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A Clinical And Etiological Study of Patients with Pancytopenia (A Study Of 50 Cases)

KEYWORDS: Pancytopenia, Megaloblastic anemia, aplastic anemia

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ABSTRACT *"Pale represents death and I as a doctor thrive to bring back the dead" –Dr. Priyank Mody.*

Pancytopenia means a disorder in which all 3 blood elements (red blood cells, white blood cells and platelets) are decreased than normal. For years panctopenia was equated with aplastic anemia, resulting to unnecessary referral to an oncologist, resulting to unnecessary financial & emotional burden to the patient & his family .to Relatively untouched topic by all prominent indigenous Textbooks of Internal Medicine & Haematology, hence we had to rely on foreign literature where the aetiology varied widely as compared to the patient profile we see in India. Hence there was an imminent need for studies to determine aetiology & generate a plan for evaluation and treatment based on local factors.

Common questions that a healthcare professionals asks are

1) What are the most common causes of pancytopenia? And

2) What is the best diagnostic approach to the pancytopenia patient?

In the present study, I have attempted to answer these questions. I studied 50 patient admitted in a general medical ward with pancytopenia with different aetiology and varied clinical presentations, .On the basis of the findings and available literature I have tried to study common causes of pancytopenia in general medical ward, their clinical presentations, physical examination findings and have formulated approach to the problem of pancytopenia.

INTRODUCTION:

Although it is a common clinical problem with an extensive differential diagnosis, there is a relatively little discussion of this abnormality in major textbooks of internal medicine and haematology.

The spectrum of primary and secondary disorder that affect the bone marrow may manifest with pancytopenia.[3] Pancytopenia can be due to decrease in Hematopoietic cell production in the 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. ineffective haematopoiesis' and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells.

Patients usually present with complaints ascribed to anemia, thrombocytopenia and rarely leucopenia which in later stages is responsible for downhill course. Various factors encompassing geographical distribution and genetic disturbances may cause variation in the incidence of disorders causing pancytopenia.[4, 5, 6] underlying pathology determines the management and prognosis of the patients.[7]

Sometimes pancytopenia is detected as an incidental finding in a patient who has presented with symptoms of a disorder that is capable of depressing the levels of all cellular elements in the blood. Initially, mild impairment in marrow function is unapparent and pancytopenia may become apparent only during times of stress or increased demand (for example bleeding or infection). More severe degrees of cytopenias affect the peripheral blood count even in the steady state.[2]

However, major diagnostic problems occur when there are no specific features in the blood to suggest the diagnosis or when the clinical features are not sufficiently specific to point to the cause.[2]

No two studies of clinical profile of pancytopenia are the same. Apparent differences observed in profile may be due to number of factors including health care delivery system/ availability of advanced laboratory back up facility/population risk factors (like occupations - rubber factory worker / radiation exposure/agricultural pesticide exposure/exposure to drugs and chemicals/infectious diseases), geographical and environmental factors and other co morbid conditions and study factors such as the type and number of sample collected; investigation performed and interpretation of results.

AIMS & OBJECTIVES:

1. To study the clinical profile of the patient with pancytopenia.
2. To study the underlying aetiology of the pancytopenia.
3. To study various clinical presentation, physical examination findings in patient with pancytopenia.
4. To study utility of peripheral smear examination in diagnosis of pancytopenia.
5. To study the utility of the bone marrow examination in diagnosis of pancytopenia.

MATERIALS & METHODS:

This study was two year cross sectional study carried in our hospital in general medical ward from May 2008 to May 2010. I studied 50 patients of pancytopenia admitted in general medical ward having all the inclusion criteria, after taking written and informed consent.

Inclusion criteria:

1. age >13 years
2. Anemia (Hb < 10g/dl)
3. Leucopenia (total count <4000/dl)
4. Thrombocytopenia (platelet count < 1,50,000)

Exclusion criteria:

1. Patient on cancer chemotherapy

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2. Patient is taking other cytotoxic/antimetabolic drugs
3. Patient who is taking radiotherapy

Note: In every patient included in the study detailed history, physical examination was done and blood sample collected was sent for appropriate investigations:

- Haemoglobin.
- Total count, differential count and ESR.
- Platelet count.
- Peripheral smear study.
- Bone marrow smear study.

Other investigations as necessary such as;
- Bone marrow trephine biopsy.
- Peripheral smear for malarial pigment
- Serological study.
- o Rapid card test for HIV infection.
- o HBsAg & anti- HCV
- o Elisa Ig M for Dengue.
- Blood culture study.
- Chest x-ray.
- Electrophoresis.

OBSERVATIONS & RESULTS:
The study was conducted on 50 hospitalized patients presenting with pancytopenia & eligible under definition of panctopenia. Findings are as tabulated below:

ETIOLOGY	Male	Female	Total No.	%
Megaloblastic anemia	16	08	24	48%
Aplastic anemia	05	02	07	14%
Malaria	04	01	05	10%
Dengue fever	01	02	03	06%
Leukemia / Lymphoma	01	01	02	04%
Septicemia	01	01	02	04%
Hepatitis B	02	00	02	04%
Hypersplenism	00	01	01	02%
HIV Infection	00	01	01	02%
ITP	00	01	01	02%
Myelodysplastic syndrome	00	01	01	02%
Drug induced	01	00	01	02%

Inference: Megaloblatic anemia was the commonest cause of pancytopenia followed by aplastic anemia, malaria and dengue.

