

Outcome of allogeneic bone marrow transplantation in aplastic Anaemia: A Retrospective Study

Shehzad Sarwar, Uzair Ahmad, Hafiz Muhammad Nadeem, Asghar Ali, Muhammad Farhan, Muhammad Afzal

Abstract

Objective: To evaluate early outcomes of allogeneic bone marrow transplantation in patients with aplastic anaemia.

Method: The retrospective, observational study was conducted at the Department of Clinical Haematology and Bone Marrow Transplantation, Gambat Medical College in Sindh, Pakistan, and comprised data from June 2021 to June 2025 of patients who underwent allogeneic bone marrow transplantation. All procedures were conducted in isolation chambers equipped with laminar airflow and high-efficiency particulate air filtration systems, and stem cells were obtained from sibling donors fully matched for human leukocyte antigens. Data recorded from the patient files included demographics, donor characteristics, stem cell source and dosage, transplant-related complications, and post-transplant outcomes, including disease-free survival and overall survival. Data was analysed using SPSS 26.

Results: Of the 56 patients, 34(60.6%) were male and 22(39.4%) were female. The overall median age was 19 years (interquartile range: 4-41 years). Stem cells were sourced exclusively from bone marrow in 38(67.9%) patients, followed by 17(30.4%) who received a combination of bone marrow and peripheral blood stem cells. The most common early post-transplant complications were fungal infections 23(41.1%) and cyclosporine-induced hypertension 13(23.2%). In the first 100 days, there were 14(25%) deaths, leaving both the 100-day overall survival and disease-free survival rates to be 42(75%).

Conclusion: Allogeneic bone marrow transplantation was found to be a viable curative treatment for severe aplastic anaemia even in resource-limited settings.

Keywords: Aplastic anaemia, Allogeneic stem cell transplantation, post-transplant complications. (JPMA 76: 1614; 2026)

DOI: <https://doi.org/10.47391/JPMA.20686>

Introduction

Aplastic anaemia is a rare, but serious haematological disease characterised by pancytopenia and bone marrow (BM) failure. Its global occurrence ranges 2-6 cases per million individuals annually, affecting patients across diverse geographical and ethnic backgrounds.¹ Despite its low prevalence, it is associated with significant morbidity and mortality, necessitating timely and effective therapeutic intervention.² The allogeneic bone marrow transplantation (allo-BMT) is curative treatment for individuals with aplastic anaemia who are not responding to immunosuppressive therapy.³ By replacing the dysfunctional haematopoietic system with healthy donor stem cells, allo-BMT restores haematopoiesis and immune function, thereby reducing risk of life-threatening infections and haemorrhagic manifestations.⁴ However, the procedure is not without challenges. Transplant-related problems, such as opportunistic infections, graft rejection, graft-versus-host disease (GVHD) and regimen-related complications continue to pose significant risks.⁵ These

challenges are further amplified in resource-constrained settings where access to matched sibling donors, optimal conditioning regimens and comprehensive post-transplant care may be limited.⁵ Although the safety and efficacy of allo-BMT have been extensively studied, data from remote and underserved regions remain scarce. Detailed evaluations of transplant outcomes—including survival rates, engraftment kinetics, and complication profiles—are essential to inform clinical practice and optimise transplant protocols tailored to the unique constraints of such environments.⁶

The current study was planned to evaluate early outcomes of allo-BMT in patients with aplastic anaemia in a low-resource setting.

Materials and Methods

The retrospective, observational study was conducted at the Department of Clinical Haematology and Bone Marrow Transplantation, Gambat Medical College in Sindh, Pakistan, and comprised data from June 2021 to June 2025 of consecutive patients diagnosed with severe aplastic anaemia (SAA) who underwent allo-BMT. The centre serves a predominantly rural and resource-limited population. The current sample was raised using non-probabilistic consecutive sampling method and all eligible patients who met the inclusion criteria were enrolled. All procedures

Department of Clinical Haematology and Bone Marrow Transplant, Gambat Medical College, Gambat, Pakistan.

Correspondence: Uzair Ahmad. e-mail: uzaira37121@gmail.com

ORCID ID: 0009-0004-0856-6903

Submission completed: 28-09-2024 **1st Revision received:** 15-08-2025

Acceptance: 13-06-2026

Last Revision received: 12-06-2026

were conducted in isolation chambers equipped with laminar airflow and high-efficiency particulate air (HEPA) filtration systems, and stem cells were obtained from sibling donors fully matched for human leukocyte antigen (HLA).

