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# Impact of Pre- and Post-Transplant Transfusion Requirements on Outcomes in Severe Aplastic Anaemia (SAA) Patients

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## Abstract

Objective: The goal of this research shall be to assess the effects of the pre- and post-transplant transfusion requirements on the outcomes of SAA patients who underwent HSCT.
Methodology: This is a retrospective design study was conducted at Gambat Institute of Medical Sciences specializing in hematology and oncology, between 1st, December 2018 to 2nd, January 2023. Total Patients were 84, in which 45 patients were diagnosed with SAA who have undergone HSCT. Data were extracted regarding demographic features, transfusion history, transplant outcomes, and post-transplant complications. Patients were categorized into two groups: Group A (≤20 transfusions) and Group B (>20 transfusions). The diagnosis of Severe Aplastic Anemia is made using recognized criteria, which include a bone marrow cellularity of less than 25%, and the presence of at least two of the following: an absolute neutrophil count of less than 500/µL, a platelet count of less than 20,000/µL, or a reticulocyte count of less than 20,000/µL.
Results: The study group consisted of individuals aged 4 to 41 years, with a higher proportion of males, having a male-to-female ratio of 1.2:1. Majority of the patients had a sibling donor (97.8%) while fewer had unrelated (2.2%) donor. Group A demonstrated superior outcomes with a 5-year overall survival of 84.0% compared to 60.0% in Group B (p=0.02). Graft failure (4.0% vs. 20.0%, p=0.03), severe infections (12.0% vs. 30.0%, p=0.01), iron overload (8.0% vs. 25.0%, p=0.04), and alloimmunization (12.0% vs. 30.0%, p=0.03) were significantly lower in Group A.
Conclusion: Transfusion burden before and after HSCT is strongly associated with adverse outcomes in SAA patients. Strategies to minimize transfusion dependency may improve transplant success and survival.
Keywords: HSCT, Severe aplastic anemia, Transfusion Requirements, Graft Failure.

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## Introduction

Severe Aplastic Anemia (SAA) is a rare but serious hematologic condition characterized by bone marrow hypocellularity leading to pancytopenia.[1] This condition leads to severe anemia, neutropenia and thrombocytopenia, this implies that patients with such condition have high risks for life-threatening infections, bleeding, and severe fatigue.[2, 3] SAA can have various causes including idiopathic, toxic, radiation, certain drugs and viral infections. [4, 5]

Allogeneic hematopoietic stem cell transplantation (HSCT) is the treatment of choice in younger patients with matched sibling donors and offers curative potential.[6] Despite advances in transplant techniques and supportive care, HSCT is still associated with significant complications, including graft failure, graft-versus-host disease (GVHD), and severe infections.[7] Transfusion support with red blood cells and platelets remains essential both before and after HSCT. It can effectively control the manifestations of pancytopenia and show a positive impact on the patient's status before the transplantation.[8, 9]

However, repeated transfusions are not without risk—they contribute to iron overload, allo-immunization, and increased susceptibility to infections.[10] The cumulative transfusion burden may negatively affect transplant outcomes, yet the relationship between transfusion volume and post-transplant prognosis in SAA remains underexplored.[11]

This study aims to assess the impact of pre- and post-transplant transfusion requirements on outcomes in patients with SAA undergoing HSCT. It further explores associations with survival, graft failure, and post-transplant complications, thereby providing insights for optimizing transfusion strategies in transplant settings.

Authorship Contribution: [1-3] Conceived and planned the idea of the study, data drafting the work or revising it critically for important intellectual content, final approval of the version to be published, [4-6]Data Analysis, Literature Review, analysis, [7-8]Active participation in active methodology

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## Methodology

This retrospective observational study was conducted at the Department of Hematology and Bone Marrow Transplantation, Gambat Institute of Medical Sciences, from December 1, 2018, to January 2, 2023.

Out of 84 patients assessed, 45 were diagnosed with Severe Aplastic Anemia (SAA) and underwent allogeneic hematopoietic stem cell transplantation (HSCT) during the study period. Patients were included if they met the diagnostic criteria for SAA, defined by bone marrow cellularity of <25% and at least two of the following: absolute neutrophil count <500/μL, platelet count <20,000/μL, or reticulocyte count <20,000/μL. Patients with incomplete records or those who underwent a second transplant were excluded.

