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ORIGINAL ARTICLE

Survival Outcomes and Treatment Modalities in Aplastic Anaemia Patients: A Six-Year Retrospective Study at Muhimbili National Hospital, Tanzania

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ABSTRACT

Background: Aplastic anaemia (AA) is a rare bone marrow failure syndrome characterised by pancytopenia and hypocellular marrow, often resulting from immune-mediated hematopoietic stem cell destruction. Survival data for AA in Tanzania is limited. This study assessed the survival outcomes of AA patients based on available treatment regimens at Muhimbili National Hospital (MNH).

Methods: A retrospective cohort study included all AA patients identified and treated at MNH between January 2018 and December 2023. Clinical and laboratory data, along with socio-demographic information, were extracted from patients' records. Descriptive statistics of patient characteristics, Kaplan-Meier curves estimated survival outcomes, and the Cox regression model assessed factors associated with mortality risk.

Results: Among 577 patients with pancytopenia, 156 (27%) had acquired idiopathic aplastic anaemia. The median age at diagnosis was 23 years. Majority of the patients had severe AA (49.4%) and very severe AA (36.5%). Treatment regimens included cyclosporine A (59.0%), supportive care alone (21.8%), intensive immunosuppressive therapy (14.1%), and other treatments (4.5%). Only 3 (1.9%) patients underwent allogeneic hematopoietic stem cell transplant abroad. The Kaplan–Meier estimate of overall survival was 27.6%, with a median survival time of 158 days from diagnosis. Supportive care alone and cyclosporine A plus supportive care were associated with higher mortality compared to intensive immunosuppressive therapy.

Conclusion: Patients receiving intensive immunosuppressive therapy demonstrated the most favourable survival outcomes; however, these findings should be interpreted cautiously given the observational design. Expanding access to allogeneic hematopoietic stem cell transplantation and intensive immunosuppressive therapy, alongside early detection and timely referral, is crucial for improving survival of aplastic anaemia patients in Tanzania.

BACKGROUND

Acquired Aplastic Anaemia (AA) is a rare and life-threatening haematological disorder that significantly affects the well-being of affected individuals.[1] The prevalence of acquired aplastic anaemia (AA) varies depending on age and geographic location.[1] In Europe and North America, the annual incidence is approximately 2-3 cases per million individuals, while in East Asia, it is notably higher, 2-3 times that rate.[1,2] The gender distribution of AA cases is nearly equal, with a ratio of almost 1:1 between men and women.[3,4] The occurrence of AA follows a biphasic pattern, with peaks observed in two age groups: one between the ages of 10 and 25, and another in individuals aged 60 and above.[1,2,4,5] While data on the incidence of AA in Africa is limited, cases have been reported in various regions of the continent, including Northern Africa, Western Africa, Eastern Africa, and Southern Africa.[5–8]

The choice of therapy is influenced by the severity of the AA, the patient's age, the accessibility to the best therapy, and the availability of matched donors.[9] Hematopoietic Stem cell transplant (HSCT) is the recommended treatment for patients below 40-50 years with severe aplastic anaemia, provided a matched sibling donor is available.[9] In Tanzania, due to limited resources, only a few eligible patients can afford this expensive procedure.[10] Immunosuppressive therapy (IST) with horse anti-thymocyte globulin (ATG) and cyclosporine A (CSA) is the first line treatment for patients older than 40 years and for those without a matched sibling donor.[9]

In upper-middle and high-income countries, median survival ranges between 19.2 to 150 months, while in areas where supportive treatment is the mainstay of treatment, this value is quite low.[1,6,11–13] Disease severity and treatment options have been shown to affect survival.[11,14] While previous studies from Muhimbili National Hospital have described the prevalence and clinical characteristics of AA, they lacked detailed analysis of survival rates and did not compare outcomes across treatment modalities.[7] There is a critical need for locally generated evidence to guide management decisions in resource-limited settings such as Tanzania. This study aimed to describe the frequency, disease severity, treatment patterns, and survival outcomes of patients with aplastic anaemia treated at Muhimbili National Hospital between 2018 and 2023, and to explore factors associated with survival. Given the limited number of patients who received definitive therapies such as intensive immunosuppressive therapy and hematopoietic stem cell transplantation, treatment-specific survival findings should be interpreted as exploratory.

