Original Research Article

A Study on evaluation of Pancytopenia in a Teaching Hospital

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Abstract

Background: Pancytopenia is not a single disease entity,but it is a triad of findings that may result from a number of disease processes-primarily or secondarily involving the bone marrow. The presenting symptoms are usually attributable to anemia, leucopenia and/or thrombocytopenia.**Aim of the study:** To study clinical, hematological and biochemical profile of patients with pancytopenia.**Materials and Methods:**This was a prospective cross-sectional study done in the department of General Medicine for a duration of six months at Maheshwara Medical College, Patancheru, Telangana.**Results:** A total of 60 cases were studied. The patient age range was 18 years to 70 years and the male to female ratio was 1:1.06. In this study, vitamin B12 deficiency anemia was the most common disorder diagnosed clinically in 56.6% followed by dengue in 16.6% cases, Malaria in about 15%, Aplastic anemia,Hepatitis B and acute leukaemia in 3.3% each.MDS was seen in 1.6% cases.**Conclusion:** Severe pancytopenia has significant relation with the clinical outcome and can be used as a prognostic indicator.The present study concludes that detailed primary hematological investigations, the physical findings and peripheral blood picture provides precious information in the workup of patients with pancytopenia.

Keywords: Pancytopenia, Vitamin B12 deficiency anemia, Bone marrow examination

Introduction

Cytopenia is a reduction in the number in any of the three types of peripheral blood cells. A reduction in all three types of cellular components is termed as PANCYTOPENIA and this involves anaemia,leucopenia, and thrombocytopenia. Initially, mild impairment in marrow function may go undetected and pancytopenia may become apparent only during times of stress or increased demand like bleeding or infections.[1]

Pancytopenia is not a disease entity,but it is a triad of findings that may result from a number of disease processes-primarily or secondarily involving the bone marrow. The presenting symptoms are usually attributable to anemia, leucopenia or thrombo-cytopenia.[2]

The clinical symptoms of the patient can either be due to pancytopenia as such or due to the underlying cause. Pancytopenia cnnbe suspected on clinical grounds when a patient presents with pallor, prolonged fever and a tendency to bleed but the common presenting symptoms are usually due to anaemia and thrombocytopenia.[3] Pancytopenia is a common hematological problem. It has an extensive differential diagnosis and it can result from damage to bone marrow as proved by low reticulocyte count, or increased destruction of preformed blood cells peripherally with increased reticulocyte count.[2] Many severe and lethal illnesses ranging from drug induced bone marrow hypoplasia, megaloblastic anemia to fatal bone marrow aplasia and leukemias present with pancytopenia.[4]Bone marrow examination is extremely helpful in evaluation of pancytopenia. Bone Marrow Aspiration Cytology (BMA), Touch Imprint Cytology (BMI) and Trephine Biopsy (BMB) are the three main basic preparations for bone marrow evaluation. Marrow aspiration is assessed for cytology, and trephine biopsy provides overall cellularity, detection of focal lesion and infiltration. The severity of pancytopenia and underlying pathology determines the management and prognosis of patients.[5]

Pancytopenia can have various etiologies such as common diseases like nutritional anemias, drug induced myelosuppression, infections such as malaria, kalaazar or dengue, to life threatening conditions like aplasia, myelodysplasias and leukemias.[6] An early detection of underlying pathology helps in timely diagnosis and therapeutic intervention favoring a better clinical outcome.[7] Physical findings and peripheral blood picture providevaluable information in the workup of pancytopenic patients and help in planning investigations on bone marrow samples. [8] Bone marrow evaluation is a very important diagnostic procedure and provides confirmation for the etiology of suspected pancytopenia. [9]

Aim of the Study

To study clinical, hematological and biochemical profile of patients with pancytopenia.

Objectives of the study are:

- To study various clinical presentations in patients with pancytopenia.
- To evaluate causes of Pancytopenia in different patients and correlate it with the clinical presentation.
- To study hematological and biochemical profile in pancytopenia and its correlation with the cause of pancytopenia and the clinical presentation.

Materials and Methods

This was a prospective cross-sectional study done in the department of General Medicine for a duration of six months from November 2020 to April 2021 at Maheshwara Medical College, Patancheru, Telangana.The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from the all the cases included in the study. A total of sixty cases were studied.

Inclusion criteria:

- Patients willing to participate in the study.
- Age group range 18 years to 70 years.