Electronic medical records were reviewed to extract data on demographics, clinical features, etiology of SAA, transfusion history, conditioning regimen, donor type, and transplant outcomes. Transfusion requirements before and after HSCT were documented.

Patients were categorized into two groups based on the total number of red blood cell and platelet transfusions received before and after transplantation:

Group A: ≤20 total transfusions (n=25)

Group B: >20 total transfusions (n=20)

The primary endpoints were overall survival (OS) and graft failure. Secondary endpoints included the incidence of severe infections, acute and chronic graft-versus-host disease (GVHD), iron overload, and alloimmunization.

Descriptive statistics were calculated using SPSS version 26.0. Categorical variables were compared using the chi-square test, while survival analysis was performed using the Kaplan-Meier method with the log-rank test. A p-value <0.05 was considered statistically significant.

The study was approved by the Institutional Review Board of Gambat Institute of Medical Sciences. Given its retrospective nature, informed consent was waived. Patient confidentiality was strictly maintained, and all data were anonymized.

## Results

A total of 45 patients with SAA underwent HSCT during the study period. The cohort included patients aged 4 to 41 years, with a median age of 24 years, and a male-to-female ratio of 1.2:1. Most patients (71.1%) had idiopathic SAA, while 13.3% were attributed to toxins, 11.1% to drug-induced causes, and 4.4% to viral etiologies. Donor source was predominantly matched sibling (97.8%). (Table I)

Patients were stratified by transfusion burden into two groups: Group A (≤20 transfusions, n=25) and Group B (>20 transfusions, n=20). Group B had significantly higher pre-transplant (median: 20 vs. 10; p<0.001) and post-transplant transfusion requirements (median: 18 vs. 8; p<0.001) compared to Group A.

The 5-year overall survival ratio was better in Group A with 84.0% as compared to Group B with 60.0% with p=0.02. The graft failure rate was also lower in the Group A (4.0%) compared to the Group B (20.0%, p=0.03). Mentioning the comparison of the incidence of severe infections between the two groups, it should be stated that the rate in Group B was significantly higher (30.0%) in contrast to Group A (12.0%, p=0.01). The frequency of acute GVHD was also comparable in the two groups (12.0% in Group A vs. 10.0% in Group B, p=0.62) and of

Table I: Patient Demographics and Clinical Features.

| Characteristic | Total (N=45) | Group A (≤20 Transfusions, n=25) | Group B (>20 Transfusions, n=20) | p-value |
|---|---|---|---|---|
| Median Age (years) | 24 | 22 | 25 | 0.42 |
| Age Range (years) | 4-41 | 4-41 | 4-41 | |
| Male/Female Ratio | 1.2:1 | 1.3:1 | 1.1:1 | 0.56 |
| Etiology | | | | |
| Idiopathic | 32 (71.1%) | 18 (72.0%) | 14 (70.0%) | |
| Toxic | 6(13.3%) | 3 (12.0%) | 2 (10.0%) | 0.76 |
| Drug | 5 (11.1%) | 3 (12.0%) | 1 (5.0%) | |
| Viral | 2 (4.4%) | 1 (4.0%) | 2 (10.0%) | |
| Donor Type | | | | |
| Sibling | 44 (97.8%) | 25 (100%) | 19 (95.0%) | |
| Unrelated | 1 (2.2%) | 0 (0%) | 1 (5.0%) | 0.89 |

chronic GVHD (8.0% in Group A vs. 5.0% in Group B, p=0.74).

Table II shows the complication profile of the patients who developed complications after the transplant. Group B had more patients with severe infections 30.0% vs. 12.0% p=0.01, iron overload 25.0% vs. 8.0% p=0.04 and alloimmunization 30.0% vs. 12.0% p=0.03. The incidence of acute GVHD was 20.0% in Group A and 25.0% in Group B, p=0.62 and chronic GVHD was 16.0% in Group A and 20.0% in Group B, p=0.74.

