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General Medicine

CLINICAL AND ETIOPATHOLOGICAL SPECTRUM OF ADULT PATIENTS WITH PANCYTOPENIA

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ABSTRACT

BACKGROUND: Pancytopenia is diagnosed when there is a reduction in all three hematopoietic cell lines. Till date there is limited number of studies on the frequency of various causes of pancytopenia. Of these some have been reported from the Indian subcontinent. There appears to be a changing spectrum of pancytopenia over the past two decades. The objective was to study the etiopathological spectrum of adult patients with pancytopenia over a period of one and half year.

MATERIAL AND METHODS: The Prospective and retrospective observational study was conducted in the Department of General Medicine Jawahar lal Nehru medical College and Hospital Bhagalpur Bihar,. A total of 120 Patients were included in the study. All patients gave their consent to take part in the study and were subjected to a questionnaire regarding symptoms, past relevant history, lifestyle and detailed clinical examination and investigations as mentioned in materials and methods.

CONCLUSION: Pancytopenia is not a disease itself. It is a hematological feature of varying etiology with slight male preponderance. Megaloblastic anemia along with mixed nutritional anemia is leading cause of pancytopenia in India followed by infections being second and aplastic anemia and acute leukemia being third common causes.

KEYWORDS : Pancytopenia, Megaloblastic anemia, Nutritional anemia.

INTRODUCTION

Pancytopenia is diagnosed when there is a reduction in all three hematopoietic cell lines.[1] Pancytopenia is diagnosed when the following are present 1. HB <10 g/dl male & female 2. Platelet count <150*10^9 3. TLC < 4000cells /dl.[1]

A number of texts have simply defined pancytopenia as a reduction in 2 or more of the three hematopoietic cell lines.[2] Other texts have defined pancytopenia to be a reduction in all the three hematopoietic cell lines.[1,3,4]

Till date there is limited number of studies on the frequency of various causes of pancytopenia. Of these some have been reported from the Indian subcontinent. There appears to be a changing spectrum of pancytopenia over the past two decades. Some of the diseases that exhibit pancytopenia include aleukemic leukemia, myeloma. Lymphoma, myeloid metaplasia, storage reticulosis, pernicious anemia, paroxysmal nocturnal hemoglobinuria and aplastic anemia.[2] Some studies have documented drug induced cytopenia to be the most common while others have shown megaloblastic anemia / aplastic anemia to be more common. Studies done in India recently revealed megaloblastic anemia/aplastic anemia,

leukemia, leishmaniasis, myelodysplastic syndrome, paroxysmal nocturnal hemoglobinuria, overwhelming viral infections (HIV, viral hepatitis etc.) and drug induced pancytopenia as the most commonly diagnosed causes of pancytopenia.[5,6] The incidence of aplastic anemia quoted from the west is 10.25%. However studies done in India show a lower proportion of aplastic anemia in all cases of pancytopenia. Kala azar has also been reported in a large proportion of cases from India as compared to western studies. A review of international literature reveals the etiopathogenetic spectrum differs based on the geographic region. The studies in the Indian subcontinent looked at pancytopenia in a different perspective. Of particular interest are studies regarding megaloblastic anemias in India which show an increasing prevalence of this disease as a proportion of all anemias / pancytopenia. Keeping these factors in mind we plan to review the clinical and etiopathological spectrum of pancytopenia causes in adults.[7] Since the hematological and etiopathological causes of pancytopenia differs. It's planned to evaluate inpatients that were found to have pancytopenia in hematology lab reports for etiopathological presentation.

The hypothesis of this thesis is " ETIOPATHOLOGICAL SPECTRUM OF ADULT PATIENTS WITH PANCYTOPENIA" in tertiary care hospital in Bihar.

MATERIAL & METHODS

The present study "CLINICAL AND ETIOPATHOGENESIS SPECTRUM OF ADULT PATIENTS WITH PANCYTOPENIA" has been carried out in the Department of General Medicine, Jawahar lal Nehru medical College and Hospital Bhagalpur Bihar. Study design: A Prospective and retrospective observational study

a) Study period: One and half year.

b) Study material: captured from medical record of patients who have a newly diagnosed pancytopenia documented in the hematology laboratory.