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- Patients with pancytopenia.
- Hemoglobin less than 13.3 g/dl in males or 11.5 g/dl in females.
- Total leukocyte counts less than 4×10^9 /L.
- Platelet count less than 150×10^9 /L.

Exclusion criteria:

- Patients not willing to participate in the study.
- Age less than 18 years and more than 70 years.
- Pregnant and lactating women.
- Patients receiving chemotherapy for malignant tumors.

Diagnostic criteriafor Pancytopenia [10]

- Hemoglobin level less than 13.3 g/dl in males or 11.5 g/dl in females.
- Total leukocyte counts less than 4×10^9 /L.
- Platelets count less than 150×10^9 /L

Method Of Collection Of Data: Patients with pancytopenia attending General Medicine OPD and those admitted in the wards of Department of Medicine were included in the study. Cases were selected as per inclusion criteria. The study protocol was explained to the patients. Thorough clinical history was taken including age, gender, history of present illness, past history, family history and personal history including smoking, alcohol and drug history.

History suggestive of previous pancytopenia, aplastic anaemia, inherited bone marrow failure syndrome, repeated early foetal loss, cancer, liver disease, metabolic disorders, or connective tissue disorders were also noted in proforma. The patients were evaluated by thorough physical examination. Systolic and diastolic BP were measured in all of the subjects.Weight and height were measured by standard techniques. Body mass index (BMI) was calculated. All the patients were assessed for pallor, jaundice, clubbing of fingers, lymphadenopathy and splenomegaly (underlying infection, infectious mononucleosis, lymphoproliferative disorders and malignancy).

The investigations were done in the department of Pathology, Biochemistry and Microbiology of the hospital and included complete blood count (CBC) and detailed peripheral smear examination. Reticulocyte count was estimated on supravital stain (New methylene blue). Hematology slides were reported by senior pathologist and observed for

RBC- Anisopoikilocytosis, nucleated RBCs and morphological type of anemia.

WBC- Hypersegmented neutrophils, toxic granulation, relative lymphocytosis and immature cells/ blasts.

Platelets- Adequacy.

Screened for hemoparasites.

Bone marrow procedures were explained to the patients, written consent was obtained for the same and then the procedures were performed.

Statistical data analysis: Data was analysed by using IBM SPSS 20.0 version software. Results are depicted in tables and graphs.

Observations And Results

A total of 60 cases with pancytopenia were studied.

Age and gender distribution of the cases: The age of the patients ranged from 18 years to 70 years and the male to female ratio was almost equal at 1:1.06.

Majority of the cases were among 18-30 years i.e, 43.3% (26/60), followed by 31- 40 years which constituted 23.3% (14/60), 16.6% (10/60) were noted among 41-50 years age group and 11.6 % (07/60) among 51-60 years. Least were noted among 61-70 years i.e5% (03/60).In this study females i.e, 51.6% (31/60) were slightly more than males i.e,48.3% (29/60), with male to female ratio of 1:1.06.

Distribution of cases based on clinical symptoms: Generalized weakness was present in 36 (60%) cases, fever was present in 5 (8.3%) cases, fever with chills and rigors was present in 10 (16.6%) cases, abdominal distension was present in 3 (5%) cases and bleeding diathesis was present in 6 (10%) cases.

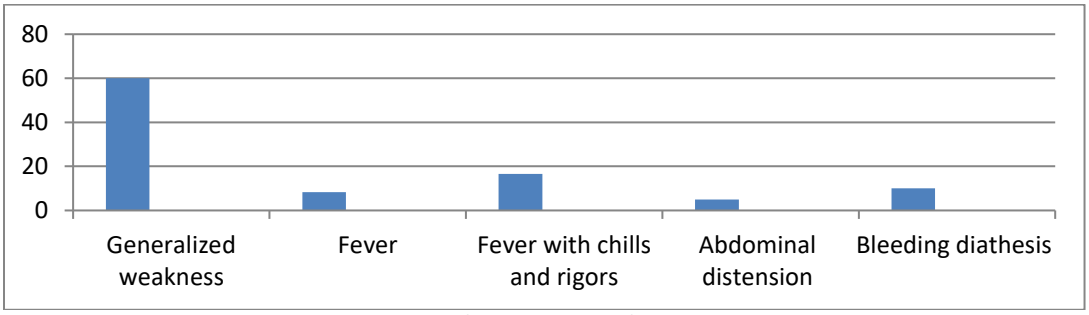

Fig 1: Clinical features in cases of pancytopenia

Table 1: Distribution of cases based on clinical signs

Signs	No. of cases	Percentage (%)
Pallor	32	53.3%
Pallor+ Splenomegaly	20	33.3%
Splenomegaly	06	10%
Hepatomegaly	02	3.3%
Total	60	100%

Pallor was the most common finding seen in the patients.