METHODS

Study Design, Area and Population

This was a retrospective cohort study that included all patients diagnosed with aplastic anaemia between January 2018 and December 2023. Patients were followed from the time of diagnosis until death, and those who were still alive at the end of the follow-up period were considered censored. The study was conducted at Muhimbili National Hospital, a national tertiary referral facility in Dar es Salaam. Adult patients were managed under the Internal Medicine–Hematology Unit, while patients younger than 14 years were treated in the Department of Pediatrics.

Inclusion Criteria

All patients confirmed to have idiopathic AA from bone marrow aspirate (BMA) and Trephine biopsy from January 2018 to December 2023.

Exclusion Criteria

Patients suspected to have inherited bone marrow failure syndromes (IBMFS) or known/suspected secondary causes of AA such as viral infections.

Disease Severity Classification

Disease severity was classified according to the modified Camitta criteria.[3,4] Non-severe aplastic anaemia (NSAA) was defined as hypocellular bone marrow without fulfilling criteria for severe disease. Severe aplastic anaemia (SAA) was defined by bone marrow cellularity below 25% together with at least two of the following: absolute neutrophil count below 0.5×10^9/L, platelet count below 20×10^9/L, or reticulocyte count below 20×10^9/L. Very severe aplastic anaemia (VSAA) fulfilled criteria for severe aplastic anaemia with an absolute neutrophil count below 0.2×10^9/L.

Sampling Method and Recruitment Process

We recruited all patients with pancytopenia, who had undergone BMA and trephine biopsy between January 2018 and December 2023 and were confirmed to have idiopathic Aplastic anaemia.

Data Collection

The data for this study were accessed between 15th January 2024 and 6th March 2024 from bone marrow and hospital registers. A data abstraction form was used to collect clinical, laboratory, and socio-demographic information from bone marrow and hospital registers. Data were entered into Microsoft Excel 2010 and then imported into STATA version 17 for statistical analysis. The authors had access to information that could identify individual participants during the data collection process, but no identifying information was retained in the final dataset used for analysis.

Treatment Definitions

Treatment groups were classified according to the treatment modality ultimately received during follow-up. Intensive immunosuppressive therapy (IST) was defined as treatment with horse antithymocyte globulin (ATG) combined with cyclosporine A (CsA), together with supportive care. Cyclosporine-based therapy included patients who received CsA without ATG. Supportive care alone consisted of blood product transfusions, antimicrobial therapy, and other supportive interventions as clinically indicated. Because this was a retrospective study focused on treatment patterns and survival outcomes, detailed information regarding ATG dosing schedules and supportive care protocols was not consistently available for all patients, particularly those who received treatment outside the study institution.

Missing Data

Due to the retrospective nature of the study, some variables contained incomplete documentation. Occupation data were missing for 58 of the 156 patients (37.2%). In addition, some patients had incomplete follow-up information, requiring contact with family members to ascertain survival status. Treatment adherence could not be reliably assessed because of incomplete documentation in medical records. Analyses were conducted using available data, and no imputation procedures were performed.

Data Analysis

Stata version 17 was used to code, clean, store and process de-identified data during analysis. Descriptive statistics were used to estimate the number of aplastic anaemia cases each year and the overall prevalence, as well as to analyze patient demographic characteristics (age, gender, etc.), disease severity, and treatment options. Survival analysis was conducted to estimate survival time from diagnosis to death. Kaplan–Meier survival curves were used to visualise survival outcomes, and the log-rank test was used to compare survival distributions according to disease severity and treatment modality. Cox proportional hazards regression was used to assess factors associated with mortality risk. Treatment modality was analyzed as a fixed exposure variable based on the treatment ultimately received during follow-up. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported. An HR of 1 indicated no difference in risk, an HR<1 indicated lower risk, and an HR>1 indicated higher risk compared with the reference group. Statistical significance was defined as a two-sided P value less than .05.

