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ORIGINAL ARTICLE

To Determine the Common Causes Leading to Pancytopenia in Patients Presenting to Tertiary Care Hospital, Lahore

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ABSTRACT

Background: New-onset pancytopenia can be caused by a wide variety of etiologies, leading to an array of prolonged and invasive investigations. Knowing the important differentials can help in targeted screening and early diagnosis. The reported frequency of common causes of pancytopenia varies among existing studies due to population and geographic differences in dietary habits and environmental and genetic factors, thus necessitating the present study. The goal is to determine the frequency of the leading causes of pancytopenia in patients presenting to the hospital.

Subjects and methods: This study is a cross sectional study involving 140 patients of both genders aged between 12 to 80 years presenting with pancytopenia to Sir Ganga Ram hospitals, Lahore. These patients underwent detailed clinical and lab evaluation to identify the underlying cause of pancytopenia e.g. aplastic anemia, megaloblastic anemia, hypersplenism and acute leukemia. The etiological spectrum of pancytopenia was stratified by various subgroups of patients based on age and gender. A written informed consent was taken from each patient.

Results: The mean age of the patients was 47.2±19.9 years. There were 90 (64.3%) male and 50 (35.7%) female patients in the study group with a male to female ratio of 1.8:1. Among the underlying causes of pancytopenia, aplastic anemia was most frequent and was observed in 54 (38.6%) patients followed by megaloblastic anemia (n=39, 27.9%), hypersplenism (n=24, 17.1%) and acute leukemia (n=23, 16.4%). Upon stratification, no statistically significant difference was observed in the frequency of various underlying causes of pancytopenia across various subgroups of patients based upon age and gender.

Conclusion: In the present study, aplastic anemia and megaloblastic anemia were found as the most frequent cause underlying pancytopenia regardless of patient's age and gender. This advocates their consideration as important differentials in the diagnostic evaluation of patients presenting with pancytopenia in future medical practice so that timely identification and management may improve the outcome of such cases.

Keywords: Pancytopenia, Etiological Spectrum, Aplastic Anemia, Megaloblastic Anemia

INTRODUCTION

Peripheral film pancytopenia is defined as reduced number of all three cell lines of blood to subnormal levels leading to anemia, leucopenia and thrombocytopenia simultaneously.[1] Thus, it is a triad of a syndrome with many different causes. The presenting symptoms are usually caused by anemia and thrombocytopenia like fatigue and bleeding or bruising. Leucopenia is a less frequent cause of initial presentation however it can prove to be fatal during the course of disease.[2] The mechanism of development of pancytopenia varies from bone marrow replacement or failure and splenic pooling or peripheral destruction of mature cells.[3] The causes of pancytopenia are many and vary according to geographical and racial distribution. The most common causes are aplastic anemia (33.3%), megaloblastic anemia (26.6%), hypersplenism (20%), acute leukemia (10%), drug induced (5%), and metastatic tumor (5%). In a study conducted at Irsa University Hyderabad, aplastic anemia (33%) was found to be the commonest cause of pancytopenia. Aplastic anemia is attributable to exposure to toxic chemicals and increasing use of pesticides.[4] Majority of the studies conducted in India showed that the most common cause of pancytopenia is megaloblastic anemia (41%) which is owing to the fact that a large proportion of Indian population is purely vegetarian. Although nutritional causes are most common in developing countries, hematological malignancies are more common in developed ones.[6]

Although pancytopenia is not an uncommon clinicohematological entity and has an exhaustive list of differential diagnoses, it is not mentioned very often in literature and even textbooks of medicine. Also, the frequency of causes varies widely in different areas owing to different eating habits, environmental exposures and prevalence of infections and other diseases.[7] This study aims to investigate and identify the common causes of pancytopenia in our set up, to assist in forming strategies to combat the common etiological factors to prevent pancytopenia. It also aims to identify the most common presenting features so that the clinicians can keep a high index of suspicion whenever these are encountered during the clinical practice, leading to timely diagnosis and treatment. The clinical outcome will be discussed in patients with treatable causes. It can also aid in establishing an effective diagnostic approach for various causes of pancytopenia.