C) Inclusion Criteria:

1. Age > 18 years of either sex
2. Patients with pancytopenia is defined by the presence of the following
   - Hb < 10 gm/dl in female & male Patients
   - Total leucocyte count < 4000cells/dl
   - Platelet count <1.5lakh/dl

d) Exclusion criteria:

- Cancer chemotherapy recipients/ on cytotoxic therapy or concomitant use of colony stimulating factors
- Recipients of multiple blood/blood component transfusions prior to 3 months presentation in our hospital
- Patients who are too sick to undergo the proposed diagnostic work up

e) Sample size: 120

f) Methodology: - Data captured from medical record.

- complete blood count (CBC) with a differential count, absolute neutrophil count (ANC), absolute lymphocyte count (ALC) including red blood cell indices MCH, MCH, MCHC will be estimated using the automatic cell count from Beckman coulter LH 780.
- A blood film to be stained by the wright stain and evaluated for red cell morphology, band forms, platelet
- Morpholog and platelet number, and any atypical cells/parasite.
- Reticulocyte count using 1% new methylene blue for supravital staining.
- Liver function tests, liver enzyme levels, renal function tests, serum ferritin, serum LDH, levels to be done in all patients.(where indicated)
- X-ray chest, USG abdomen ,blood culture.(where indicated)
- Bone marrow examination. Bone marrow aspiration and whenever required, a trephine biopsy to be performed. Findings of aspiration and trephine biopsies were interpreted in the context of history, clinical examination and peripheral blood findings.(where indicated)

Further tests to be carried out as warranted by the clinical context and the results of baseline investigations. In case of megaloblastic anemia,

these included vitamin B12 assay methodology is the ARCHITECT B12 assay is a two- step assay with an automated sample pretreatment, for determining the presence of B12 in human serum and plasma using Chemiluminescent micro particle immunoassay (CMIA) technology with flexible assay protocol referred to Chemiflex (Abbott architect J1000SR (L1SR50899) at batra hospital and medical research Centre, New Delhi) and folate assays by CMIA.(where indicated) Viral markers of HbsAg, anti HCV antibody, HIV 1 &2.(where indicated)

- Malaria serology ,dengue serology.(where indicated)
- SPEP (serum protein electrophoresis).(where indicated)

OBSERVATIONS

The present study was conducted in the Department of General Medicine, Jawahar lal Nehru medical College and Hospital Bhagalpur Bihar. The objective was clinical etiopathological spectrum of adult patients with pancytopenia over a period of one and half year. A total of 120 Patients were included in the study. All patients gave their consent to take part in the study and were subjected to a questionnaire regarding symptoms, past relevant history, lifestyle and detailed clinical examination and investigations as mentioned in materials and methods.

Table 1: Distribution of patients with pancytopenia according to gender

Gender	No(n=120)	%
Male	82	68.3
Female	38	31.7

68.3% patients were male and 31.7% were female.

Table 2: Distribution of patients with pancytopenia according to age

Age in years	No. (n=120)	%
<30	58	48.3
31-40	30	25.0
41-50	14	11.7
51-60	9	7.5
>60	9	7.5
Mean±SD (Range)	33.72±15.64 (18-80)	100

48.3% were less than 30 year, 25% were between 31-40 years, 11.7%were between 41-50 years and 7.5% were between 51-60 years or greater than 60 years.

Table 3: Etiological diagnosis in pancytopenia

Diagnosis	No.(n=120)	%
Megaloblastic anaemia	62	51.7
Aplastic anaemia	14	11.7
Acute leukaemia	10	8.3
HIV-AIDS	5	4.2
Kala Azar	1	0.8
Disseminated Koch's	6	5
Complicated malaria	7	5.8
Lymphoma	1	0.8
Myelodysplastic syndrome	1	0.8
Metastatic anaplastic carcinoma	1	0.8
postpartum sepsis with macrocytic anaemia	1	0.8
Primigravida with anaemia	1	0.8
SDH with altered sensorium	1	0.8
Acute promyelocytic anaemia	1	0.8
DCMP with multiple deficiency	1	0.8
Febrile illness with HSM	3	2.4
Signet ring cell Ca	1	0.8
Hypersplenism with multiple deficiency	2	1.6
Multiple deficiency anaemia	5	4.2