Ethics Statement

We obtained ethical clearance to conduct the study from the Institutional Review Board (IRB) at Muhimbili University of Health and Allied Sciences (MUHAS-REC-11-23-1981) on November 28, 2023. Following clearance, authorisation to gather data was obtained from the Muhimbili National Hospital- Clinical Research and Training Consultancy Unit to access patient files and records (MNH/CRTCU/Perm/2023/571) on December 6, 2023. Verbal consent was obtained from family members when contacted to ascertain survival status among patients with incomplete follow-up information. This procedure was approved by the Institutional Review Board as part of the study protocol, and the requirement for written consent was waived because of the retrospective nature of the study.

RESULTS

Frequency of Aplastic Anaemia

Between January 2018 and December 2023, 577 patients with pancytopenia underwent bone marrow evaluation at Muhimbili National Hospital. Bone marrow failure syndromes accounted for 189 (32.8%) of these cases. Among them, 156 patients (27.0%) were diagnosed with idiopathic aplastic anaemia and were included in the analysis.

Twenty patients (3.5%) had clinical features suggestive of inherited bone marrow failure syndromes (such as short stature, café au lait macules, or radial abnormalities) and were excluded. An additional 13 patients (2.3%) had viral infections (HIV, Hepatitis B, or Hepatitis C) and were excluded to avoid misclassification of secondary causes of pancytopenia.

Other causes of pancytopenia included hematological malignancies (30.5%), peripheral destruction or consumption (15.9%), myelodysplastic syndrome (5.9%), nutritional deficiencies (5.7%), and myelofibrosis (2.6%). In 6.6% of cases, bone marrow aspiration yielded non-diagnostic samples due to insufficient cellularity (Figure 1).

Socio-demographic Characteristics

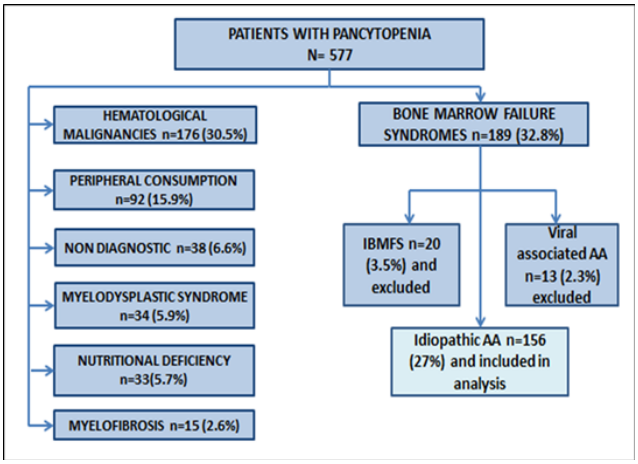
The study included 156 patients diagnosed with aplastic anaemia, of whom 94 (60.3%) were male and 62 (39.7%) were female (male-to-female ratio 1.5:1). The median age was 23 years. Overall, 54 patients (34.6%) were younger than 18 years, and 69 (44.2%) were aged 18–39 years. Most patients (90; 57.7%) were referred from outside Dar es Salaam, although Dar es Salaam contributed the highest number of cases from a single geographical location (Table 1, Figure 2). Students represented the largest occupational group (28.9%). Additionally, 59 patients (37.8%) had health insurance coverage, while 97 (62.2%) lacked insurance.

Disease Severity at Presentation

Among the 156 patients included in the study, 49.4% had severe aplastic anaemia (SAA), 36.5% had very severe aplastic anaemia (VSAA), and 14.1% had non-severe aplastic anaemia (NSAA) (Figure 3). Nearly all patients (99.4%) presented with symptoms of anaemia, while 63.5% had bleeding manifestations, 41.0% reported fever, and 4.5% exhibited jaundice (Figure 4).