Table 2:Distribution of cases based on clinical diagnosis

Clinical diagnosis	No. of cases	Percentage (%)
Vitamin B12 deficiency anemia	34	56.6%
Hepatitis B	02	3.3%
Malaria	09	15%
Aplastic anemia	02	3.3%
Acute leukemia	02	3.3%
Dengue	10	16.6%
Myelodysplastic syndrome	01	1.6%
Total	60	100%

In this study, vitamin B12 deficiency anemia was most common disorder diagnosed clinically and was seen in 56.6% (34/60) cases.

Distribution of cases based on hemoglobin level: In this study, Severe anemia (<6g/dl) was seen in 36.6% (22/60) cases, Moderate anemia with hemoglobin level of 6.0-8.9 gm/dl was seen in 53.3% (32/60) cases and Mild anemia with hemoglobin level of 9-11 g/dl was seen in 10% (06/60)cases.

Table 3:Distribution based on peripheral smear diagnosis

Peripheral smear findings	No. of cases	Percentage (%)
Normocytic Hypochromic anemia	09	15%
Microcytic hypochromic anemia	03	5%
Macrocytic anemia	44	73.3%
Dimorphic anemia	04	6.6%
Total	60	100%

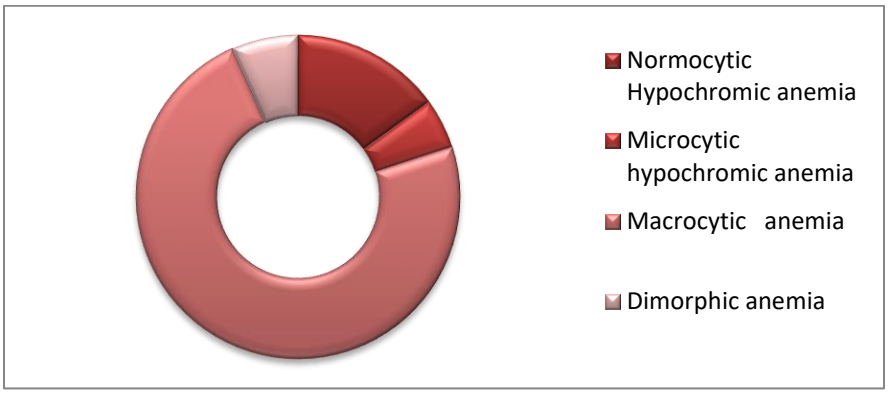

Fig 2:Peripheral smear RBC features in cases of pancytopenia

In this study, macrocytic RBCs were the most common finding and was seen in 73.3% cases.

Total leukocyte count: In this study, 60% cases (36/60) showed WBC count between 2000-4000 /cumm. WBC count between 1000-2000/cummwas seen in 23.3% cases (14/60) and 16.6% cases (10/60) had WBC count of <1000/cumm.

Platelet count: In this study, 33.3% (20/60) cases had platelet count between 20000 to 50000 /cumm (Moderate thrombocytopenia), 48.3%(29/60) cases had platelet count less than 20000/cumm (Severe thrombocytopenia) and 18.3%(11/60) had platelet count between 50000 to 1lakh /cumm (mild thrombocytopenia).

Table 4:Distribution of cases based on bone marrow aspiration diagnosis

Bone marrow Diagnosis	No. of cases	Percentage (%)
Aplastic anemia	01	8.3%
Megaloblasticanemia	07	58.3%
Acute leukemia	01	8.3%
MDS	01	8.3%
Infective etiology	02	16.7%
Total	12	100%

In this study, among 60 cases of Pancytopenia, only 12 cases were sent for Bone marrow Aspiration. The most common diagnosis on Bone marrow aspiration was megaloblastic anemia in 58.3% (7/12) cases.In our study, serum vitamin B12 level was decreased in 34 (56.6%) cases of vitamin B12 deficiency cases.