Table II: Incidence of Complications Post-Transplant.

| Complication | Group A (≤20 Transfusions, n=25) | Group B (>20 Transfusions, n=20) | p-value |
|---|---|---|---|
| Severe Infections | 3 (12.0%) | 6 (30.0%) | 0.01 |
| Acute GVHD (Grade I-II) | 5 (20.0%) | 5 (25.0%) | 0.62 |
| Chronic GVHD | 4 (16.0%) | 4 (20.0%) | 0.74 |
| Iron Overload | 2 (8.0%) | 5 (25.0%) | 0.04 |
| Alloimmunization | 3 (12.0%) | 6 (30.0%) | 0.03 |

As shown in the Kaplan-Meier survival analysis in Table 3, it was identified that the survival rate of the Group A was significantly better than that of the other groups. The median of survival at 6 months was 84.0% in Group A to 50.0% in Group B with a p=0.02. The survival to the first year was 96.0% in group A and 80.0% in Group B (p=0.04). The 3 year survival rate was 92.0% in Group A and 70.0% in Group B, (p=0.03). The five year survival rate was 84.0% in Group A and 60.0% in Group B (p=0.02). (Table III)

Table III: Kaplan-Meier Survival Analysis.

| Survival Analysis | Group A (≤20 Transfusions n=25) | Group B (>20 Transfusions n=20) | (p-value) |
|---|---|---|---|
| Median Survival (6 months) | 21 (84.0%) | 10 (50.0%) | 0.02 |
| 1-Year Survival Rate N (%) | 24 (96.0%) | 16 (80.0%) | 0.04 |
| 3-Year Survival Rate N (%) | 23 (92.0%) | 14 (70.0%) | 0.03 |
| 5-Year Survival Rate N (%) | 21 (84.0%) | 12 (60.0%) | 0.02 |

Alloimmunization was checked through a series of serological tests. Initially, the process was started by obtaining a complete blood count (CBC) and performing antibody screening via Indirect Antiglobulin Test (IAT) to find if any unexpected antibodies are present. Patients with detectable antibodies underwent anti-human globulin cross-matching to identify the antibody or antibodies present.

## Discussion

This study highlights the prognostic significance of transfusion burden in patients with Severe Aplastic Anemia undergoing HSCT. Previous studies have also indicated that the higher transfusion burden is a poor prognostic factor for outcome of HSCT in patients with SAA. Bacigalupo et al., (2015) noted that patient in their study who had previously received more than 20 units of blood prior to HSCT had a poor survival compared with other patients in the study who had received relatively small measure of blood.[12] These results parallel our study because Group A (≤20 transfusions) had a 5-year overall survival of 84.0% though the group B (>20 transfusions) had survival rate of 60.0% (p=0.02).

Lee et al. (2016), which evaluated 221 adult SAA patients undergoing allogeneic stem cell transplantation. The study demonstrated that patients who received a higher number of pretransplant packed red cell (PRC) units (>32) had significantly lower overall survival (72.3% vs. 91.9%, p<0.001) and higher transplant-related mortality (24.8% vs. 6.8%, p<0.001) compared to those with fewer transfusions (≤32 units). While their study did not find a difference in engraftment failure, it did reveal a significantly higher incidence of acute GVHD (grades II–IV) in the high transfusion group (p=0.04).[13] Our study similarly demonstrated that patients with greater transfusion exposure (>20 transfusions) experienced poorer survival outcomes and a higher rate of complications.

Higher incidence of severe infections, iron overload, and alloimmunization observed in Group B indicates that SAA patients require proper management of transfusion therapy. Repeated transfusions are associated with complications such as iron overload and alloimmunization which results to increased morbidity and mortality among the patients. The current study revealed that the prevalence of iron overload was 25.0% of the patients in Group B as opposed to 8.0% of the individuals in Group A (p = 0.04), whereas alloimmunization was detected in 30.0% of Group B as compared to 12.0% of Group A (p= 0.03).[14]

The Kaplan-Meier survival analysis also confirms the negative impact of high transfusion dependency on survival. The one year survival rate was 96.0% in Group A compared to 80.0% in Group B (p = 0.04), 3-year follow up 92.0% vs. 70.0% (p = 0.03) and 5-year follow up 84.0% vs. 60.0% (p = 0.02). These outcomes are in line with the results of Camitta et al. (2017), who also reported the comparable unfavorable impact on the survival of patients with increased transfusion requirements.[15]

These results show for the first time that increased pre- and post-transplant transfusion burden is related to worse outcomes in SAA patients receiving HSCT

## Conclusion

This study demonstrates that a high transfusion burden before and after HSCT adversely affects clinical outcomes in patients with Severe Aplastic Anemia. Patients with >20 transfusions had significantly lower survival, higher rates of graft failure, and increased post-transplant complications, including infections, iron overload, and alloimmunization.

Reducing transfusion dependency through early diagnosis, optimized supportive care, and timely transplantation is essential to improving prognosis.

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