At the time of diagnosis, 97.4% of patients had received red blood cell transfusions and 66.7% had received platelet transfusions, indicating a high level of transfusion dependence. The mean haemoglobin concentration was 6.3 ± 2.3 g/dL (Table 2). Additionally, 36.5% of patients presented with very severe neutropenia, 88.5% had reticulocytopenia, and 66% had very severe thrombocytopenia.

FIGURE 1: Flow Diagram Showing the Frequency of Aplastic Anaemia Among Patients with Pancytopenia Who Underwent Bone Marrow Aspiration at Muhimbili National Hospital

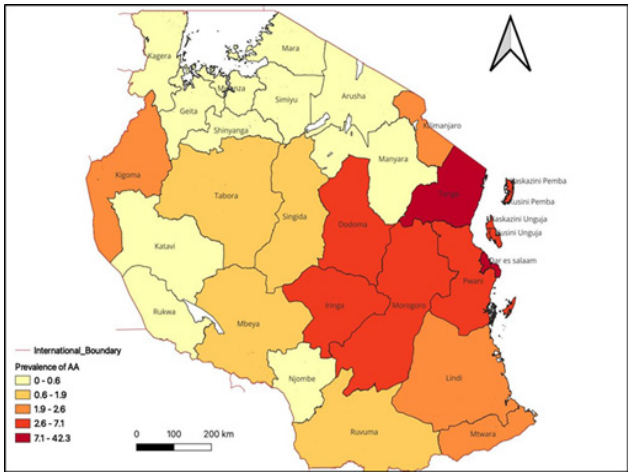


Key: IBMFS, Inherited Bone Marrow Failure Syndromes; AA, Aplastic Anaemia

TABLE 1: Socio-Demographic Characteristics of Patients Diagnosed With Aplastic Anaemia (N=156)

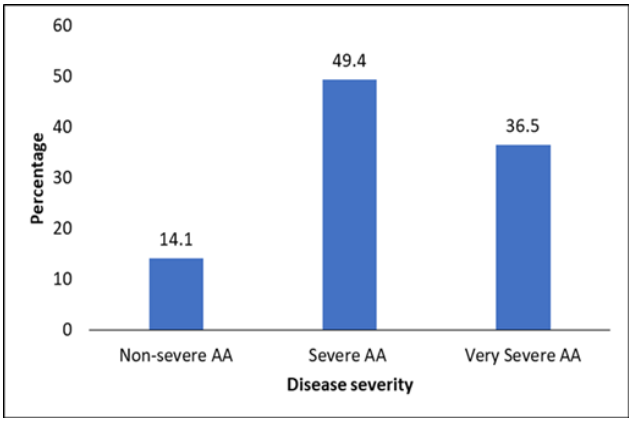
Variable	Frequency (n)	Percentage (%)
Sex		
Male	94	60.3
Female	62	39.7
Age group (years)		
Below 18	54	34.6
18-29	52	33.3
30-39	17	10.9
40 and Above	33	21.2
Median and Interquartile range	23 (15,33)	
Place of residence		
Dar es Salaam	66	42.3
Out of Dar es Salaam	90	57.7
Occupation		
Employed	10	6.4
Self employed	23	14.7
Student	45	28.9
Unemployed	20	12.8
Missing	58	37.2
Insurance status		
Insured	59	37.8
Not insured	97	62.2

FIGURE 2: Geographic Distribution of Aplastic Anaemia Cases by Region of Residence in Tanzania.



Darker shades indicate a higher number of aplastic anaemia cases

FIGURE 3: Distribution of Aplastic Anaemia Severity at Diagnosis



Nonsevere AA, Non severe aplastic anaemia; Severe AA, Severe aplastic anaemia; Very Severe AA, Very severe aplastic anaemia

Treatment Modalities

Most patients (59.0%) received cyclosporine A (CsA) in combination with supportive care. Supportive care alone, consisting primarily of blood product transfusions and antimicrobial therapy, was provided to 21.8% of patients (Figure 5). Intensive immunosuppressive therapy with antithymocyte globulin (ATG) plus CsA, along with supportive care, was administered to 14.1% of patients. Additionally, 4.5% of patients received alternative therapies, including androgens with or without CsA or eltrombopag. Only 1.9% of patients underwent allogeneic hematopoietic stem cell transplantation, which was performed outside the country.

