documented dimorphic blood picture as the lowest proportion (9%) [13]. Nucleated RBCs were predominantly seen in cases of MDS followed by malaria in present study, while Khunger et al and Gayatri et al noted them mostly in MDS and leukemic cases [4, 10]. Hypersegmented neutrophils were observed in 46.6% of total cases, whereas Tilak et al documented them in 84.9% of cases, on the contrary Khunger et al didn't document in any case of pancytopenia [10,14].

Immature WBCs were more commonly seen in cases diagnosed with leukemia, followed by MDS and megaloblastic anemia which was comparable to the studies of Khunger et al and Gayatri et al [4, 10]. Majority of cases of hypoplastic / aplastic anemia (95%) had relative lymphocytosis whereas Tilak et al and Khunger et al reported lower percentage (50% and 85.71%)[10, 14]. There are limited number of studies in literature regarding platelet morphology in cases of pancytopenia. Hemoparasite induced pancytopenia was documented in 46 cases (3.25%), where all were diagnosed as malaria – i) On peripheral smear examination in 38 cases, among which gametocytes of P. falciparum were detected in 28 cases while gametocyte, trophozoite and schizont forms of P. Vivax in 10 cases and ii) By Rapid card test in 8 cases which included P. falciparum in 5 cases and P. vivax in 3 cases. Similar study by Gayatri et al documented malaria in 1.9% of cases and noted gametocytes of P. falciparum on peripheral smear examination, while Anita Javalgi et al observed the same in 3.7% of cases on both peripheral smear and BMA smears; whereas Tilak et al reported malaria in 3.8% and kala azar in 2.5% of cases in their study [4, 6, 14]. The peripheral smear findings with respect to etiologies were comparable with other studies [4, 10] (Refer table 5).

**Table-5: Comparison of peripheral smear findings of varied etiologies.**

**Study groups: (1) Khunger et al [10] (2002), (2) Gayatri et al [4] (2011), (3) Present study (2016-2017).**

| Etiologies | Anisopoikilocytosis | | | Nucleated RBC | | | Hypersegmented Neutrophils | | | Immature WBC | | | Relative Lymphocytosis | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| Megal. A | 97.2% | 88.3% | 76% | 12.5% | - | 8% | - | 49.3% | 62% | 12.5% | 25.7% | 6% | 97.2% | 7.8% | 22% |
| Aplastic A | 0.07% | 89.4% | 10% | - | - | - | - | 26.3% | 1% | - | - | - | 85.7% | 52.6% | 95% |
| MDS | - | - | 1% | 50% | - | 20% | 25% | - | - | 75% | - | 15% | - | - | 12% |
| Leukemia | 0.1% | 25% | 5% | 40% | 25% | 1% | 40% | - | 12% | 100% | 50% | 75% | - | - | - |
| Malaria | - | 100% | - | - | - | 11% | - | - | - | - | - | - | - | - | - |

iii) Cases with normal Reticulocyte count (650 cases; 47.5%) was more common in this study, compared to those with higher (436 cases; 31.9%) and lower values (282 cases; 20.6%), which corroborated with study by Gayatri et al who also documented predominantly normal values (82 cases; 77.4%) followed by lower values (24 cases; 22.6%) [4].

iv) Bone marrow: Pancytopenia may be either due to cellular or hypocellular marrow, thus mandating the exploration of various etiologies. Out of the cases in which bone marrow aspiration was performed, cases with **h**ypercellularity was more common (**71.2**%) followed by hypocellularity (**23.6**%) and normocellularity (**5.2**%). This was comparable to Anita et al, who documented hypercellular in 68.8%, hypocellular in 16.2% and normocellular marrow in 15% of cases **[6].**

The morphological features of bone marrow were comparable with other studies. (Refer Table 6).