Discussion

The evaluation of pancytopenia starts with clinical history, physical examination and hematological, biochemical, radiological examination, bone marrow aspiration and biopsy. Pancytopenia can happen due to various primary or secondary causes affecting the bone marrow. It is a characteristic feature of many serious and life-threatening diseases.which vary in different population groups with differences in age pattern and nutritional status. The prevalence of certain infections may lead to pancytopenia. The severity of disease and underlying pathology regulate the management and prognosis of these patients.

Comparative studies related to age distribution: In our study, the age of the patients ranged from 18 years to 70 years. Majority of the cases were among 18-30 years i.e, 43.3% followed by 31 - 40 years which constituted 23.3%, 16.6% were noted among 41-50 years age group and 11.6 % among 51-60 years. Least were noted among 61-70 years i.e only 5%casse. In a similar study conducted by Agarwal et al [11], 11-20 years was the most common age group affected, whereas Gayathri BN et al [6] observed a mean age of 41 years among patients ranging from 2 to 80 years. Mandli et al [12] noted11-30 years as most common affected age group in their study.

Comparative studies related to gender distribution: In our study, females i.e, 51.6% were predominant when compared to males i.e,48.3% with male to female ratio of 1:1.06. A study by Gayathri BN et al [6]reported males to be slightly more affected than females and also Mandli et al [12] observed predominance of males over females, whereas Agarwal et al [11] observed female predominance in their study, the findings were corroborating with our study.

Comparative studies related to Clinical symptoms: In our study, 60% presented with generalized weakness followed by fever with chills and rigors in16.6%,only fever in 8.3% abdominal distension in 5% cases and bleeding in 10% cases.

In a study conducted by Patel RR et al [13] the most common clinical features were weakness (80%), fever (72.1%), pallor (100%) and hepatomegaly (62.8%). Katti TV et al {14] observed most frequent

clinical symptom as generalized weakness (90%) and least was bone pain (2%). These findings were corroborating with our study. In a study done by AgarwalR et al [11] most of the patients presented with fever and pain in legs. The commonest physical finding was pallor. In the study by Gayathri BN et al [6] most of the patients presented with generalized weakness and fever. The commonest physical finding was pallor, followed by splenomegaly and hepatomegaly. MohantyN et al [15] observed generalized weakness and fatigue (140 patients, 93.3%) as the commonest clinical symptom, whereas Swetha et al [16] noted commonest mode of presentation was generalized weakness with fatigue, which was present in all patients constituting 100%.

Comparative studies related to Pancytopenia: Santra and Das [17] defined anemia as mild (Hb:9-10g/dl), moderate (Hb: <9g/dl) and severe (Hb: <5g/dl).Leucopenia was defined as mild (4000-2000/cu.mm), moderate (< 2000-1000/cu.mm) and severe (<1000/cu.mm). Thrombocytopenia was defined as mild (1lakh-50000/cu.mm), moderate (<50000-20000/cu.mm) and severe (<20000/ cu.mm). In our study, severe anemia (<6g/dl) was seen in 36.6% (22/60) cases, 53.3% (32/60) cases showed Hb level of 6.0-8.9 gm/dl (moderate anemia) and 10% (06/60)cases showed Hb of 9-11 g/dl (mild anemia). In a study conducted by Thakkar and Bhavsar et al [18] mild anemia was observed in 25 % cases, moderate in 51% cases and severe anemia in 24% cases respectively. In the study by Patel RR et al study [13] mild, moderate and severe anemia were noted in 22.1%, 70.8% and 7.1% cases respectively.

Present study showed anisopoikilocytosis in 51 cases. The studies by Tilak and Jain et al [19]showed anisopoikilocytosis in 64 cases. Khunger et al [20] noted it in 150 cases, GayathriBN et al [6] notedin 90 cases and Khodke et al [7] noted in 30 cases respectively.

