ORIGINAL RESEARCH

Clinico-Aetiological Profile of Pancytopenia in Elderly- Tertiary Care Hospital Based Study

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Received: 05December, 2022 Accepted: 16January, 2023

ABSTRACT

Background: Pancytopenia is a common problem in clinical practice. Pancytopenia is defined as Hemoglobin less than 10 g/dL, total leucocyte counts less than 4,000/dL and platelet count less than 1.5 lakhs/dL. Causes of pancytopenia vary from nutritional deficiencies, bone marrow failure status and malignancies. Pancytopenia is a common problem in geriatric population also. In this study, we try to find common causes of pancytopenia in geriatric population in a tertiary care hospital. Objectives: To study the clinic-aetiological profile of pancytopenia in elderly population in a tertiary care hospital. **Methods:** 100 patients who are more than 60 years of age attending General Medicine Outpatient Department were included in the study. Diagnosed cases of any malignancies and Patients on chemotherapy were excluded from the study. These patients were subjected to detailed history taking and clinical examination. Routine investigations like complete blood count, peripheral smear, reticulocyte count, Coombs test, serum cobalamin level's renal function tests and liver function tests were done. Bone marrow examination was done in cases where indicated. Upper gastrointestinal endoscopy was done in cases wherever indicated. **Result:** Out of 100 patients included in the study ,73 were males and 27 were females. 63% of Patients were below 65 years and 37% of patients were above 65 years. The mean age of the patients were 64.9 .Fatigue was the most common symptom (73%).Followed by paraesthesia (28%) ,Fever (19%) ,Weight loss (20%) and Bleeding (9%) .Most common cause of pancytopenia was cobalamin deficiency (62%) .Other causes were MDS(12%) Disseminated TB (9%) ,HIV (5%) ,Chronic liver disease (5%), Acute promyelocytic leukemia (3%), Aplastic anemia (2%), Hairy cell leukemia (1%) and SLE (1%).**Conclusion:** Vitamin B12 deficiency is the most common cause of pancytopenia in elderly population Symptoms of Vitamin B12 deficiency may be non specific in elderly. High index of suspicion is required for the diagnosis. Mean corpuscular volume may not be highly elevated in all patients. Hence all patients in geriatric population presenting with pancytopenia should be tested for Serum Vitamin B12 levels.

Key words: Pancytopenia, Vitamin B12, Bone marrow, Elderly.

INTRODUCTION

Pancytopenia is the condition characterized by anemia, leucopenia and thrombocytopenia. The causes of pancytopenia ranges from infections, bone marrow infiltrations, drugs, malignancies ,vitamin deficiencies etc. Prompt identification of the cause for pancytopenia is very much important in determining the treatment as well as to predict the prognosis. Worldwide the most common cause for pancytopenia is reported as aplastic anemia. In contrast many Indian studies have revealed Vitamin B12 deficiency as the most common cause for pancytopenia in Indian population. All these studies are being conducted in general population. But the vast majority of patients that have diagnosed with pancytopenia belongs to the geriatric population, which add on to the morbidity related to the older age. If the reversible causes such as infections and nutritional deficiencies are identified earlier, the morbidity and mortality related to this condition can be decreased significantly and helps to improve the health of the geriatric population.

Aims and Objectives of Our Study

To study the clinic-aetiological profile of pancytopenia in elderly population in a tertiary care hospital.

MATERIALS AND METHODS

Source of Study

Data has been gathered by the primary investigator from 100 cases of pancytopenia patients aged more than 60 admitted in the medical wards of Coimbatore medical college hospital.

Design of Study: Observational/Cross sectional study

Period of Study

One Year(MARCH 2020- MARCH 2021)

Sampling Method: Random sampling

Methodology

After getting permission from the Institutional ethical committee and with the informed written consent from the patients a Cross sectional/Observational study has been conducted among 100 PANCYTOPENIA patients aged more than 60 admitted in the medical ward.