**Table-6: Comparison of marrow morphological categories.**

| Marrow picture | Lakey et al [9] (2010) | Verma N et al [15] (2012) | Present study |
|---|---|---|---|
| 1. Normocellular/ Normoblastic erythroid hyperplasia | 18.5% | 18.1% | 5.4% |
| 2. Micronormoblastic and Megaloblastic erythroid hyperplasia | - | - | 18.5% |
| 3. Megaloblastic erythroid hyperplasia | 24.2% | 40.2% | 34.2% |
| 4. Leukemia | 20.3% | - | 10.4% |
| 5. Myelodysplasia | 7.4% | 9.7% | 7.9% |
| 6. Hypoplastic/aplastic anemia | 29.6% | 26.3% | 23.6% |
| 7. Plasmacytosis | - | 2.7% | - |
| 8. Myelofibrosis | - | 2.7% | - |

Results of biochemical and serological tests were in accordance with similar study by GPK Reddy et al [11].

**Etiologies**

**Table-7: Comparative study showing distribution of etiologies**

| Etiologies | Khunger et al [10] (2002) | Gayatri et al [4] (2011) | Shinwari et al [12] (2012) | Reddy GP et al [11] ( 2016 ) | Present study |
|---|---|---|---|---|---|
| Megaloblastic anaemia (with and without micronormoblastic erythroid hyperplasia) | 72 | 74 | 27 | 38.1 | 68.4 |
| Dengue fever | - | - | - | - | 10.3 |
| Aplastic anaemia | 14 | 18 | 21 | 26.2 | 7.8 |
| Leukemia | 5 | 3.5 | 23 | 9.5 | 3.2 |
| Myelodysplastic syndrome | 2 | 3.5 | 1 | - | 2.5 |
| Septicemia | - | - | 2 | 2.4 | 4.5 |
| Malaria | 1 | 1.7 | - | 7.1 | 3.2 |
| Others | 6 | - | 26 | 16.7 | - |

The incidence of megaloblastic anemia in pancytopenic patients varies in literature from 0.8% to 32.26% **[10].** Megaloblastic anaemia was observed to be the commonest cause of pancytopenia (68.4%), which is in accordance with similar studies by Khunger et al (72%), Tilak et al (64%) and Gayatri et al (74%) **[4,10,14].** Among these cases, exclusive category was more common (52.2%) when compared to those **combined with iron deficiency anemia (16.2% ). In a similar study by** Nazish Shinwari et al, megaloblastic anemia was documented in 27% of total cases where exclusive (20%) was predominant followed by combined category (7%) **[12].** Hence there should be a periodical assessment to diagnose the nutritional anemias considering the diverse ethnic populations, different dietary habits and social customs in India **[6, 10]. T**he second common etiological group was dengue (10.3%). This was in contrast to other studies which documented aplastic anemia (Refer table 5). The higher incidence of dengue in this region was likely due to lower socioeconomic status, poor sanitation, lack of awareness about the spectrum of clinical manifestations and increasing frequency of vague & non-specific symptoms.

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The **incidence of** aplastic/ hypoplastic anemia **according to the literature varies from 10% to 52.7%** [4,11]. The present study reported the same as the third common cause (7.7%), whereas Gayatri et al (18.26%) and Khunger et al (14%) reported as second common etiology [4, 10]. Aplastic/ hypoplastic anemia may be due to triggering of aberrant immune response by viral infections, exposure to chemicals and drugs or endogenous antigens generated by genetically altered bone marrow cells, leading to active destruction of blood forming cells by lymphocytes [7,10]. Drug induced aplastic anemia is commonly seen in cases receiving therapy for rheumatoid arthritis, hyperthyroid conditions, tuberculosis, convulsive disorders and various inflammatory disorders. The outcome depends on:

i) Dose and duration of exposure and
ii) Susceptibility or idiosyncracy to the myelotoxin.

These usually cause mild reversible marrow suppression, but may occasionally progress to more severe damage [16]. Present study reported four cases of drug induced aplastic anemia accounting to 0.2% of total cases, among which two were on gold and two on steroid therapies; while Tilak et al also documented four such cases in 5.1% of pancytopenic patients among which, three were on chloramphenicol and one on streptomycin. Verma Nidhi et al reported three cases accounting to 4.2% and all were on chloramphenicol [14, 15].

