# ORIGINAL ARTICLE Frequency of Aplastic Anemia Among Adults Patient with Pancytopenia: A Cross-Sectional Study Design

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### ABSTRACT

Objective: To determine the frequency aplastic anemia among adult patients with pancytopenia.

Place and duration of study: The study is conducted at Department of Medicine, MTI-Lady Reading Hospital, Peshawar and the duration of study is From 25-04-2018 to 25-10-2018.

**Material and Method:** It is a Descriptive cross sectional study design having sample size of 135 patients, this study using 95% confidence level and 7% margin of error, under WHO software for sample size determination. The sampling technique we have used in this study is the non-probability consecutive sampling. All adult patients with newly diagnosed pancytopenia of any duration, Age group above 18 years to 60 years belongs to any gender are included in this study design. SPSS 23 was used to evaluate all the data.Mean and Standard Deviation was calculated frequency and percentages were calculated. Using the chi square test results are examine the effect modification. A p-value of 0.05 or below was considered significant.

**Results**: At the MTI-Lady Reading Hospital in Peshawar's Department of General Medicine, 135 patients participated in this study. According to descriptive data, the mean and SDs for age were recorded as 55+12.85 and 3+1.18, respectively. In the 18–30 age range, there were 27 (20%) patients, whereas the 31–60 age group had 108 (80%) individuals. In a similar manner, 44 (32.59%) patients were recorded as female and 91 (67.40%) patients were recorded as male. According to frequency and prevalence rate for aplastic anaemia, 103 (76.29%) patients were identified as having this condition.

**Practical Implications:** The current study's objective is to determine the prevalence of aplastic anaemia in people with adult pancytopenia. Despite the availability of study, statistics show that the severity of aplastic anaemia varies from population to population, and pancytopenia is not uncommon in our society.

**Conclusion:** This study evaluated that aplastic anaemia is the most prevalent cause of pancytopenia in the Khyber Pukhtunkhwa population, and that bone marrow aspiration is a recognised diagnostic method for the assessment of pancytopenia.

**Keywords:** Aplastic anemia, Bone marrow, Megaloblastic Anemia, Pancytopenia, Bone marrow failure Syndrome, . Myelophthisic anemia, Thrombocytopenia.

## INTRODUCTION

Aplastic anemia (AA) is a rare bone marrow failure syndrome of unknown etiology characterized by hypocellular marrow and severe persistent pancytopenia in the absence of major dysplastic signs or marrow fibrosis<sup>1</sup>. Different epidemiological studies are conducted to determine the comprehensive incidence of aplastic anemia, providing result of an increase in population with 2-3 times higher ratio in asian countries<sup>2</sup>.Pediatric apalstic anemia seen more frequently in adolescents and young adults<sup>3</sup>. Hypocellularity and bone marrow aplasia are thought to be primarily triggered by immune-mediated death of hematopoietic stem cells<sup>4</sup>. Compared to adults, paediatric patients with acquired AA had better results<sup>5</sup>.

Pancytopenia refers to a reduction below normal values of all 3 peripheral blood lineages i.e. leukocytes, platelets and erythrocytes<sup>6</sup>. Pancytopenia may be acquired inherited (genetic but not necessarily present at birth)<sup>7</sup>. The pathogenesis of pancytopenia is either a failure of production of hematopoietic progenitors or peripheral destruction of cellular element due to infection, immune mediated damage or hypersplenism<sup>8</sup>. Pancytopenia requires microscopic examination of a bone marrow biopsy specimen and a marrow aspirate to assess overall cellularity and morphology<sup>6</sup>. Bone Marrow Examination is one of the important diagnostic procedures for many hematological disorders.

A decrease in all three cell lines is the most common manifestation of bone marrow failure. Aplastic or hypoplastic anemia can be idiopathic in nature, or it can develop from secondary causes. Myelodysplastic anemia also can cause pancytopenia. Myelophthisic anemia may result from marrow destruction because of tumor invasion or granulomas.