MATERIALS AND METHODS:

This cross sectional study was conducted in Medical unit 2 in Sir Ganga Ram Hospital/ Fatima Jinnah Medical University Lahore for a period of 6 months from 2.05.2020 to 1.11.2020 after approval by the institutional ethical review committee. Sample size of 140 cases was calculated with a 95% confidence interval and 5% margin of error while taking expected frequency of acute leukemia as 10.0%. Patients were selected by a nonprobability consecutive sampling technique. The study included all the male and female patients presenting with pancytopenia on complete blood count to the OPD and emergency, aged between 12 to 80 years, except those with diagnosed cases of malignancy or undergoing chemotherapy or radiotherapy. **Diagnosed cases of bleeding disorders and pregnant females with pancytopenia.** After taking informed consent, patient history and examination were done and venous blood was sent for investigations such as CBC, peripheral film etc. followed by ultrasound abdomen. Bone marrow aspiration studies were done only where indicated, avoiding the cases where the cause of pancytopenia was obvious. Likewise, serum folate was done only where indicated (MCV >100fL). All the collected data was entered and analyzed through SPSS version 21.0. Numerical variables; age were presented by mean ±SD. Categorical variables i.e. gender and common causes of pancytopenia were described using percentage and frequency. Effect modifiers were addressed using data stratification for age and gender. A p-value of ≤0.05 as significant was used for chi-square test.

RESULTS

Patient age ranged from 12 years to 80 years, mean value 47.2±19.9 years. Majority (n=68, 48.6%) of the patients were

aged above 50 years followed by 47 (33.6%) patients aged between 25-50 years and 25 (17.8%) patients aged under 25 years.

The study group contained 90 male (64.3%) and 50 female (35.7%) patients with a male-female ratio of 1.8:1 as shown in Table 8.1.

Among the underlying causes of pancytopenia, aplastic anemia was most frequent and was observed in 54 (38.6%) patients followed by megaloblastic anemia (n=39, 27.9%), hypersplenism (n=24, 17.1%) and acute leukemia (n=23, 16.4%) as shown in Table 8.2.

When stratified, there was no statistically significant difference in the frequency of various underlying causes of pancytopenia across various subgroups of patients based upon age and gender as shown in Tables 8.3 – 8.6.

Table 0.1: Baseline Characteristics of Study Sample

Characters	Participants n=140
Age (years)	47.2±19.9
• <25 years	25 (17.8%)
• 25-50 years	47 (33.6%)
• >50 years	68 (48.6%)
Gender	
• Male	90 (64.3%)
• Female	50 (35.7%)

Table 0.2: Frequency of various underlying Causes in Patients with Pancytopenia n=140

Underlying Cause of Pancytopenia	Frequency (n)	Percent (%)
Megaloblastic Anemia	39	27.9%
Aplastic Anemia	54	38.6%
Hypersplenism	24	17.1%
Acute Leukemia	23	16.4%
Total	140	100.0%

Table 0.3: Stratification of Megaloblastic Anemia across various subgroups of Pancytopenic Patients n=140

Subgroups	n	Megaloblastic Anemia n (%)	P-value
Age			
• <25 years	25	7 (28.0%)	0.999
• 25-50 years	47	13 (27.7%)	
• >50 years	68	19 (27.9%)	
Gender			
• Male	90	25 (27.8%)	0.978
• Female	50	14 (28.0%)	

Chi-square test, observed difference was statistically insignificant

Table 0.4: Stratification of Aplastic Anemia across various subgroups of Pancytopenic Patients n=140

Subgroups	n	Aplastic Anemia n (%)	P-value
Age			
• <25 years	25	10 (40.0%)	0.987
• 25-50 years	47	18 (38.3%)	
• >50 years	68	26 (38.2%)	
Gender			
• Male	90	35 (38.9%)	0.918
• Female	50	19 (38.0%)	

Chi-square test, observed difference was statistically insignificant

DISCUSSION

Pancytopenia is characterized by subnormal levels of erythrocytes, leukocytes and platelets. Instead of a disease, it is a triad of cytopenias originating from various deficiencies and disease processes[1]. It does not have any specific signs and symptoms; instead they are directly proportional to the severity of the underlying cytopenias as well as the etiology[2]. As underlying causes are difficult to assess without extensive invasive procedures, patient management remains very challenging and time consuming for physicians[3].

Pancytopenia commonly requires bone marrow examination. Cytotoxic treatments such as radiotherapy and chemotherapy, are often causative factors for pancytopenia in patients being treated for neoplasia. Outside this setting, new-onset pancytopenia can be difficult to diagnose, with a myriad of causes: autoimmune disorders, bone marrow failure syndromes, marrow space-occupying lesions, peripheral destruction of hematopoietic cells, infections etc. The workup of new-onset pancytopenia often requires a detailed clinical, medication, recreational drug and environmental exposure history[10]. Knowing the important differentials can help in targeted screening and early diagnosis. The reported frequency of frequent causes of pancytopenia varied[3-6] among existing studies due to population and geographic differences in dietary habits and environmental and genetic factors which necessitated the present study.