HSM-hepatosplenomegaly, DCMP-dilated cardiomyopathy, Ca-carcinoma, SDH-subdural hematoma

Table 4: Distribution of patients with pancytopenia according to final diagnosis

Diagnosis	No. (n=120)	%
Megaloblastic anaemia(D1)	69	57.5
Aplastic anaemia(D2)	14	11.7
leukaemia/lymphoma (D3)	14	11.7
Infections (D4)	18	15.0
Myelophthisis/Storage disorder(D5)	1	0.8
Other (D6)	4	3.3

57.5% of patients with pancytopenia were diagnosed as megaloblastic anemia. 15% of patients with pancytopenia were diagnosed with infections such as complicated malaria cases (7), HIV (5), disseminated Koch's (4), viral (2). 11.7% of patients with pancytopenia were diagnosed as Aplastic anemia & leukemia/lymphoma such as lymphoma (1), metastatic anaplastic carcinoma (1), acute leukemia (11), and metastatic gastric carcinoma (1), 3.3% were other such as reactive marrow (4) and 0.8% was Myelophthisis/Storage disorder as myelodysplastic syndrome (1).

DISCUSSION

Pancytopenia has multiple etiologies. The purpose of this thesis work was to capture the spectrum of diseases causing pancytopenia in adult patients and to identify useful clinical and hematological correlates of these diverse illnesses. It also highlights the importance of early recognition and treatment of reversible causes. Data regarding pancytopenia in adult Indian population in North India is not enough which prompted this study also prevalence of disease is changing.

The study population consisted of 120 patients with mean age 33.72±15.64 years with range of 18-80years. 68.3% (82) patients were male and 31.7%(38) were female in the study group (M:F ratio 2.17:1). It may be possible that male patients with pancytopenia are more likely to present to hospital. 48.3% were less than 30 year of age, 25% were between 31-40 years, 11.7%were between 41-50 years and 7.5% were between 51-60 years or greater than 60 years. Similar results were obtained in Kumar et al,[8] Khanduri et al.[7]

Six broad diagnostic groups were identified in this study. The largest group 57.5% of patients with pancytopenia was diagnosed as having megaloblastic anemia. 15% of patients with pancytopenia were diagnosed with infections such as complicated malaria (7), HIV (5), disseminated Tuberculosis (4), viral fever (2). 11.7% of patients with pancytopenia were diagnosed as Aplastic anemia. 11.7% of patients with pancytopenia were diagnosed as leukemia/lymphoma. These were lymphoma (1), metastatic anaplastic carcinoma (1), acute leukemia (11), and metastatic gastric carcinoma (1), 3.3% were others namely reactive marrow (4) and 0.8% was Myelophthisis/Storage disorder such as myelodysplastic syndrome (1). Similar results were seen in Khanduri et al[7] Khunger et al,[9] Verma et al,[10] Khodke et al[11] Kumar et al,[8] Gayathri BN, Rao KS12 Saini T, Kumhar M, Barjartya HC et al13

In a study done by Khunger et al,[9] the commonest cause of pancytopenia in 200 patients was found to be megaloblastic anemia (72%) followed by aplastic anemia (14%) and others.[9]In a study done by Kumar et al,[9] the four major causes were aplastic anemia in 49, megaloblastic anemia in 37, aleukemic leukemia or lymphoma in 30, and hypersplenism in 19 cases.[9]

Similar findings were reported by Verma et al, Aplastic anemia (40.6%), megaloblastic anemia (23.26 %) and acute myeloblastic leukemia (12.8%) together accounted for most of the cases.

CONCLUSION

Pancytopenia is not a disease itself. It is a hematological feature of varying etiology with slight male preponderance. Megaloblastic anemia along with mixed nutritional anemia is leading cause of pancytopenia in India followed by infections being second and aplastic anemia and acute leukemia being third common causes.

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