



ORIGINAL ARTICLE

Evaluation of pancytopenia based on bone marrow examination in adults in a tertiary care hospital in Islamabad.

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ABSTRACT... Objective: To evaluate etiological spectrum of pancytopenia in adults using bone marrow aspiration biopsy. **Study Design:** Randomized Prospective study. **Setting:** Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad. **Period:** October 2018-October 2020. **Material & Methods:** Eight hundred bone marrow biopsies were performed out of which 250 patients came with pancytopenia. 135 patients out of these were in adult age group which are included in this study. **Results:** Out of 250 patients adults were 135 that presented with pancytopenia. Male to female ratio came out to be 1.22:1. The most common disorder that results in pancytopenia came out to be megaloblastic anemia that was 29.6%, after that 26.6% were infection related changes, 10.3% aplasia, 9.6% reactive marrow, 5.9% acute leukemia, 3.7% chronic leukemia and iron deficiency anemia followed by 2.9% myelodysplastic syndromes and hypersplenism, 2.2% multiple myeloma, 1.4% mixed deficiency anemia and 0.74% myelofibrosis. We also analyzed patients on their presenting complaints as well. Most common complaint of presentation was fever (54.8%), (31.85%) with fatigue and malaise, (31.1%) pallor, vomiting and diarrhea (25.9%) followed by bleeding (14.8%). On clinical examination 12% cases presented with hepatomegaly and 16.6% with splenomegaly. **Conclusion:** Pancytopenia is a common hematological finding in our setup with megaloblastic anemia to be the most common cause of it. Therefore, it's very important to diagnose it as this is a curable (reversible) deficiency and patients can easily be managed to prevent serious hematological and neurological abnormalities.

Key words: Bone Marrow Aspiration, Infections, Megaloblastic Anemia, Pancytopenia.

INTRODUCTION

Patients presenting with pancytopenia are relatively common issue in our setups. It is a challenge to timely evaluate and find the underlying cause of pancytopenia in routine clinical practice.¹ It can be defined as decrease values in all the cell lines that is red blood cell count/hemoglobin, white blood cell count and platelet count leading to decrease in hemoglobin, total leucocyte counts and platelet levels causing anemia, leukopenia and thrombocytopenia in patients.^{2,3} Usually the patients with pancytopenia presents with signs of easy bruising, pallor, history of repeated infections and bleed.^{4,5}

Patients with pancytopenia usually present with unexplained fatigue, weakness, difficulty in breathing, history of repeated infections, easy

bruising, easy gum bleeds owing to decline in values of all the cell lines.^{6,7,8}

Pancytopenia can be defined as hemoglobin less than 10g/dl, with an absolute neutrophil count of $1.5 \times 10^9/L$ or less and a platelet count of less than $100 \times 10^9/L$.^{9,10} The etiology of pancytopenia in all individuals ranges from brief marrow suppression to marrow infiltration by metastatic carcinomas.¹¹ It results from failure of production of hemopoetic stem cells due to their replacement by tumor cells or fibrosis. It can be constitutional, resulting from an inherited genetic defect or can be acquired that can be due to immune related damage to stem cells or their surrounding microenvironment.^{12,13}

The presence of pancytopenia apart from chemotherapy or radiotherapy is a common

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diagnostic dilemma and a bone marrow aspiration biopsy is recommended.^{14,15}

Some of the important causes of pancytopenia includes aplastic anemia, cancers, autoimmune diseases, chemotherapy, infections, megaloblastic anemia, fanconi's anemia and many more.¹⁶

We conducted a study in our hospital to know the percentage of possible causes of pancytopenia in our population because many of them are easily treatable which we encounter in routine practice.

MATERIAL & METHODS

A prospective hospital based study was done at department of pathology in Pakistan Institute of Medical Sciences, Islamabad over a period of two years from October 2018 to October 2020. All the patients presented in OPD were diagnosed with pancytopenia on complete blood picture along with peripheral film.

Total 800 bone marrow biopsies were performed in our pathology department in these two years out of which a total of 135 patients were adults that presented with pancytopenia. Using automated cell counter (Sysmex) pancytopenia was confirmed in patients. Pancytopenia is defined as hemoglobin of less than 10g/dl, an absolute neutrophil count of equals to or less than $1.5 \times 10^9/L$ and platelet count less than $100 \times 10^9/L$ (3). Decreased platelet count was confirmed manually by performing peripheral blood film exam. Bone marrow aspiration and biopsy was done in all cases of pancytopenia. Special stains were used like myeloperoxidase where necessary. Various related causes/diagnoses of pancytopenia were recorded, and results were drawn accordingly. Mean and standard deviation both were calculated for quantitative variables e.g. age. Frequencies and percentages were calculated for qualitative variables like diagnosis and gender. Data was scrutinized using SPSS version 20. Approval from ethical review board was obtained (No. F. 1-1/2015/ERB/SZAMBU) along with informed consent was taken from patients.

Patients of age 15 year and above, including both sexes and fulfilling the criteria for pancytopenia were all included in this study. Patients whose bone marrow aspirate sample was not enough or could not give any proper diagnosis were excluded from this study. All the patients who were on radiotherapy, chemotherapy and are already diagnosed patients of pancytopenia were also removed from the study.

RESULTS

Out of 135 pancytopenia patients presented, 1.2:1 was the male to female ratio. Common conditions that are related with pancytopenia was macrocytic (megaloblastic) anemia, following infections, aplastic anemia, reactive marrow, acute leukemia and hypersplenism.

Most associated symptom with which patients presented was fever (54.8%), followed by fatigue with malaise (31.8%), (31.1%) patients presented with pallor, vomiting and loose stools (25.9%) and bleeding from gums and various other sites (14.8%).