Patient morbidity and mortality are increased by bone marrow failure that prevents the production of one, two, or all three blood cell lines. Low amounts of mature blood cells contribute to the morbidity and mortality of pancytopenia. A high-output heart failure and tiredness might result from severe anaemia. Infections with bacteria and fungi can be more likely to affect people who have neutropenia. Spontaneous bleeding and haemorrhage can occured by thrombocytopenia. Severe pancytopenia is a medical emergency, requiring rapid institution of definitive therapy (ie, early determination of supportive care and bone marrow transplant candidates).

Aplastic anemia is a syndrome of bone marrow failure characterized by peripheral pancytopenia and marrow hypoplasia (see the image below). Although the anemia is often normocytic, mild macrocytosis can also be observed in association with stress erythropoiesis and elevated fetal hemoglobin levels.

**Operational Definitions:** Pancytopenia: A patient is said to have Pancytopenia, when peripheral smear of blood shows all of the following features;

- Hemoglobin< 10g/dl</p>
- Total leucocyte count < 4,000</p>
- Platelets < 150,000</p>
- Reticulocyte count <2%</p>

Aplastic anemia: Hypocellularity i.e. decrease in the hematopoetic cells below 70% of the bone marrow on bone marrow aspiration.

#### MATERIAL AND METHODS

The study is conducted at Department of Medicine, MTI-Lady Reading Hospital, Peshawar and the duration of study is From 25-04-2018 to 25-10-2018.

It is a Descriptive cross sectional study design having sample size of 135 patients, this study using 95% confidence level and 7% margin of error, under WHO software for sample size determination. The sampling technique we have used in this study is the non-probability consecutive sampling. All adult patients with newly diagnosed pancytopenia of any duration, Age group above 18 years to 60 years belongs to any gender are included in this study design.

Patient already on treatment for diseases like cancer chemotherapy, Aplastic anemia and leukemias as detected by history and medical record, Already diagnosed cases of iron deficiency anemia, aplastic anemia, Megaloblastic anemia, leukemias and infectious diseases are excluded in this investigative study as they may create biasness in the study results.

After approval of study from research committee of CPSP, informed consent of patients are taken, all patients were explained that the study was done for data publication and research purpose. The privacy implications of the collected information was clearly explained to the patients.

A sample of venous blood from each patient was taken, and it was sent to the hospital laboratory for the peripheral smear examination. An experienced haematologist with at least five years of experience performed the bone marrow aspiration.

All the above mentioned information including name, Age, Sex, hematological profile, duration of illness and Address was recorded on pre-designed Performa.

SPSS 23 was used to evaluate all the data that was gathered.Mean and Standard Deviation was calculated for numerical variable like age. For gender and aplastic anaemia, frequency and percentages were calculated. Using the chi square test, aplastic anaemia was stratified by age, gender, and duration of sickness to examine the effect modification. A p value of 0.05 or below was considered significant. The current study's objective is to determine the prevalence of aplastic anaemia in people with adult pancytopenia. Despite the availability of study, statistics show that the severity of aplastic anaemia varies from population to population, and pancytopenia is not uncommon in our society. From this study design, we will learn the local magnitude of AA in adult pancytopenia patients. In order to inform them of the seriousness of the issue and help them plan for future research and treatment recommendations, the study's findings will be distributed to local health professionals.

#### RESULT

At the MTI-Lady Reading Hospital in Peshawar's Department of General Medicine, 135 patients participated in this study. According to descriptive data, the mean and SDs for age were recorded as 55+12.85 and 3+1.18, respectively. (Table No.1).

In the 18–30 age range, there were 27 (20%) patients, whereas the 31–60 age group had 108 (80%) individuals. In a similar manner, 44 (32.59%) patients were recorded as female and 91 (67.40%) patients were recorded as male. According to frequency and prevalence rate for aplastic anaemia, 103 (76.29%) patients were identified as having this condition. (Table No.2).

Stratification of aplastic anemia with respect to age, gender and duration of illness is determined and quoted in Table No.3.