FIGURE 4: Clinical Characteristics of Patients With Aplastic Anaemia at Diagnosis (N=156)

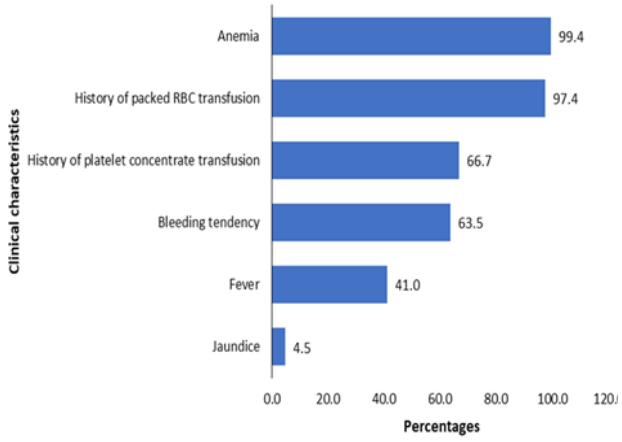
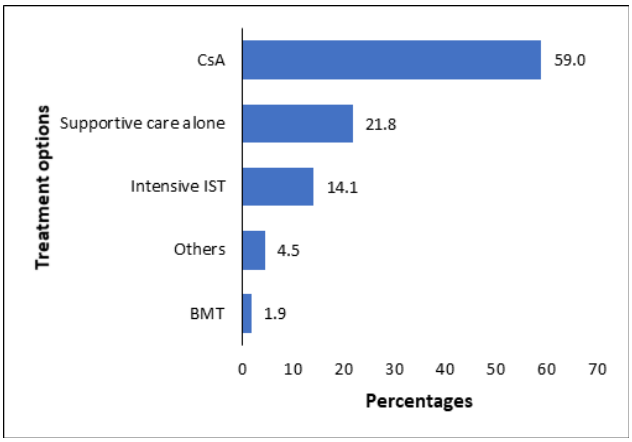


FIGURE 5: Treatment Modalities Received by Patients With Aplastic Anaemia (N=156)



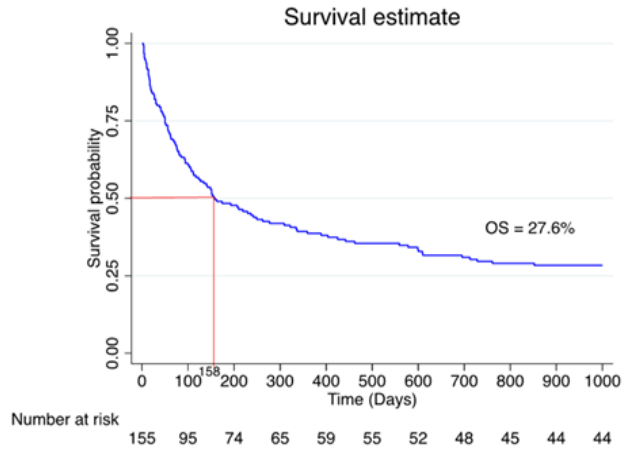
Abbreviations: BMT, Bone Marrow Transplant (hematopoietic stem cell transplantation, HSCT); Others include patients who received Androgens with or without Cyclosporine A and eltrombopag. IST, intensive immunosuppressive therapy. Supportive care alone, included blood transfusion products and antimicrobial medications. CsA, Cyclosporine A.