Age: Patient's age ranged from 15 to 95 years. Maximum number of cases were in the age group of 15 to 24 years (26%) followed by age group of 35 to 44 years (22%). Average age at presentation was 41.2 ± 20.62 years.

Sex: Out of 50 patients, 31 patients (62%) were males and 19 patients (38%) were females. Accounting to a ratio of male to female of approximately 3:2.

Symptoms	No.	%
Easy fatigability	44	88%
Decreased appetite	34	68%
Fever	30	60%
Exertional breathlessness	26	52%
Body ache	22	44%
Bleeding tendencies	21	42%
Vomiting	18	36%
Abdominal pain	16	32%
Weight loss	11	22%
Lower limb edema	11	22%
Palpitations	11	22%
Cough	08	16%
Loose stool	05	10%
Easy fatigability	44	88%

The commonest symptom was easy fatigability (88%) followed by decreased appetite (68%), fever (60%), exertional breathlessness (52%), body ache (44%), bleeding tendencies (42%), and lower limb oedema (22%). Hence most patients presented with symptoms of anemia, followed by thrombocytopenia & lastly Leucopenia.

SIGN'S	No.	%
Pallor	50	100%
Splenomegaly	28	56%
Hepatomegaly	19	38%
Petechiae	15	30%
Edema feet	11	22%
Icterus	09	18%
Glossitis	08	16%
Haemic murmur	08	16%
Lymphadenopathy	04	08%
Ascites	04	08%

Commonest physical sign was anemia followed by splenomegaly and hepatomegaly.

Anemia: Haemoglobin level ranged from 2 gm% to 10 gm%. The mean haemoglobin level was 5.42 ± 2.38 gm%. Hence majority presented with severe anemia (<6)

Leucopenia: Total leucocyte count ranged from 700 cells to 3900 cells/cmm. The mean total leukocyte count was 2526 ± 829.26 cells/cmm. Total leucocyte count 2100 to 3000 cells/cmm was associated with more incidence of fever. But correlation between total leucocyte count and incidence of fever was statistically non significant (p=0.6592).

Thrombocytopenia: Platelet count ranged from 1000 to 130000 cells/cmm. Mean platelet count was 50400 ± 39476.67 cells/cmm. Majority (58%) patients had platelet count less than or equal to 50000 cells/cmm. Majority of patients with bleeding tendencies had platelet count ≤ 50000 cells/cmm (80.95%). This correlation was statistically significant (p=0.0190).

Diet: Megaloblastic anemia was more common in patients with vegetarian diet. Also MCV turned out to be a better predictor of megaloblastic anemia. In present study, MCV had a sensitivity of 79.16%, specificity of 92.30% and positive predictive value of 90.47% for diagnosis of megaloblastic anemia.

Peripheral Smear examination: Peripheral smear was conclusive to arrive at diagnosis of pancytopenia in most of the cases. Majority (44%) of the patients had normocytic hypochronic blood picture on peripheral smear followed by macrocytic/megaloblastic (24%). Hyper segmented neutrophils in peripheral smear were very sensitive and specific for diagnosis of megaloblastic anemia.

Bone marrow Examination: Bone marrow study/trephine biopsy was done only in few of the cases. Of the bone marrow performed, majority of patients with aplastic anemia had hypocellular marrow.

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DISCUSSION:

In the present study of 50 patients it was observed that megaloblastic anemia was the most common cause of pancytopenia (48%), followed by infection (16%) (Malaria plus dengue and aplastic anemia 3rd (14%).

Similar results were found in various studies done in Asian countries due to common socio-economic, environalmental, and cultural differences eg. *Osama I et a*[8,] *Sen. R et al*[9] , *Tilak et al*[7] *Department of Pathology, Dr RML Hospital, New Delhi study*[11]

Whereas various studies of the west showed aplastic anemia and leukaemia as the most common cause of pancytopenia. Eg. *International agranulocutosis and aplastic anemia study*[4] *Imbert M et al*[10]

Common presenting symptoms in our study were easy fatigability (88%) followed by decrease appetite (68%), fever (60%), exerctional breathlessness (52%), bleeding tendencies (42%), bodyache (44%) and lower limb oedema (22%). i.e . symptoms due to anemia were most common followed by thrombocytopenia and lastly leucopenia . Pallor as sign was present in all the patients followed by splenomegaly and hepatomegaly.

The mean haemoglobin in the present study was 5.42 ± 2.38 gm%, the mean total leukocyte count was 2526 ± 829.26 cells/cmm and mean platelet count was 50400 ± 39476.67 cells/cmm. Similar results were seen in Hamid GA et al[12]

CONCLUSION:

- Megaloblastic anemia is the most common cause of pancytopenia
- Deficiency of Vit B12 & folic acid is the most common cause of megaloblastic anemia
- Malaria including p. vivax apart from p. falciparum & Dengue are common and important causes of reversible pancytopenia in endemic region like ours
- Hyper segmented neutrophils is more sensitive and specific than MCV in diagnosis of megaloblastic anemia
- Of all patients of megaloblastic anemia 88 % were pure vegetarians with even dairy products less than 200 ml day
- PS CM – mc normocytic hypo chromic picture
- Marrow biopsy : mc hypocellular / a cellular in aplastic anemia and hyper cellular in megaloblastic.

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