Table	1 · 1	Descri	otive	statistics	(n=135)	۱.
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Quantitative Variables	Mean & SDs	
Age	55+12.85	
Duration of illness	12.85	

Table 2: Frequencies and percentages for aplastic anemia (n=135)

Variables		Frequency	Percentage	
Age	Age groups			
Distribution	18-30 Years	27	20%	
	31-60 years	108	80%	
Gender distribution	Gender			
	Male	91	67.40%	
	Female	44	32.59%	
Occurrence of Aplastic	Aplastic Anemia			
Anemia	Yes	103	76.29%	
	No	32	23.70%	

•	Table 3: Stratification of aplastic anemia (n=135)								
	Variables	Aplastic anemia	Frequency	Percentage	P-value				

with Respect					0.294
to Gender	Gender				
	Male	YES	67	49.62%	
		NO	24	17.77%	
	Female	YES	36	26.66%	
		NO	08	5.29%	
with Respect to Age	Age groups				0.478
	18-30 Years	YES	22	16.29%	
		NO	05	3.70%	
	31-60 years	YES	81	60%	
		NO	27	20%	
with Respect to Duration of Illness	Duration of illness				0.578
	< 3 months	YES	72	53.33%	
		NO	24	15.68%	
	> 3 months	YES	31	22.96%	
		NO	08	5.92%	

#### DISCUSSION

In the absence of significant dysplastic symptoms or marrow fibrosis, aplastic anaemia (AA) is a rare bone marrow failure illness of unclear cause defined by hypocellular marrow and severe consistent pancytopenia. Different epidemiological studies are conducted to determine the comprehensive incidence of aplastic anemia, providing result of an increase in population with 2-3 times higher ratio in asian countries<sup>2</sup>.Pediatric apalstic anemia seen more frequently in adolescents and young adults<sup>3</sup>. Hypocellularity and bone marrow aplasia are thought to be primarily triggered by immune-mediated death of hematopoietic stem cells<sup>4</sup>. Compared to adults, paediatric patients with acquired AA had better results<sup>5</sup>.

Three kinds of peripheral parameters are become decresing in number in the medical state of pancytopeniai.e. leukocytes, platelets and erythrocytes<sup>6</sup>. These parameters also proividing evidence of getting multiple different medical conditions. It is possible for pancytopenia to be acquired or inherited (genetic, but not always present at birth)<sup>7</sup>. Pancytopenia's aetiology is either a loss of hematopoietic progenitor formation or peripheral cellular element death brought on by infection, immune-mediated injury, or hypersplenism<sup>8</sup>.

Microscopic evaluation of bone marrow specimen and marrow aspirate are required to diagnose pancytopenia, this microscopic examination provides morphological and cellular compositions of specimen to analyze the outcome<sup>6</sup>.

One of the crucial diagnostic techniques for many haematological illnesses is the bone marrow examination. Most of the time, it provides the precise diagnosis; however, occasionally, additional tests are needed. Anemia, thrombocytopenia, or leucopenia are the medical state which can be predicted as per the symptoms observed<sup>9</sup>.

Geographical distribution and genetic anomalies affect the pancytopenia aetiology spectrum differently. Megaloblastic anaemia (14.6%) was shown to be a less frequent haematological condition than Aplastic anaemia (20.2%)<sup>10</sup>. Aplastic anaemia (78.04%) and megaloblastic anaemia (9.75%) were the two most frequent causes of pancytopenia among adult patients in a different study<sup>11</sup>. According to the frequencies and percentages for aplastic anaemia in our study, 103 (76.29%) patients were identified as having the condition. (Table Number 02).

Pancytopenia is a rare blood disorder in clinical practice and should be evaluated when individual having complains of undetermined pallor, fever from along time and having a tendency to bleed<sup>5</sup>. A common test required to identify the aetiology of pancytopenia is a bone marrow examination. The MTI-Lady Reading Hospital in Peshawar's Department of General Medicine conducted this study on 135 individuals. According to descriptive statistics, the average age and standard deviations were 55+12.85 and 3+1.18, respectively(Table No. 1). In the 18–30 year age range, there were 27 patients (20%), while 108 patients (80%) were in the 31–60 year age group. The second table. Similarly, 44 (32.59%) patients were recorded as female patients, compared to 91 (67.40%) patients who were recorded as male patients.(Table No. 2). As per frequencies and percentages for aplastic anemia, 103 (76.29%) patients were recorded having aplastic anemia(Table No. 2). Niazi et al.<sup>[11]</sup> and Dahake et al.<sup>[12]</sup> made similar observations, however in other studies by Khodke et al.<sup>[8]</sup> and Hamid et al.<sup>[13]</sup>, the most prevalent clinical symptoms were fever, widespread weakness, and bleeding signs, respectively.