Survival Outcomes and Factors Associated with Mortality

The Kaplan–Meier estimated overall survival at the end of the study period was 27.6%, with a median survival time of 158 days (5.2 months) (Figure 6). The median follow-up time estimated using the reverse Kaplan–Meier method was 1,090 days (3.0 years). Survival differed significantly by disease severity (P<.001). Patients with

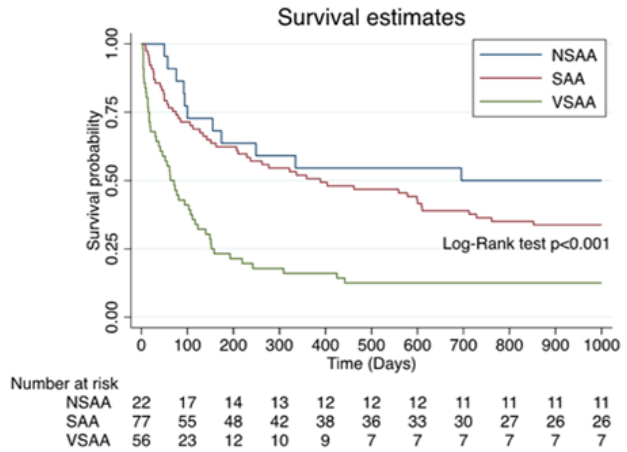
non-severe aplastic anaemia (NSAA) had the longest survival, with a median survival time of 695 days. Patients with severe aplastic anaemia (SAA) had a median survival of 389 days, while those with very severe aplastic anaemia (VSAA) had the shortest survival, with a median survival of 46 days (Figure 7).

FIGURE 6: Kaplan–Meier Overall Survival Curve for Patients With Aplastic Anaemia



Key: OS, overall survival.

FIGURE 7: Kaplan–Meier Survival Curves According to Aplastic Anaemia Severity

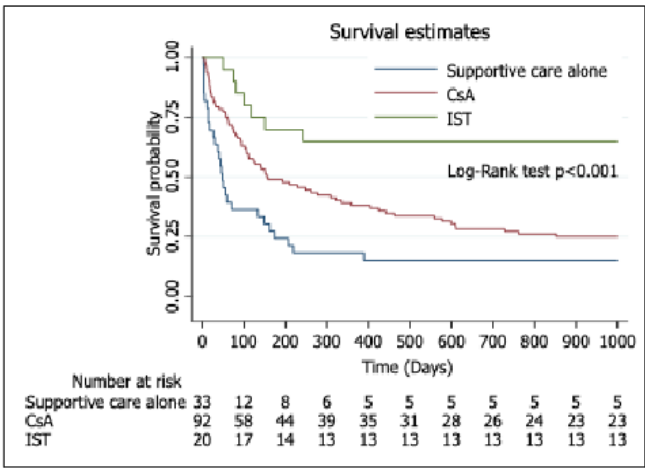


Key: NSAA = Non-severe aplastic anaemia; SAA = Severe aplastic anaemia; VSAA = Very severe aplastic anaemia.

Treatment modality also had a significant impact on survival (Figure 8). Patients who received supportive care alone had a median survival of 48 days. Those treated with cyclosporine A (CsA) and supportive care had a median survival of 155 days. Intensive immunosuppressive therapy with ATG plus CsA demonstrated the greatest survival benefit. Because more than half of the patients remained alive at the end of follow-up, the median survival time was not reached. Three patients underwent allogeneic hematopoietic stem cell transplantation abroad; one died from early transplant-related complications, while two achieved long-term remission.

In the Cox regression model, intensive IST served as the reference category. Supportive care alone (aHR 6.40; 95% CI, 2.61 to 15.73; *P*<.001), CsA plus supportive care (aHR 3.25; 95% CI, 1.42 to 7.45; *P*=.005), and other therapies including androgens with or without CsA and/or eltrombopag (aHR 4.20; 95% CI, 1.51 to 11.69; *P*=.006), were each associated with significantly higher mortality. Allogeneic HSCT was not significantly associated with mortality reduction (aHR 0.41; 95% CI, 0.05 to 3.70, *P*=.428), likely due to the very small sample size. VSAA significantly increased the mortality risk (aHR 4.77, 95% CI, 2.23 to 10.22, *P*<.001), whereas SAA did not (aHR, 1.67; 95% CI, 0.82 to 3.43; *P*=.159). Age, sex, and region of residence were not significantly associated with survival (Table 3).

