SEVERITY AND CLINICO-HAEMATOLOGICAL FEATURES OF APLASTIC ANEMIA IN ADULTS PRESENTING TO PUBLIC SECTOR TERTIARY CARE HOSPITAL OF LAHORE: A DESCRIPTIVE CROSS SECTIONAL STUDY

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Abstract

Background & Objective: Aplastic anemia is a rare and heterogeneous disorder. Literature shows inconsistencies in frequency and its clinico-hematological findings. Objective of this study was to assess frequency of different severity grades and clinico-hematological features in newly diagnosed cases of aplastic anemia in adults.

Methods: In this descriptive, cross-sectional study, conducted in Allama Iqbal Medical College Lahore from October 2021 through April 2022, a total of 100 diagnosed cases of acquired aplastic anemia were included. Modified Camitta's criteria were applied to assess the severity of aplastic anemia. Clinical features such as pallor, fever and bleeding manifestations were determined by history and physical examination. About 3ml whole blood was collected in EDTA vial and run for complete blood count on automated hematology analyzer for hematological Parameters (Hb, Platelets, total leukocyte count and absolute Neutrophil count). Data were entered and analyzed using SPSS version 20. Quantitative variables like age, Hb, TLC and platelet count were expressed as mean ±Standard deviation. Qualitative variables such as gender, severity of aplastic anemia and clinical features were expressed as percentages.

Results: In this study, 55% participants were male and 45% were female. All patients had pallor, 61% had fever and 66% had bleeding on presentation. Regarding severity of aplastic anemia, 56% were categorized as severe, 24% as very severe and 20% were as non severe aplastic anemia.

Conclusion: Severe aplastic anemia is frequent among male population and at younger age. This information has prognostic implications. Therefore, all patients with aplastic anemia should be assessed for severity for further clinical management.

Keywords: Aplastic anemia, pallor, severity, clinico-haematogical, cross sectional study

Aplastic anemia is a rare and heterogeneous disorder. It is defined as pancytopenia with a hypo-cellular bone marrow in the absence of an abnormal infiltrate or marrow fibrosis.[1] The incidence of aplastic anemia is 2-3 per million per year in European countries while very high in East Asian countries and its peak was seen at 10-25 years and above 60 years. In Pakistan, young males are more affected by aplastic anemia and idiopathic severe aplastic anemia is the most common type.[2] Where Patients were commonly found with symptoms of anemia and thrombocytopenia, the majority of cases were idiopathic, therefore a careful drug occupational exposure with family history should be obtained. There is usually no hepatosplenomegaly or lymphadenopathy except in infection.[1] The Modified Camitta criteria is used to assess severity as: Severe AA

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(SAA), Very-severe AA (VSAA) and Non-severe AA (NSAA).[1] Internationally, Das et al. showed frequency of severity in adult patients as: Severe AA 35%, Very-severe AA 10% and Non-severe AA 55%.[3] In another study by Mahapatra et al. showed Severity of AA as: Severe (SAA): 75%, Very severe (VSAA): 15%, Non-severe (NSAA):10%.[4] Whereas, Biswajit et al. reported that the frequency of severity in aplastic anemia as: Severe AA (34.21%), Very-severe AA (21.05%), Non-severe AA (44.74%).[5] In Pakistan, a cross sectional study conducted in Karachi by Taj et al. reported the frequency of aplastic anemia severity as: Severe AA (61.32%), Very- Severe AA (22.9%), Non-severe AA (15%),[6] whereas Wali et al. in Aga Khan University Hospital, on pediatric patients, showed frequency of severity as: Severe (SAA) 28.9%, Very-severe (VSAA) 32.2% and Moderate aplastic anemia 18.9%.[7] A study in Lahore by Ayesha et al. has reported the frequency of severity as: Severe AA 68%, Non-severe AA 20%, Very-severe AA 12%.[2]

Regarding the frequency of clinico-hematological features of aplastic anemia, Das et al. in India reported that 55% of adults with aplastic anemia manifested fever, 25% with minute bleeding, and 25% with gross bleeding. Mean values of hematological parameters include: Haemoglobin (4.8 g/dl), total leucocyte count (2814/microliter), absolute neutrophil count (628/microliter), and total platelet count (23,832 /microliter).[3] The study by Mahapatra showed pallor (97%), bleeding manifestations (69.6%) and fever (54%), while haematological parameters came out as: median level of Haemoglobin (5.9gm/dL), WBC (2700/microliter), ANC (380/microliter), platelet (10000/microliter).[4] Similarly, Wali et al. reported fever in 72.2%, pallor in 58.8%, skin bleeding in 54.4% and epistaxis in 34.4% of pediatric patient.[7] Further, Ayesha et al. showed fever in 36.6%, history of bleeding manifestations in 52.4% aplastic anemia cases. Moreover, mean values of hematological parameters included: Haemoglobin (7.15g/dl), total leucocyte count (2.41×10^3/microliter), absolute neutrophil count (0.56/ microliter), Platelet count (25.85×10^3/microliter).[2] Current literature showed inconsistencies between the frequency of aplastic ane-

mia and its clinico-hematological findings, both on international and local level. Moreover, previous studies have been conducted on either pediatric group or generalized population with no specific information available on adult group. Thus, this study will provide baseline information on adult group in Pakistani population and will help clinicians for subsequent management and improving the quality of life of aplastic anemia patients. The objective of this study was to assess frequency of different severity grades and clinico-hematological features in newly diagnosed cases of aplastic anemia in adults.