The common cause of pancytopenia is the in our study is aplastic anemia as seen in table 2. A well-known and wellestablished cause of cytopenias is megaloblastic anaemia brought on by a vitamin B12 and folic acid deficiency.

It was the main contributor to pancytopenia in our investigation. Other research from India made similar observations. The Indian subcontinent appears to have a higher frequency of nutritional inadequacy, which may be reflected in the high incidence of megaloblastic anaemia there. Various chronic inflammatory conditions of the gut, such as chronic diarrhoea, parasite infections, and malabsorption syndromes, in addition to poor nutrition, may be the lack of vitamin B12 and folic acid in this area. In our analysis, the second most typical cause of pancytopenia was aplastic anaemia. The literature from Nepal and other subcontinental nations also provided the same outcomes.

The goal of the current Study is to identify the prevalence of aplastic anaemia in adult pancytopenia patients. Pancytopenia is not unusual in our population, and despite the existence of research, statistics indicate that the severity of aplastic anaemia varies from population to population. We will learn the local magnitude of AA in adult pancytopenia patients from this study design. The results of this study will be shared with local health professionals to make them aware of the gravity of the problem and design future research and treatment recommendations.

### CONCLUSION

This study evaluated that aplastic anaemia is the most prevalent cause of pancytopenia in the Khyber Pukhtunkhwa population, and

that bone marrow aspiration is a recognised diagnostic method for the assessment of pancytopenia.

#### REFERENCES

- Killick SB, Bown N, Cavenagh J, Dokal I, Foukaneli T, Hill A, et al. Guidelines for the diagnosis and management of adult aplastic anaemia. Br J Hematol 2016;172(2):187-207.
- Ruiz E, Ramalle-Gomara E, Quinones C, Rabasa P, Pison C. Validation of diagnosis of aplastic anaemia in La Rioja (Spain) by International Classification ofDiseases codes for case ascertainment for the Spanish National RareDiseases Registry. Eur J Haematol 2015;94(5):400–03
- Young NS. Current concepts in the pathophysiology and treatment of aplastic anemia. Hematology Am Soc Hematol Educ Program.2013;2013:76–81.
- Jalaeikhoo H, Khajeh-Mehrizi A. Immunosuppressive therapy in patients with aplastic anemia: a single-center retrospective study. PLoS One. 2015;10(5):e0126925.
- Burroughs LM, Woolfrey AE, Storer BE. Success of allogeneic marrow transplantation for children with severe aplastic anaemia. Br J Haematol. 2012;158(1):120–128.
- Gupta N, Khajuria A. Pancytopenia: clinico-haematological evaluation and correlation with bone marrow examination. leukemia. 20151;3:6
- Young NS, Dumitriu B, Ogawa S. Acquired aplastic anemia: new genetics, new genomics. Blood. 2014;124(21):SCI-21.
- Wang YH, Fu R, Dong SW, Liu H, Shao ZH. Erythroblastic islands in the bone marrow of patients with immune-related pancytopenia. PloS one. 2014;9(4):e95143.
- Ojha S, Haritwal A, Meenai FJ, Gupta S. Bone marrow examination findings in cases of 82 pancytopenia-a study from central India. Ind J Path Oncol 2016;3(3):479-84.
- Ahmad A, Idrees M, Afridi IG, Rehman G. To determine the etiology and frequency of pancytopenia in pediatric population and compare it with other studies. Khy J Med Sci. 2016;9(2):186.
- Patra M, Mohanty L, Mohanty P. Hematological diversity in pancytopenia: a tertiary care hospital experience. J Evol Med Dent Sci 2015;4(34):5892-9.
- Young NS. Acquired bone marrow failure. Handin RI, Stossel TP, Lux SE, eds. Blood: Principles and Practice of Hematology. Philadelphia, Pa: JB Lippincott; 1995. 293-365.
- Richardson C, Yan S, Vestal CG. Oxidative stress, bone marrow failure, and genome instability in hematopoietic stem cells. Int J Mol Sci. 2015 Jan 22. 16 (2):2366-85.