During clinical examination organomegaly was observed in 52 patients out of 135 patients. In total 17% patients presented with hepatosplenomegaly, 8.8 % with hepatomegaly and 12.5% with splenomegaly.

Average age of study sample is from 18 years to 67 years with an average age of 46 years + 15.4 SD.

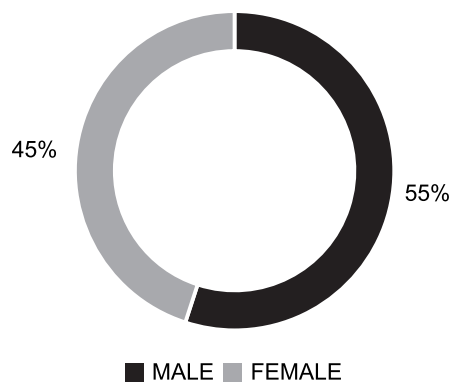


Figure-1. Representing gender distribution among patients

Disease	No of Cases (n=137) (%)
Myelofibrosis	1 (0.74%)
Mixed Deficiency Anemia	2 (1.48%)
Multiple Myeloma	3 (2.22%)
MDS	4 (2.96%)
Hypersplenism	4 (2.96%)
Chronic Leukemia	5 (3.70%)
IDA	5 (3.70%)
Acute Leukemia	8 (5.93%)
Reactive Marrow	13 (9.63%)
Aplasia	14 (10.37%)
Infection Related Changes	36 (26.67%)
Megaloblastic Anemia	40 (29.63%)

Table-I. Etiological spectrum of diseases in adults presented with pancytopenia

Symptoms	No of Cases (n=137)	Percentage
Fever	74	54.8 %
Bodyaches	43	31.8 %
Pallor	42	31.1 %
Diarrhea & Vomiting	35	25.92 %
Bleeding	20	14.8 %

Table-II. Distribution of cases according to their presenting complaints

DISCUSSION

Pancytopenia is very common hematological condition in our population.^{17,18} Patients with symptoms like bleeding, bruises, fever etc must be investigated for pancytopenia using complete blood count.¹⁹ As a wide variety of malignant and non- malignant diseases can be presented with complaints related to pancytopenia. For a confirmative diagnosis bone marrow examination should be done.²⁰

There are various studies that has been done to view the etiological spectrum of pancytopenia. There are various diseases that results into pancytopenia which vary depending upon the health status, genetic variation and difference in the geographical areas.^{20,21}

In present study, commonest cause related to pancytopenia came out to be megaloblastic anemia (29.6%), second being the infections (26.6%), followed by aplasia (10.3%). All these conditions were diagnosed on evaluating

complete blood count, peripheral film and bone marrow examination. For diagnosis of leukemia's special stains were used along with immunohistochemistry.

A similar study was conducted by Farooque R, Iftikhar S, Herekar F, Patel MJ in Karachi, Pakistan in which megaloblastic anemia (41.7%) was the leading cause for pancytopenia like in our study, followed by cases of hypersplenism (16.6%) as the second most common cause, ours being the infection.³

In 2018 a study was conducted in India studying the spectrum of pancytopenia in adults in which the leading cause of pancytopenia again came out to be megaloblastic anemia that was a similar to the result of ours. In this study the commonest mode of presentation was weakness/fatigue (55%) followed by fever (33%). However the leading complaint in our study is fever (54.8%) followed by body aches (31.8%).⁶

Jain A. did a study in India to study the spectrum of pancytopenia presenting in their hospital. The commonest complaint in this study is same as in our study that is fever (60%). The result of their study is quite similar to ours as megaloblastic (macrocytic) anemia was the most common cause resulting pancytopenia (37%), second being the dimorphic anemia (26%).⁵

More of such studies were done by Zeeshan R in 2019 in Pakistan and by Doshi D in 2012. Both the studies showed very similar results as compared to our study. Megaloblastic anemia (27.8% and 45%) was again the leading cause resulting into pancytopenia.^{7,13}

All the above studies were conducted in Asian countries including ours too. So we can possibly say that megaloblastic anemia one of the leading cause resulting into pancytopenia that can be explained in terms of poor health and nutritional status in these developing countries which is the possible reason of developing megaloblastic anemia in them.

However, a study conducted in Mexico in 2019

by C.J.VARGAS-CARRETERO et al. in which in contrast to this study, their leading cause resulting into pancytopenia came out to be myelodysplastic syndrome (20.2%) followed by megaloblastic anemia (18.3%) and acute leukemia's (12.8%). The most common presenting complaint was pallor (82%) in contrast to ours which was fever.⁸

Nell EM did a similar study in South Africa in 2022 to know the causes of pancytopenia in which came out as 25%, chemotherapy, 18% sepsis and 9% malignancy cases.¹²

That was also quite contrary to our study and other studies that were done in Asian countries in which megaloblastic (macrocytic) anemia was among the leading cause resulting into pancytopenia in patients.

CONCLUSION

Pancytopenia is a common hematological finding in our setup with megaloblastic anemia to be the most common cause of it. Therefore, it's very important to diagnose it as this is a curable (reversible) deficiency and patients can easily be managed to prevent serious hematological and neurological abnormalities.






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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Maryam Zulfiqar	Data collection, Analysis, Article writing.	
2	Bushra Anam Ali	Conceived and Designed the analysis, Data collection.	
3	Shahzad Ali Jiskani	Study design, Interpretation of data.	
4	Maryam Waqar	Data collection, Data analysis.	
5	Maliha Saad	Data interpretation, Discussion.	
6	Humera Javed	Paper review, Data collection.	