METHODS

This cross-sectional study was conducted at Department of Hematology, Allama Iqbal Medical College, Jinnah Hospital Lahore from October 2021 to April 2022. Total 100 diagnosed cases of acquired Aplastic anemia having age 15-60 years, both male and female patients were included.

Patients of aplastic anemia with paroxysmal nocturnal hemoglobinuria clones diagnosed on flow cytometry, post chemotherapy and radiotherapy induced marrow aplasia, i.e., within 6 months of remission induction therapy in leukemia, lymphomas and solid tumors, constitutional anemia such as Fanconi's Anemia diagnosed by physical examination, for skeletal deformity (absent thumb, radial hypoplasia, scoliosis and Fanconi's faces) and confirmation by cytogenetic studies were excluded.

Informed consent was obtained from every patient. Demographic information like age, sex, contact number and address was obtained. All of the data were collected on specially designed Performa. Modified Camitta's criteria were applied to assess the severity of aplastic anemia. Clinical features such as pallor, skin bleeding, epistaxis and fever were determined by history and physical examination. For hematological parameters such as Hb, Platelets, total leukocyte count and absolute neutrophil count, we used 03 ml of whole blood sample in EDTA vial using aseptic measures. Whole blood EDTA sample was run for complete blood count (CBC) on automated hematology analyzer. Effect modifiers

like age, gender were explored through stratification of data. All the information was entered in a structured proforma. The data was entered and analyzed through SPSS (Statistical Package for Social Sciences) version 20. Quantitative variables like age, Hemoglobin, white cell count, platelet count were expressed as mean ± Standard Deviation (SD). Qualitative variables like gender, severity of aplastic anemia, clinical features like fever, bleeding manifestation and pallor were expressed as percentage. Chi-square test was used to examine difference of proportions between the categories. A p-value < 0.05 was taken as statistically significant.

RESULTS

Mean age of the sample was 29.6 ± 14.3 years. Among hematological parameters, mean value of Hb was 6.8±1.41 g/dl, Total Leukocyte Count (TLC) was 2.2±0.79×109/l, and Absolute Neutrophil Count (ANC) was 0.4±0.40×109/l and platelet count was 16±14.1× 109/l. About 79% of patients were referred from ward and remaining 21% were OPD referral. Regarding clinical presentation of patients, all patients had pallor, 66% had bleeding manifestation on presentation, majority had epistaxis and 61% had fever. Regarding severity of aplastic anemia, majority 56 (56%) were categorized as having severe disease, 24 (24%) were characterized as very severe aplastic anemia and 20 (20%) were having non severe disease (Figure 1).
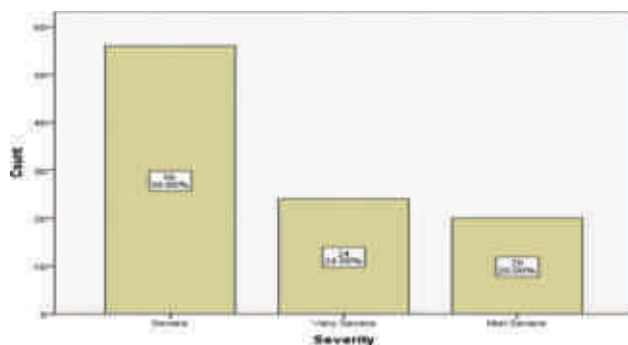

Figure 1. *Severity of Aplastic Anemia Observed in Study*

Table1 shows severity of aplastic anemia stratified by age. Total of 66 patients were aged 15-30 years, 15 patients were aged 31-45 years and 19 patients were aged more than 45 years. In age group 15-30 years, severe anemia was noted in 42(63.6%) patients followed by very severe in 16 (24.2%) patients and non-severe in 8(12.1%) patients. In age group 31-50 years, severe anemia was found in 6(40%) patients, very severe anemia in 4 (26.7%) patients, while non-severe anemia in 5(33.3%) patients. In age group >45 years, severe, very severe and non-severe anemia was found in 8(42.1%) patients, 4(21.1%) patients and 7 (36.8%) patients respectively. Association of severity of anemia with age groups was not significant (P=0.084).