Inclusion Criteria

1) Patients aged more than 60 years.

2) Patients with Hb <10 g%,Total leucocyte count <4000 cells/mm3,platelet count < 1,50000 cells/mm3.

Exclusion Criteria

1) Patients with age less than 60 years.

2) Patients who have already been diagnosed with malignancy and on chemotherapy.

3) Patients not willing to give the consent

Methods of study:

Pretest proformas were used for the collection of data according to the objectives of the study. Detailed history and examination was done in 100 patients after getting informed written consent.The aim and purpose of the study was explained to the patients .Need for invasive procedures like Bone marrow aspiration study , biopsy and OGD scopy if indicated were explained to the patient via informed written consent. Patients were selected based on the inclusion criteria and some cases were excluded based on the exclusion criteria.

Investigations

1.COMPLETE BLOOD COUNT includes Hemoglobin, Total count, Platelet count and Mean corpuscular volume

2. ESR

RETICULOCYTE COUNT, SERUM LDH

SERUM VITAMIN B12 LEVEL, HIV-1 AND HIV 2 TEST (ICTC)

2. BIOCHEMICAL INVESTIGATIONS Blood Urea Nitrogen, Liver Function Test

Total/direct/indirect bilirubin, SGOT, SGPT

Total Protein including S.Albumin, S.Globulin

Alkaline phosphatase

3. ELECTROCARDIOGRAM

4. IMAGING STUDIES

ULTRASOUNG ABDOMEN PELVIS

Chest X ray PA view

5. PERIPHERAL SMEAR FOR PATHOLOGIST OPINION

6. BONE MARROW ASPIRATION CYTOLOGY

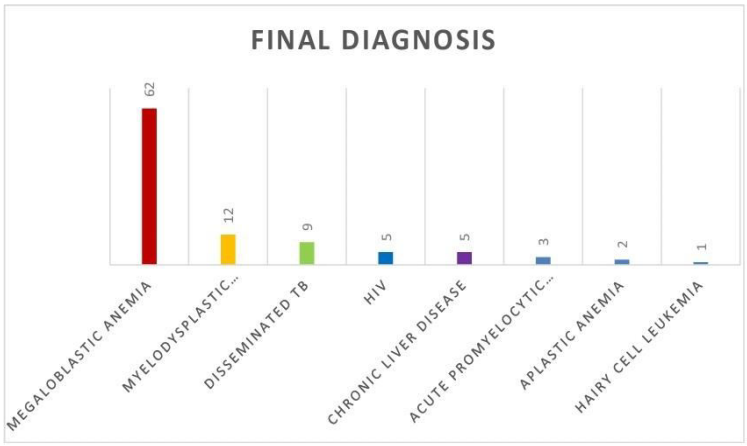
7. BONE MARROW TREPHINE BIOPSY (if necessary)

8. SPECIAL INVESTIGATIONS like ANA, THYROID FUNCTION TEST, SERUM PROTEIN ELECTROPHORESIS, CD4 COUNTS, UPPER GI ENDOSCOPY, SPUTUM FOR AFB STAINING was done only for appropriate needed patients.

RESULT

TABLE -5.1

FINAL DIAGNOSIS	NO OF PATIENTS	PERCENTAGE
MEGALOBLASTIC ANEMIA	62	62%
MYELODYSPLASTIC SYNDROME	12	12%
DISSEMINATED TB	9	9%
HIV	5	5%
CHRONIC LIVER DISEASE	5	5%
ACUTE PROMYELOCYTIC LEUKEMIA	3	3%
APLASTIC ANEMIA	2	2%
HAIRY CELL LEUKEMIA	1	1%
SLE	1	1%