FIGURE 8: Kaplan–Meier survival curves according to treatment modality



Key: IST-Intensive immunosuppressive therapy with supportive care, CsA-Cyclosporine A with supportive care.

TABLE 2: Laboratory Characteristics of Patients With Aplastic Anaemia at Diagnosis (N=156)

Variable	Reference range	Frequency (n)	Percentage (%)
Hb (g/dl)			
Mean SD		6.3±2.3	
ANC (x109/L)			
Very severe	<0.2	57	36.5
Severe	0.2-0.49	51	32.7
Moderate	0.5-0.9	31	19.9
Mild	>1.0	17	10.9
ARC (x109/L)			
Reticulocytopenia	<60	138	88.5
Normal	>60	18	11.5
PLT (x109/L)			
Very severe	<20	103	66
Severe	20-49	39	25
Mild to moderate	>50	14	9

Abbreviations: Hb, Hemoglobin; ANC, Absolute neutrophil count; ARC, Absolute reticulocyte count; PLT, Platelet count.

TABLE 3: Cox Regression for Factors Associated With the Survival of Aplastic Anaemia Patients

Variable	cHR	*P Value*	aHR(95% CI)	*P Value*
Sex				
Female	Ref		Ref	
Male	1.05(0.72-1.54)	.784	0.72(0.48-1.08)	.112
Age group				
Age (per year)	1.00(0.99-1.01)	.745	1.00(0.99-1.01)	.929
Place of residence				
Dar es Salaam	Ref		Ref	
Out Dar es Salaam	1.01(0.68-1.48)	.978	1.26(0.83-1.91)	.278
Treatment options				
Intensive IST	Ref	Ref		
Supportive care alone	5.48(2.25-13.37)	<.001	6.40(2.61-15.73)	<.001
CsA + Supportive care	3.06(1.38-6.79)	.006	3.25(1.42-7.45)	.005
BMT (Abroad)	0.79(0.12-4.98)	.800	0.41(0.05-3.70)	.428
Others	2.91(1.14-7.41)	.026	4.20(1.51-11.69)	.006
Disease severity				
Non severe Aplastic anemia	Ref		Ref	
Severe Aplastic anemia	1.37(0.73-2.57)	.325	1.67(0.82-3.43)	.159
Very Severe Aplastic anemia	3.31(1.75-6.25)	<.001	4.77(2.23-10.22)	<.001

Abbreviations:
cHR, crude Hazard Ratio; aHR, adjusted Hazard Ratio; Ref, Reference group; Intensive IST, Intensive immunosuppressive therapy which includes ATG and CsA; ATG, Antithymocyte globulin,
CsA, Cyclosporine A; BMT, Bone marrow transplant (hematopoietic stem cell transplantation, HSCT);
Others include patients who received Androgen with or without CsA and eltrombopag

DISCUSSION

This study is the first to evaluate median survival among patients with idiopathic aplastic anaemia in a resource-limited setting in East and Central Africa. This study found that patients who received intensive immunosuppressive therapy (IST) experienced better survival outcomes than those receiving supportive care alone or cyclosporine A-based therapy. These findings support the importance of improving access to standard IST protocols in resource-limited settings. However, because treatment allocation was not randomised, the observed associations should not be interpreted as evidence of a causal treatment effect.

A notable demographic feature of this cohort was the young age distribution, with most patients being under

30 years of age and a median age of 23 years. This aligns with findings from a South African study reporting a median age of 24.5 years.[15] Unlike the biphasic age distribution often reported in Europe, the age distribution in our population was unimodal, which is similar to trends observed in Asian populations.[1,16,17] This pattern may be largely influenced by demographic structure: Tanzania has a predominantly young population, with a national median age of approximately 18 years, in contrast to Europe where the median age is about 44.5 years.[18,19] Thus, the predominance of younger affected individuals may partly reflect broader population age dynamics rather than disease-specific factors alone.