Male patients were 55 while female patients were 45. In male patients, severe anemia was noted in 34

Table 1: Severity of aplastic anemia stratified by age (n=100)

| Age group | Severity | | | P value |
	Severe (%)	Very Severe (%)	Non-Severe (%)	
15-30 years	42 (63.6)	16 (24.2)	8 (12.1)	
31-45 years	6 (40.0)	4 (26.7)	5 (33.3)	0.084
>45 years	8 (42.1)	4 (21.1)	7 (36.8)	
Total	56 (56.0)	24 (24.0)	20 (20)	

(61.8%) patients, very severe anemia in 13 (23.6%) patients and non-severe anemia in 8 (14.5%) patients. Among female patients, severe anemia was found in 22(48.9%) patients, very severe anemia in 11(24.4%) patients and non-severe anemia in 12(26.7%) patients. Association of severity of anemia with gender was not significant (P=0.278) (Table-2).

Table 2: Severity of aplastic anemia stratified by gender (n=100)

| Gender | Severity | | | P value |
	Severe (%)	Very Severe (%)	Non-Severe (%)	
Male	34 (61.8)	13 (23.6)	8 (14.5)	
Female	22 (48.9)	11 (24.4)	12 (26.7)	0.278
Total	56 (56.0)	24 (24.0)	20 (20.0)	

DISCUSSION

The clinical severity of aplastic anemia classification is based on peripheral blood counts and results of bone marrow examinations. Aplastic anemia is

classified as non-severe (NSAA), severe (SAA) and very severe based on the degree of the peripheral blood cytopenias according to Cammita's Criteria. The 2-year mortality rate with supportive care alone for patients with SAA or very severe AA approaches 80%,[8] with invasive fungal infections and overwhelming bacterial sepsis being the most frequent causes of death. The clinical course of NSAA is quite variable; it is seldom life-threatening and in many instances, requires no therapy.[9] The data from study in Korea suggest that low pre-treatment levels of white blood cells and absolute neutrophils are associated with progression to more severe disease. Furthermore, patients with thrombocytopenia that did not respond to treatment with immunosuppression had a higher frequency (33%) of progression to SAA.[10]

Among 100 patients included in this study, 56% had SAA, 24% had VSAA and 20% had NSAA at the time of presentation. In Pakistan, cross sectional study conducted by Ayesha et al. in Lahore studying 82 patients over 7 years showed frequency of severity in adult patients as: Severe AA 68%, Very-severe AA 20% and Non-severe AA 12%,[2] and study conducted by Taj et al. in NIBD Karachi on 318 patients, reported the frequency of severity as: Severe AA 61.32%, Very-Severe AA 22.9%, Non-severe AA 15%.[6] These studies showed consistent results as our study regarding the severity of disease. On the other hand, study conducted by Wali et al. at Aga Khan University Hospital, on pediatric patients, showed frequency of severity as: Severe (SAA) 28.9%, Very-severe (VSAA) 32.2% and Non-severe aplastic anemia 18.9%.[7] Internationally, a multicenter prospective study conducted by Das et al. in India on adult revealed frequency as SAA: 35%, VSAA 10% and NSAA 18.9%.[3] While another study in the identical age group conducted by Mahapatra et al. on 1501 patients over 7 years in India showed fre-quency as: SAA (75%), VSAA (15%) and NSAA (10%).[4] These inconsistencies in results are due to different study settings, different time frames and different age groups of study population.

Regarding clinical features, pallor was present in all patients, bleeding manifestation in 66% of cases and fever was present in 61%. Among hematological features, mean value of Hb was 6.8±1.40g/dl, TLC was 2.2±0.79×109/l, Platelet count 16±14.19×109/l and ANC was 0.4±0.40×109/l. The study conducted by Mahapatra et al. in India showed pallor as a predominant feature (97%) followed by bleeding and fever as in our study, while hematological parameters came out as: median level of Hb: 5.9gm/dl, total leukocyte count:2700/µl, ANC:380/µl, platelet:1000/µl.[4] Whereas, another study conducted in India by in- patient age group of 3-86 years revealed results as: fever in 55% patients and bleeding manifestation in 25% patients. Mean values of hematological parameters were: Hb (4.8 g/dl), Total leukocyte count (2814/µl), Absolute Neutrophil count (628/µl), total platelet count (23,832 / µl.[3]). Whereas, the results of study in Pakistan revealed fever as a predominant clinical feature that is 72.2%, followed by pallor and bleeding manifestation in pediatric age group.[7] While another study in Pakistan in adults showed pallor as a predominant feature followed by bleeding manifestations and fever as in our study. Mean values of hematological parameters include: Hb 7.15g/dl, Total leukocyte count: 2.41×103/µl, Absolute neutrophil count:0.56/µl, Platelet count: 25.85×103/µl.2 The inconsistencies in results are due to different study setting and age groups and different population size and study period.

CONCLUSION

Most patients had severe aplastic anemia with younger age and male population being affected more but there is a non- significant statistical relationship between age, gender and severity of anemia.

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