AGE DISTRIBUTION

TABLE-5.2

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 65	63	63%
> 65	37	37%

SEX DISTRIBUTION

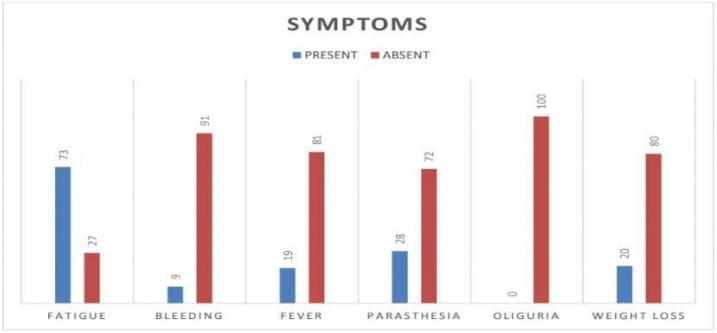
TABLE-5.3

SEX	NO OF PATIENTS	PERCENTAGE
MALE	73	73%
FEMALE	27	27%

SYMPTOMS

TABLE-5.4

SYMPTOMS	PRESENT	ABSENT
FATIGUE	73	27
BLEEDING	9	91
FEVER	19	81
PARAESTHESIA	28	72
OLIGURIA	0	100
WEIGHT LOSS	20	80



COMORBIDITIES

TABLE-5.6

CO MORBIDITIES	NO OF PATIENTS	PERCENTAGE
DIABETES	36	36%
HYPERTENSION	38	38%
COPD	2	2%
CAD	5	5%
PLHA	5	5%
DCLD	5	5%
OTHER	3	3%

BLOOD PARAMETERS

TABLE-5.9

BLOOD PARAMETERS	MEAN	SD
HEMOGLOBIN	6.43	1.54
TOTAL COUNT	2460	5.36
PLATELET COUNT	36940	11309
RETICULOCYTE COUNT	2.3	0.88
MCV	97.87	12.28
ESR	36.36	11.61
UREA	31.69	6.03
CREATININE	0.99	0.35
TOTAL BILIRBIN	1.41	0.4
DIRECT BILIRUBIN	0.56	0.32
SGOT	49.23	19.11
SGPT	45.05	15.73
LDH	304.75	99.29
VITAMIN B12	143.24	30.9

OTHER FINDINGS

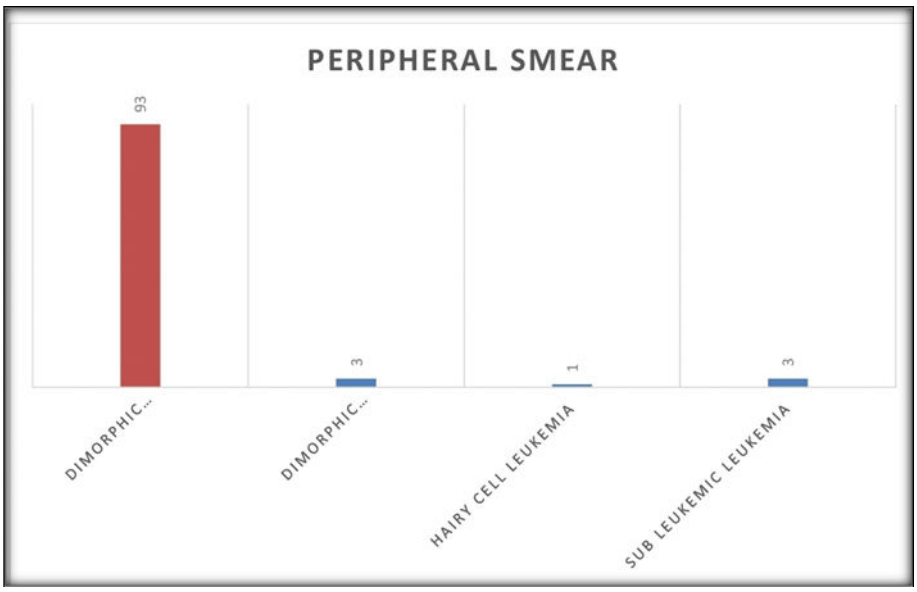
TABLE-6.8

OTHER FINDINGS	NO OF PATIENTS	PERCENTAGE
SPUTUM AFB	9	9%
ANA	1	1%
OESOPHAGEAL VARICES	5	5%
REDUCED CD4 COUNT	5	5%

PERIPHERAL SMEAR

TABLE-6.9

PERIPHERAL SMEAR	NO OF PATIENTS	PERCENTAGE
DIMORPHIC ANEMIA (MICRO/MACRO)	93	93%
DIMORPHIC ANEMIA (MICRO/NORMO)	3	3%
HAIRY CELL LEUKEMIA	1	1%
ACUTE PROMYELOCYTIC LEUKEMIA	3	3%



BONE MARROW CELLULARITY

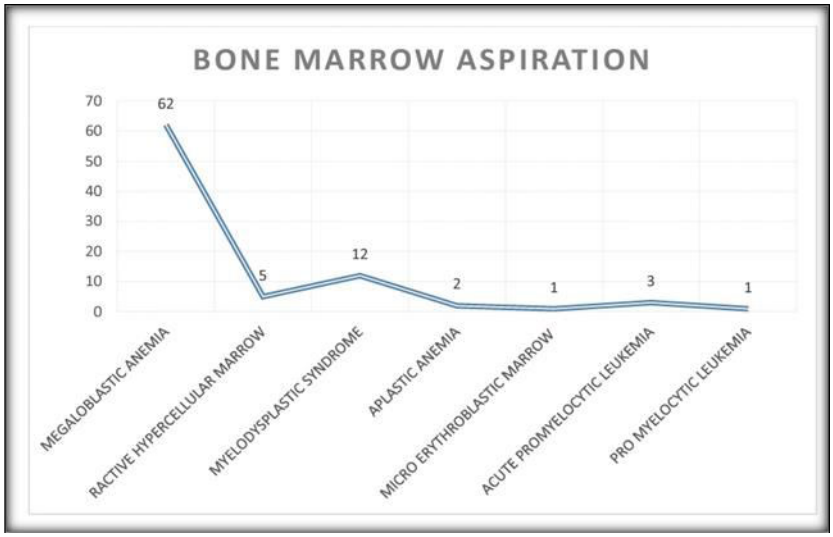
TABLE-7.1

BONE MARROW CELLULARITY	NO OF PATIENTS	PERCENTAGE
HYPERCELLULAR	84	84%
HYPOCELLULAR	2	2%
NORMAL	14	14%

BONE MARROW ASPIRATION

TABLE-7.2

BONE MARROW ASPIRATION	NO OF PATIENTS	PERCENTAGE
MEGALOBLASTIC ANEMIA	62	62%
RACTIVE HYPERCELLULAR MARROW	5	5%
MYELODYSPLASTIC SYNDROME	12	12%
APLASTIC ANEMIA	2	2%
MICRO ERYTHROBLASTIC MARROW	1	1%
ACUTE PROMYELOCYTIC LEUKEMIA	3	3%
HAIRY CELL LEUKEMIA	1	1%



MEAN AGE

TABLE-7.3

FINAL DIAGNOSIS	AGE IN YRS	
	MEAN	SD
MEGALOBLASTIC ANEMIA	65.05	4.01
MYELODYSPLASTIC SYNDROME	65.92	3.55
DISSEMINATED TB	64.67	3.67
HIV	64.4	1.81
CHRONIC LIVER DISEASE	64.2	3.27
ACUTE PROMYELOCYTIC LEUKEMIA	64	4.35
APLASTIC ANEMIA	58	5.65
HAIRY CELL LEUKEMIA	68	0
SLE	61	0

In this present study of 100 cases of pancytopenia, we have noted the following observations. Of the 100 cases, 63 patients were under the age of 65, 37 patients were of age more than 65 years. Thus this study reveals that the incidence of pancytopenia increases as the age advances. Of the 100 cases, 73 cases were males, remaining 27 patients were females. Majority of the patients in this study consumes mixed diet (79%) and majority of patients did not consume alcohol (61%) which reveals the different causes of pancytopenia, in addition to alcoholism. Majority of patients in this study (97%) have comorbidities such as Diabetes, Hypertension, COPD, CAD, HIV Disease, DCLD.

Most common comorbidity is Diabetes mellitus followed by Systemic hypertension. Major symptoms encountered in our patients were fatigue(73%), bleeding (9%), fever(19%), paresthesia(28%), weight loss(20%). Of signs, Pallor was present in all patients (100%), next common sign was lymphadenopathy (9%), Jaundice and splenomegaly was present in 5% of patients, Hepatomegaly in (7%) of patients ,Sternal tenderness was present in 2% of cases. serum LDH was elevated in most of the patients (99 %) with a mean serum LDH of 304.75 IU/L .CD4 count was low in all the five HIV positive patients presented with pancytopenia.

Chest x-ray was normal in majority of patients (89%) patients (27¾) had. Fibrocavity changes were present in 9% of patients. Pneumocystis jirovecii pneumonia associated chest x-ray findings were noted in HIV patients. Regarding bone marrow cellularity, 2% of patients had hypocellular marrow and 84% had hypercellular marrow. In remaining 14% of patients, bone marrow aspirations were not done because it was not clinically needed and they had, TB, HIV as their cause of pancytopenia. Bone marrow trephine biopsy was done only in patients who bone marrow aspiration yielded dry tap and subsequently the biopsy reported as Aplastic anemia.(68).By this study, probable cause of pancytopenia or primary diagnosis of these 100 cases of pancytopenia were as follows:(in descending order of frequency) a. MEGALOBLASTIC ANEMIA (62%) b. MYELODYSPLASTIC SYNDROME (12%) c. DISSEMINATED TB (9%) d. HIV (5%) e. CHRONIC LIVER DISEASE (5%) f. ACUTE PROMYELOCYTIC LEUKEMIA (3%)
g. APLASTIC ANEMIA (2%) h. HAIRY CELL LEUKEMIA (1%) i. SLE (1%).

DISCUSSION

Wide variety of disorders which primarily or secondarily affect the bone marrow can cause Peripheral pancytopenia. The causes of pancytopenia depend on the nutritional as well as socio-economic status, alcohol consumption, medications as well as the underlying bone marrow pathology. Causes of pancytopenia are not well defined in India Studies revealing the causes for pancytopenia in elderly population are limited in India. Even though many studies regarding the causes of pancytopenia in general have been published, studies on the clinical and aetiological profile on pancytopenia in elderly population in India is limited.

Increase in the geriatric population, poor socioeconomic status as well as passive attitude from the family members in elderly population might be the reason for lack of such studies in India. In this present study Megaloblastic anemia has found to be the most common cause for pancytopenia (62%) ,followed by Myelodysplastic syndrome(12%),Disseminated TB(9%) ,HIV disease(5%) ,Chronic liver disease(5%) ,Acute promyelocytic leukemia(3%) ,Aplastic anemia(2%),Hairy cell leukemia(1%) .Unlike in younger populations , acute infections were not found to be a cause for pancytopenia in this case. Autoimmune diseases were not found as a cause for

pancytopenia in elderly population. Decreased survival in patients with autoimmune disease might be the cause for absence of such cases as cause for pancytopenia in elderly population.

A comparison of the most common causes of pancytopenia in different studies:

Study group	Country	Year	No. of cases	Commonest cause
IAASG	Israel & europe	1987	319	Hypoplastic anemia
Hossain et al	Bangladesh	1992	50	Hypoplastic anemia
Verma &Dash	India	1992	202	Hypoplastic anemia
Tilak & Jain	India	1999	77	Megaloblastic anemia
Kumar et al	India	1999	166	Hypoplastic anemia
Khodke et al	India	2000	50	Megaloblastic anemia
Bajracharya et al	Nepal	2005	23	Hypoplastic anemia
Present study	**India**	**2020**	**100**	**Megaloblastic anemia**

IAASG-International Agranulocytosis and Aplastic Anemia Group

Various studies conducted throughout the world has reported aplastic anemia as the most common cause for pancytopenia. This is contrary to the reports from the Indian studies, which reveals Vitamin B12 deficiency as the most common cause for pancytopenia. Result obtained from the present study is also same as the other Indian studies, which is Vitamin B12 deficiency. This reflects the prevalence of nutritional deficiency in Indian population and also make us to think regarding the lacunas in geriatric medicine in our public health system.

Incidence of megaloblastic anemia in the present study is 62%. Khunger JM et al have reported an incidence of 72% and Tilak V et al have Indian reported an incidence of 68%. All these studies conducted in India shows the gravity of megaloblastic anemia in Indian population. Early detection and prompt treatment of this potentially curable disease in elderly population is rewarding for the physician as well as improves the quality of life in elderly population. Among pancytopenic patients the incidence of aplastic anemia varies from 10-52%.In our study the incidence is 2% , which doesn't correlate with the available studies . Kumar R et al have documented a higher incidence of 29.5%. Aplastic anaemia was idiopathic in most of the cases. Western studies have reported higher incidence of aplastic anaemia compared to the Indian studies on pancytopenia. Increased exposure to toxic chemicals might be the reason for higher incidence of aplastic anaemia in the western world. An Indian study have revealed the incidence of Myelodysplastic syndrome in about 5% of cases ,In our study the incidence has found to be 12%, which is comparatively higher compared to other Indian studies as well as Western studies . Now the commonest clinical condition associated with pancytopenia in a central referral hospital in Zimbabwe {30} and AIDS was diagnosed in 25¾ of the study cases in patients with multilineage blood cytopenia. In our study 5% patients has found to be having HIV infection. CD4 count was reduced in all the five patients with a mean CD4 count of 204.6. Two patients had chest X-Ray suggestive of Pnemocystis jirovecii pneumonia. The CD4 count in both the patients with Xray features s/o pnemocystis jirovecii was less than 100 .Drug induced aplasia , Cryptococcosis and HIV infection can be the other causes of pancytopenia in HIV infection].Hence it is important to r/o disseminated tuberculosis and other opportunistic infections in case of patients with HIV infection.

In 84% of cases bone marrow was hypercellular in our study which is in concordance with Imbert et al in which 66% of cases had hypercellular bone marrow. Megaloblastic anemia has been observed as the most common cause for pancytopenia in this study and most of the patients were consuming a vegetarian diet. This study also shows a higher prevalence of Megaloblastic anemia in Tamil Nadu compared to other states of India. Higher incidence of MDS is also documented in this study compared to other Indian study, which necessitates further studies for detecting underlying pathologies behind a higher incidence of MDS. Hence, in India, this study has very much importance in the public health as well as the health of geriatric population. If megaloblastic anemia is addressed at an earlier stage, it can improve the quality of life in elderly population and decreases the mental stress as well as financial burden in the family members

CONCLUSION

Pancytopenia is not an uncommon hematological problem encountered in clinical practice. 62 out of 100 patients in this study had low serum Vitamin B12 level. Unlike in young population, bone marrow failure syndromes and leukemias should be considered as a differential diagnosis for pancytopenia in elderly population. This study concludes that vitamin B12 deficiency as the most common cause for pancytopenia in elderly population. Detailed history, clinical features, primary haematological investigations along with bone marrow examination in pancytopenic patients is helpful for understanding the disease process, to diagnose or to rule out the causes of pancytopenia and helpful in planning further investigations and management of patients with pancytopenia.

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