The aim of this study was to find out the frequency of common causative factors of pancytopenia in patients presenting to Sir Ganga Ram Hospital Lahore.

The mean patient age in our study was 47.2±19.9 years. Our observation is in line with that of Arshad et al.[87] (2016) who reported similar mean age of 46.6±18.9 years among such patients at Department of Hematology (Pathology), Army Medical College, Rawalpindi. In an Indian study, Deshpande et al.[88] (2019) reported similar mean age of 48.5±15.1 years among pancytopenic patients in line with the present study. Our observation also matches with that of Hossain et al.[89] (2017) who observed similar mean age of 47.3±15.0 years among Bangladeshi such patients. Similar mean age of 49.4±20.7 years has been reported by Vargas-Carretero et al.[90] (2019) among Mexican patients with pancytopenia.

Our study had a male to female ratio of 1.8:1 and a similar male preponderance was observed by Tareen et al.[91] (2012) at Combined Military Hospital Quetta. In another local study, Jan et al.[92] (2013) reported a similar ratio of 1.8:1 among such patients presenting at Rehman Medical Institute Peshawar while Khan et al.[93] (2018) observed it to be 1.9:1 at The Children's Hospital and Institute of Child Health, Lahore. Comparable male predominance has also been reported by Shinwari et al.[94] in 2012 (2:1) at Hayatabad Medical Complex, Peshawar. In similar Indian studies involving pancytopenic patients, Bijaya et al.[95] (2017), Dasgupta et al.[96] (2015) and Barik et al.[97] (2014) also reported similar male predominance with male to female ratio of 1.5:1, 1.6:1 and 1.5:1 respectively. A much higher male predominance with male to female ratio of 2.6:1 has been reported by Jain et al.[1] (2013) in India.

We observed that among the underlying causes of pancytopenia, aplastic anemia was most frequent and was observed in 38.6% patients followed by megaloblastic anemia (27.9%), hypersplenism (17.1%) and acute leukemia (16.4%). Upon stratification, no statistically significant difference was observed in the frequency of various underlying causes of pancytopenia across various subgroups of patients based upon age and gender.

Our observation is in line with a previously published local study where Ujjan et al.[4] (2010) reported similar distribution of aplastic anemia (33.3%), megaloblastic anemia (26.6%), hypersplenism (20.0%) and acute leukemia (10.0%) among pancytopenic patients presenting at Isra University Hospital, Hyderabad. In another local study, Niazi et al.[3] (2011) observed similar frequency of aplastic anemia, megaloblastic anemia, hypersplenism and acute leukemia and reported it to be 38.3%, 24.7%, 16.0% and 13.6% respectively at Lady Reading Hospital Peshawar. Our observation is also in line with that of Dasgupta et al.[96] (2015) who reported comparable frequency of aplastic anemia (33.5%), megaloblastic anemia (21.0%) and hypersplenism (13.7%) among pancytopenic patients in India. In another Indian study, Singh et al.[98] (2016) observed similar frequency of aplastic anemia, megaloblastic anemia, hypersplenism and acute leukemia

and reported it to be 44.0%, 20.0%, 12.0% and 12.0% respectively.

The present study adds to the limited already published local research evidence on the topic. In the present study, aplastic anemia and megaloblastic anemia were found as the frequent cause undying pancytopenia regardless of patient's age and gender. This has multiple implications. On one side, we need to focus on the preventive aspects of aplastic and megaloblastic anemias like avoidance of exposures to environmental and chemical agents and drugs which can cause aplastic anemia along with nutritional improvement to prevent megaloblastic anemia. On the other side, the results of the present study advocates consideration of aplastic and megaloblastic anemia as important differentials in the diagnostic evaluation of patients presenting with pancytopenia in future medical practice so that timely identification and management may improve the outcome of such cases.

The strengths of the present study were its large sample size of 140 cases and strict exclusion criteria. We also stratified the data to address effect modifiers like age and gender. A very strong limitation to the present study was that we didn't consider other effect modifiers like patient's occupation, residence, smoking and family history which could have helped us to identify potential attributable factors of pancytopenia. Such a study is highly recommended in future clinical research.

CONCLUSION

In the present study, aplastic anemia and megaloblastic anemia were found as the most frequent cause underlying pancytopenia regardless of patient's age and gender which advocates their consideration as important differentials in the diagnostic evaluation of patients presenting with pancytopenia in future medical practice so that timely identification and management may improve the outcome of such cases.

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