In terms of inclusion criteria, confirmed SAA diagnosis was based on the standard elements, like BM cellularity <25%, presence of two or more cytopenias, like absolute neutrophil count $<0.5 \times 10^9/L$, platelet count $<20 \times 10^9/L$, and reticulocyte count $<20 \times 10^9/L$, and the absence of significant marrow fibrosis or malignant infiltration. Besides, a fully HLA-matched (10/10) sibling donor had to be available and confirmed by high-resolution deoxyribonucleic acid (DNA) typing, age 3-45 years, and with adequate organ function, including left ventricular ejection fraction (LVEF) $\geq 45\%$, creatinine clearance $\geq 60 \text{ mL/min}$, bilirubin $\leq 1.5 \times$ upper limit of normal, and transferrin saturation $<80\%$.

Those excluded were individuals with the presence of active uncontrolled infection at time of transplantation, prior allogeneic stem cell transplantation, concurrent malignancy or myelodysplastic syndrome, positive cross-match against donor, and incomplete medical records or follow-up data.

All patients underwent comprehensive pre-transplant assessment including complete blood count (CBC) with differential, BM aspiration and trephine biopsy, cytogenetic analysis, HLA typing by low-resolution PCR-SSP method, cardiac evaluation through echocardiography (ECG), pulmonary function tests, renal and hepatic function panels, viral serology (CMV, HBV, HCV, HIV), iron studies (serum ferritin, transferrin saturation), and nutritional assessment.

All the patients received a fludarabine-based reduced-intensity conditioning regimen that comprised Fludarabine $30 \text{ mg/m}^2/\text{day}$ intravenously (IV) for 4 days (total 120 mg/m^2), cyclophosphamide 60 mg/kg/day IV for 2 days (total 120 mg/kg), and antithymocyte globulin (ATG) 2.5 mg/kg/day IV for 4 days (total 10 mg/kg).

High-risk regimen was given to patients with ≥ 2 risk factors. The risk factors included duration between diagnosis and Date of transplant, ≥ 20 prior red cell transfusions, active infection at transplantation, prior platelets transfusion ≥ 25 , previous transplant and previous Immunosuppressant therapy.

For high-risk patients, cyclophosphamide was escalated to 80 mg/kg/day for 2 days (total 160 mg/kg), and ATG was escalated to 3.75 mg/kg/day for 4 days (total 15 mg/kg).

All the donors underwent complete medical evaluation, including physical examination, CBC, infectious disease screening, HLA confirmation by high-resolution typing, and psychological assessment.

Stem cells were collected from either BM or peripheral blood based on donor preference and institutional protocol.

BM harvest was performed under general anaesthesia (GA). The target volume was $5\text{--}10 \text{ mL/kg}$ donor body weight, while the minimum target was 2.0×10^8 nucleated cells/kg recipient weight.

For peripheral blood stem cell (PBSC) collection, the donors received G-CSF $10 \mu\text{g/kg/day}$ for 4-5 days. Apheresis was performed using Spectra Optia. The target was $\geq 4.0 \times 10^6$ cluster of differentiation (CD)34+ cells/kg recipient weight.

Primary GVHD prophylaxis included cyclosporine A, with a starting dose of 3 mg/kg/day IV from day-1, which was adjusted to maintain trough levels of $200\text{--}300 \text{ ng/mL}$, and then converted to oral formulation when tolerated (dose $1.5 \times \text{IV}$). It also includes ATG as per the conditioning regimen.

Bacterial infection prophylaxis included cefixime 400 mg twice daily from day-0 until neutrophil recovery, and broadspectrum IV antibiotics for febrile neutropenia as per institutional protocol.

Fungal infection prophylaxis included fluconazole 400 mg/day from day-1 to day +75, amphotericin B (liposomal) 3 mg/kg/day for breakthrough infections, and caspofungin for azole-refractory cases.

Viral infection prophylaxis included acyclovir 400 mg twice daily for HSV prophylaxis, valganciclovir 900 mg/day for CMV seropositive patients, and pre-emptive CMV monitoring through weekly PCR from day +7 to +100

For *Pneumocystis jirovecii*, co-trimoxazole was given twice daily, thrice weekly from engraftment to day +180.

Transfusion support was provided through red blood cells (RBCs) to maintain Haemoglobin $\geq 8 \text{ g/dL}$, and platelets to maintain a count of $\geq 20 \times 10^9/L$ ($\geq 50 \times 10^9/L$ for active bleeding). All products were leuko reduced, irradiated (25Gy) and CMV-negative.

Parenteral nutrition was provided if oral intake $<50\%$ of the requirement for 3 days. Besides, standardised oral supplement protocol was followed, and weekly monitoring of weight, albumin and pre-albumin was ensured.

Neutrophil engraftment was taken as the first of three consecutive days with absolute neutrophil counts

$\geq 0.5 \times 10^9/L$. Platelet engraftment was taken as the first of seven consecutive days with platelet count $\geq 20 \times 10^9/L$ without transfusion. Primary graft failures defined as failure to achieve ANC $\geq 0.5 \times 10^9/L$ by day +28. