PANCYTOPENIA – CLINICAL & HAEMATOLOGICAL STUDY AT TERTIARY CARE CENTRE.

Pathology

**Dr Chaitnya
Dnyanesh Khillare**

Assistant Professor, Department Of Pathology, SKNMCGH, Narhe, Pune.

**Dr Amardeep
Ajinath Patil**

Assistant Professor, Department Of Pathology, SKNMCGH, Narhe, Pune.

**Dr Bageshri
Parikshit Gogate***

Professor & HOD, Department Of Pathology, SKNMCGH, Narhe, Pune.*Corresponding Author

**Mrudul
Nagapurkar**

Student Academy Of Healthcare Science, Denville, New jersey, USA

ABSTRACT

INTRODUCTION: Pancytopenia is the simultaneous presence of anaemia, leucopenia and thrombocytopenia. This study was carried out to evaluate bone marrow findings in patients with pancytopenia. **MATERIALS AND METHODS:** This is retrospective study carried out on 100 pancytopenia patient over the period of two years. Peripheral blood smears (PBS), Bone marrow aspiration (BMA) & Trepine Biopsy slides were retrieved from storage. Data analysed was compared with various studies published in literature. **RESULTS:** The maximum cases of pancytopenia were in the age group up to 20 years with male preponderance. Megaloblastic anaemia (43%) was found to be most common aetiology of pancytopenia and followed by iron deficiency anaemia (23%). **CONCLUSION:** Present study concludes that basic primary haematological investigations along bone marrow aspiration/trepine bone biopsy in the pancytopenia patients are helpful in understanding the disease process. This plays a key role in planning the further management.

KEYWORDS

Pancytopenia, Megaloblastic Anaemia, Haematology.

INTRODUCTION

Sir William Harvey described blood as 'the fountain of life and the primary seat of the soul. The marrow of our bones is the seedbed of our blood.'⁽¹⁾

A multitude of disorders primarily or secondarily affecting the bone marrow manifests with various haematological derangements, which is reflected in the peripheral blood, commonly as pancytopenia.²

Pancytopenia was not a discrete haematological entity till as late as 1919. The term was used almost synonymously for Aplastic anaemia, it being the major cause of pancytopenia in Western countries.^{3,4}

Pancytopenia is the simultaneous presence of anaemia, leucopenia and thrombocytopenia. It exists in adults when haemoglobin concentration is less than 13.5 g/dl in males, 11.5 g/dl in females, the leukocyte count <4000/Cumm and platelet count <1.5 lakhs/cumm.¹

Various etiological factors have been implicated in the causation of pancytopenia. Major factors include reduction in blood cell production, infiltration of bone marrow (BM) by abnormal cells, suppression of bone marrow (BM), ineffective haematopoiesis with cell destruction, antibody mediated destruction of cells, and sequestration of cells in the reticulo-endothelial system.⁵

Various studies have done in India shows Megaloblastic Anaemia as major cause of pancytopenia. It is simple and treatable cause and reduces mortality and morbidity.⁶

Aim of the study is evaluate the clinico- haematological profile and causes of pancytopenia in adult patients from the population of this region at tertiary care hospital.

MATERIALS AND METHODS

Retrospective cross sectional study was carried out in department of pathology Smt. Kashibai Navle Medical College and General hospital (SKNMCGH), Narhe Pune. The retrospective data of 208 bone marrow aspiration and bone marrow biopsy (BMA & BMB) cases from January 2016 to January 2018 was collected.

During this period, patients who full fill the following criteria were provisionally selected in the study.

Criteria

1. Hgb ≤ 13.5 gm/dl (Male) or ≤ 11.5 gm/dl (Female)
2. Leucocytes count $< 4 \times 10^9/L$
3. Platelet $< 150 \times 10^9/L$

Cases having dry tap /inadequate biopsy are excluded from our study. Total 100 cases were included in study.

Peripheral blood smears (PBS), Bone marrow aspiration (BMA) & Trepine Biopsy slides were retrieved from storage.

Bone marrow aspiration (BMA) smears were stained with Leishman stain & Biopsy slides were stained with H&E stains. All BMA slides were also stained with Pearls stain to grade iron. Periodic acid-Schiff (PAS), Ziehl-Neelsen stain (ZN), Reticulin stains were used whenever required. Data analysis done on Microsoft excel sheet Data analysed was compared with various studies published in literature.

RESULTS

Age range in our study was from 2.3 months to 18 years.

The commonest age group of presentation of pancytopenia was < 20 years. With total 21% of cases.

Total 100 patient with pancytopenia were studied. Of these patient 57% were male & 43% were female. Male to female ratio (1.3:1).

The most common cause of pancytopenia in our study was Megaloblastic Anaemia (43%),

Followed by Iron Deficiency Anaemia (23%). Other causes include anaemia of chronic disease (2%), Dimorphic anaemia (18%), Aplastic anaemia (2%), Lymphoma (1%).

Marrow cellularity was evaluated on the Bone marrow Aspiration & Biopsy. Majority patient had Hyper cellular marrow (72%), followed by Normocellular (19%), & Hypo cellular (8%).

Bone marrow Aspiration were stained by Pearle's Prussian blue to evaluate Iron grade. It is observed that in Iron deficiency Anaemia (IDA) it is in the range of 0-2%, in Megaloblastic anaemia it is 0-4%, in cases of Dimorphic Anaemia 0-5%.

Table No 1

Age distribution among patient with pancytopenia

Age (Years)	Frequency	Percentage
<20	21	21%
21-30	18	18%
31-40	08	08%
41-50	18	18%
51-60	16	16%
61-70	15	15%
>70	04	04%

Table no 2**Causes of pancytopenia in study population**

Cause	Frequency	Percentage
IDA	23	23%
MA	43	43%
DA	18	18%
HS	01	1%
SA	04	04%
Lym	01	01
BMhypoplasia	01	01
Acute Leukemia	03	3%
ACD	02	2%
AA	02	2%
CDA	02	2%

(IDA- Iron deficiency Anaemia, MA- Megaloblastic Anaemia, DA- dimorphic Anemia, HS- Hypersplenism, SA- sideroblastic anemia, Lym- lymphoma, BM hypoplasia- bone marrow hypoplasia, ACD- Anemia of chronic disease, AA- aplastic anemia, CDA- congenital dyserythropoietic anemia)

Table no 3**Age and sex Distribution in comparison with other cases**

Sno	Author	Age distribution	No of cases	Predominant Age group affected	M:F ratio
1	Khodke et al.(2001) ⁷	3-69 yrs	50	12-30yrs	1.3:1
2	Khunger et al.(2002) ⁸	2-70yrs	200	21-30yrs	1.2:1
3	Hamid et al. (2008) ⁹	3-85 yrs	75	16-30yrs	1.03:1
4	Desalphine et al.(2014) ¹⁰	6-78 yrs	50	10-30 yrs	1.8:1
5	Dagdial et al.(2016) ¹¹	1-80 yrs	75	21-40yrs	0.87:1
6	Present study	2.3month-79yrs	100	2.3months-20 yrs	1.3:1

Table 4**Comparison of aetiology of pancytopenia found in the present study with that in other Indian studies.**

	Tilak & Jain (1999) ¹²	Khodke et al(2001) ⁷	Kumar et al (2001) ¹³	Niazi and Faizi & Raziq (2004) ¹⁴	Present study
No of cases	77	50	166	89	100
Commonest cause	Megaloblastic Anemia (68%)	Megaloblastic Anemia (44%)	Aplastic anemia (29.5%)	Aplastic anaemia (38.3%)	Megaloblastic anemia (56%)
2nd mc cause	Aplastic anemia (7.7%)	Aplastic anemia (14%)	Megaloblastic anemia (22.2%)	Megaloblastic Anemia (24.7%)	Iron Deficiency anemia (23%)

Fig.1 Hyper cellular marrow Micronormoblastic erythropoiesis **Fig.2 Lymphoma infiltrating bone marrow** **Fig.3 Megaloblastic anaemia with hypersegmented neutrophil** **Fig.4 Dimorphic anemia with anisopoikilocytosis****DISCUSSION**

Extensive studies have been conducted for the different etiological factors of pancytopenia.

In present study patient with age < 20 years (1st decade of life) are affected most commonly. Commonest age group affected by various study ranges from 10 to 40 years.

In our study male preponderance with M:F ratio 3.1:1. In most of the other studies also male preponderance was noted, except in the study by Dagadia et al.¹¹

The significant finding on physical examination included hepatomegaly (17%), splenomegaly (19%) & Lymphadenopathy (1%) in our study.

Gayathri et al.¹⁵ observed hepatomegaly in 26.9%, splenomegaly in 35.5% & Lymphadenopathy in 0.96% of patient in his study.

Khodake et al.⁷ noted hepatomegaly in 38% & splenomegaly in 48% & Lymphadenopathy in 14.7% of patient in his study. Variation in the clinical findings could be related to the spectrum of lesion in particular setup.

On the analyzing cause of pancytopenia we have come across Megaloblastic anaemia (43%) IDA (23%), marrow involvement in acute leukaemia, Lymphoma is 2% each.

Tilak & Jain et al.¹², Khodke et al.⁷, found in their studies, Megaloblastic anaemia (68% & 44%) as a most common cause of pancytopenia.

2nd most common cause of pancytopenia in the present study is IDA (23%).

In study done by Tilak & Jain et al.¹² second most common cause of pancytopenia is aplastic anaemia (7.2%). Same results are found in study done by Khodake et al.⁷

Study done by Kumar et al.¹³ shows Megaloblastic anaemia (22.2%) is 2nd most common cause of anaemia in the study.

We came across neoplastic aetiology for pancytopenia in 4% of our cases. These were NHL (Non Hodgkin's Lymphoma), acute leukaemia. Similar observations were made by various other workers like Khunger et al⁸, Pathak R et al¹⁶ who showed incidence of lymphoma 1% and 2.9% respectively. Other similar studies by Subrahmanyam et al.¹⁷ and Desalphine et al¹⁰ had incidence of lymphoma 3.7% and 4% respectively. While the Indian studies done by Kale p et al¹⁸, and Kumar et al¹³ show high incidence of acute leukaemia as 14.5% and 18% respectively.

The present study shows two cases (2%) of Anaemia of chronic disease. On analyzing various other studies the incidence of anaemia of chronic disease was negligible, where in a study done by Subrahmanyam et al.¹⁷ it was 7.5%.

In our study patients with megaloblastic anaemia had iron store grade in marrow in range of 0-4. Study done by Pujara et al¹⁹ also showed iron store grade in marrow in range of 1-4 in Megaloblastic anaemia patients.

CONCLUSION

Pancytopenia is a common hematological presentation encountered in day today's clinical practice. It should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed. After routine haematological examination, Bone marrow aspiration/trephine bone biopsy is an important diagnostic tool in haematology which helps to evaluate various causes of pancytopenia.

In this study Megaloblastic anaemia was diagnosed in 43% patients who constituted the commonest aetiology of pancytopenia. This was followed by IDA in 23%.

Megaloblastic anaemia due to vitamin B12 /Folate deficiency seems to reflects higher prevalence of pancytopenia in Indian subjects.

Present study concludes that basic primary haematological investigations along with bone marrow aspiration/trephine bone biopsy and biochemical parameters in the pancytopenia patients are helpful in understanding the disease process. This plays a key role in planning the further management.

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