A male predominance was also observed, with a male-to-female ratio of 1.5:1. This finding is consistent with several reports from Sub-Saharan Africa and parts of Asia.[6,8,20] However, sex distribution in aplastic anaemia varies across regions, with some studies reporting a near-equal ratio and others demonstrating a male excess.[17,21] The reasons behind this disparity remain unclear and warrant further investigation.

A notable finding was that idiopathic aplastic anaemia accounted for 27% of all cases in the study cohort. This proportion is comparable to reports from South Asian populations but higher than the prevalence documented in North America and Western India (11%–12.8%).[22–24] These differences may reflect geographical and environmental influences, and the single-center design of our study may also have contributed to underestimation.

Most patients presented with severe or very severe disease at diagnosis. This pattern is consistent with reports from other African settings but differs from high-income countries, where non-severe AA is more frequently observed at presentation.[7,15,25] Although these factors were not directly assessed in this study, the predominance of severe disease may be related to delays in seeking care, restricted access to diagnostic evaluation, socio-cultural influences, and financial barriers that impede timely presentation.

Over the past five years, treatment options for AA in Tanzania have improved significantly.[7] Intensive IST is now available locally, although uptake remains low, with only 14.1% of patients receiving this regimen. The majority continues to receive cyclosporine A (CsA) with supportive care, and a substantial proportion relies solely on supportive care alone. Within Sub-Saharan Africa, South Africa is the only country with longstanding access to ATG-based IST.[8,15] In other countries, the cost and availability of ATG remain challenging.[26–28] Since 2021, bone marrow transplant (BMT) services have expanded in Tanzania. MNH initially established autologous transplantation, and Benjamin Mkapa Hospital subsequently began performing allogeneic transplants for sickle cell disease.[10,29] Within the region, only three countries namely Tanzania, South Africa, and Nigeria, currently offer BMT services, but access remains limited due to high treatment costs and constrained capacity.[29–31]

The median survival of 158 days observed in this study highlights the substantial disparities in outcomes between resource-limited settings and high-income countries. In upper-middle- and high-income regions, reported median survival times range from 19.2 to 150 months, a striking contrast that largely reflects greater access to definitive therapies such as ATG-based IST and stem cell transplantation.[1,11–13] Our findings also showed that patients receiving supportive care alone had the poorest outcomes, similar to reports from Nigeria.[6] Financial constraints, lack of insurance coverage, and treatment non-adherence likely contributed to the lower survival observed among patients receiving CsA with supportive care.

Patients diagnosed with NSAA demonstrated markedly longer survival compared to those with SAA or VSAA. This pattern is consistent with international findings, including studies from China, where NSAA was similarly associated with better overall survival.[25] These differences underscore the strong prognostic value of disease severity and its influence on treatment response.

Limitation

This study has several limitations. First, treatment allocation was not randomised, and patients who received intensive immunosuppressive therapy may have differed systematically from those receiving supportive care alone or cyclosporine-based therapy. Consequently, confounding by indication may have influenced the observed associations between treatment modality and survival. Second, treatment exposure was analyzed as a fixed variable based on the treatment ultimately received during follow-up. Because treatment initiation occurred at varying times after diagnosis, the possibility of immortal time bias cannot be excluded. Third, socioeconomic factors influencing treatment access and outcomes were not systematically assessed, and treatment adherence could not be reliably evaluated because of incomplete documentation in medical records. Finally, although patients were classified as having idiopathic aplastic anaemia, inherited bone marrow failure syndromes such as Fanconi anaemia could not be completely excluded because confirmatory genetic testing was not routinely available.

CONCLUSION

Aplastic anaemia in this setting predominantly affects a young population and is frequently diagnosed at a severe stage. Patients who received intensive immunosuppressive therapy demonstrated better survival outcomes than those receiving supportive care alone or cyclosporine-based therapy; however, these findings should be interpreted cautiously given the retrospective design and potential for confounding. These findings underscore the need to improve early diagnosis, enhance access to intensive therapies, and strengthen treatment pathways to optimise outcomes for patients with severe forms of the disease.

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