In the present study, macrocytic anemia was noted in 73.3 % cases (44/60), microcytic hypochromic in 5% cases (03/60) and normocytic hypochromic anemia constituted 15%(09/60) and dimorphic anemia was seen in 6.6%(04/60) cases. Katti TV et al [14] revealed predominantly macrocytic blood picture in 47.9% cases. In a study conducted by Reenal R Patel et al (13) the predominant blood picture was normocytic normochromic (38.5%) followed by dimorphic (32.7%), macrocytic (17.3%), microcytic hypochromic (5.8%) and normocytic hypochromic anemia(5.8%). A study by Shweta et al [16]showed macrocytic anemia in 49% cases, whereas, Khodke et al study [7] showed dimorphic picture as the predominant blood picture.Present study reported hyper-segmented neutrophils in 44 cases of macrocytic anemia cases whereas Patel RR et al [13] reported hyper-segmented neutrophils in 40 cases of megaloblastic anemia and in one case of iron deficiency anemia. Rani and Sureshkumar et al [21]studyreported hyper-segmented neutrophils in peripheral smear of 92% patients with megaloblastic anemia.

In this study, 60% cases showed WBC count between 2000-4000 /cumm. WBC count between 1000-2000/cummwas seen in 23.3% cases and 16.6% cases had WBC count of <1000/cumm. Thakkar and Bhavsar study [18] observed mild, moderate and severe leucopenia in 46%, 52% and 2% respectively. Present study observed that relative lymphocytosis was seen in dengue (10 cases) and malaria (09cases).The studies done by Tilak and Jain et al [19] observed relative lymphocytosis in 11 cases and, Khunger et al [20] noted in 38 cases.

In the present study, 33.3% cases had platelet count between 20000 to 50000 /cumm (Moderate thrombocytopenia), 48.3% cases had platelet count less than 20000/cumm (Severe thrombocytopenia) and 18.3% had platelet count between 50000 to 1lakh /cumm (mild thrombocytopenia. In the study done by Patel RR etal [13] moderate thrombocytopenia in 26%.cases, severe thrombocytopenia was seen in 8% cases and mild thrombocytopenia was seen in 66% cases.

Comparative studies related to Diagnosis: In this study, vitamin B12 deficiency anemia was most common disorder diagnosed clinically in 56.6% cases, followed by dengue in 16.6% cases,Malaria in about 15% cases, Aplastic anemia,Hepatitis B and acute leukaemia in 3.3% each, and myelodyspalstic syndrome in 1.6% cases. In a study conducted by, Varma A et al [22], among all the hematological disorders causing pancytopenia, the most common noted was megaloblastic anemia (98/202, 48.51%) followed by dimorphic anemia (36/202, 17.8%) and aplastic anemia (18/202, 8.9%). Least common causes included hemolyticanemia (2/202) and disseminated intravascular coagulation (2/202), that is, 0.99% each.

In a study by Swetha et al [16] megaloblastic anemia was commonest cause constituting 47.05% followed by Hypersplenism (22.05%), SLE (4.90%), malaria (4.90%), subleukemicleukemia (3.92%), HIV (2.94%), Aplastic anemia{(idiopathic) 2.94%}, NHL (1.96%), MDS (0.98%), Disseminated tuberculosis (0.98%), Paroxysmal nocturnal hemoglobinuria(0.98%), enteric fever (0.98%), Hepatitis B (0.98%) and Multiple Myeloma (0.98%).In Patel RR et al [13] study, the most common causes of pancytopenia were malaria (50%), megaloblastic anemia (18.6%) and dengue (18.1%) followed by aplastic anemia (1.3%), leptospirosis (0.9%), dimorphic anemia (0.9%), dyskeratosis congenita (0.4%) and myelodysplastic syndrome (0.4%).In the study by Katti TV et al [14], 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%), 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%).

Bone marrow: In the present study, Hypocellular marrow was noted in one case of Aplastic anemia and one case of MDS. Dry tap was observed in one case of Aplastic anemia. Hypercellular marrow was noted mostly in all megaloblastic anemia cases (06) and in one case of Iron deficiency anemia. Normocellular marrow was noted in one case which was reported as infectiveetiology.

In a study conducted by Graham S et al [23] the most common aetiology of pancytopenia was normoblasticerythroid hyperplasia (30%), followed by megaloblastic anemia (20%), followed by acute myeloid leukemia (13.3%) and closely by micro-normoblastic erythroid maturation (10%).

Conclusion

The present study concludes that detailed primary hematological investigations, the physical findings and peripheral blood picture provides precious information in the work up of patients with pancytopenia. Complete hematological examination including bone marrow aspiration should be done to recognize and diagnose this disease early so that proper intervention and medical treatment for these patients can be done.Early identification of pancytopenia would help in early planning for management thereby improving the survival rates.

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