Next common cause included leukemia which comprised of 46 cases, where 38 were AML M2 and 8 were ALL L1; whereas Gayatri et al reported 4 cases where three were AML M2 and one was ALL L2 [4].

The least common etiologies were septicemia (4.5%), malaria (3.25%) and MDS (2.5%); while Reddy P et al documented septicemia in 2.4% and malaria in 7.1% of cases, respectively [11]. The incidence of malaria in other studies were : Khunger JM et al - 1%; Tilak V et al -3.9% and Kumar R et al - 3% respectively [3,10,14]. MDS in this study was detected in thirty four cases (2.5%) which was similar to Khunger et al (2%), whereas Anita et al documented the same in 0.9% of total cases [6,10].

The clinical features of pancytopenic cases considerably varied according to the spectrum of different etiologies. However, cases presenting with organomegaly and lymphadenopathy were comparable with the studies of Khunger et al and Gayatri et al [4, 10].

Clinical findings as per etiologies were compared. In cases of megaloblastic anemia, splenomegaly was more predominant in this study (45.4%) compared to Khunger et al (28.5%) and Gayatri et al (27.7%), while hepatomegaly (22.2%) was in accordance with the said authors' studies (29.1% and 29.8%) and lymphadenopathy was more common in present study (5.9%) compared to Khunger et al (0.6%) and Gayatri et al (3.8%) [4, 9].

The present study had no organomegaly in cases of aplastic anemia, whereas Gayatri et al documented both splenomegaly (21%) and hepatomegaly (15.7%), while Khunger et al documented only hepatomegaly (3.5%). Lymphadenopathy in this study was more common (26.4%) compared to Gayatri et al (5.2%).

In cases diagnosed as leukemia, Khunger et al documented higher incidence of splenomegaly (80%) and hepatomegaly (100%) compared to the present study (52.1%; 25%) and Gayatri et al (25%; 25%). Lymphadenopathy was observed more commonly in the study by Khunger et al (60%) compared to present study (21.7%).

The cases of MDS showed splenomegaly and hepatomegaly more frequently in the study of Khunger et al (75%; 50%) when compared to present study (58.8%; 23.5%). Lymphadenopathy was not seen in this study as well as the authors' studies.

Cases of malaria had splenomegaly more commonly in the studies of Khunger et al (100%) and Gayatri et al (100%) compared to this study (65.2%), whereas hepatomegaly and lymphadenopathy was not seen in either of the said studies [4,9].

Among the frequent etiologies of pancytopenia in the world scenario, aplastic anemia is documented to be the commonest especially in countries like Israel, Europe, Bangladesh and India. Myelodysplastic syndrome and neoplastic diseases are the next common ones in Israel & Europe, chronic malaria and kala azar in Bangladesh; while on the contrary, it was megaloblastic anemia in India [5].

## Conclusion

Keeping in mind the probable etiologies and large proportion of pancytopenia being reversible, a **thorough evaluation** is warranted **to identify the** underlying pathology **at the earliest, thus** guiding the clinicians to **implement preventive strategies and help the patients in achieving** better clinical outcome.

### Contribution Details

| Names of Authors | Study Concept | Design | Acquisition of data | Analysis & Interpretiation of data | Compiled literature sources | Drafting the manuscript | Checked References | Critical Revision |
|---|---|---|---|---|---|---|---|---|
| Dr. Trupti V Katti | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Dr. A.S. Anand | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Dr. Tejeshwini Patil | - | ✓ | ✓ | - | - | - | ✓ | ✓ |
| Dr. Sangeeta Seshagiri | - | - | - | - | ✓ | - | ✓ | - |

**What this study add to existing knowledge-** Based on assimilation of data from previous studies and current research, there exists an overlap of certain clinico-hematological findings. As etiological spectrum of pancytopenia is varied and confounds the pathologists and clinicians, routine along with bone marrow and etiological based laboratory evaluation is warranted. The frequency of this hematological condition Pancytopenia, is on the rise and hence needs global attention.

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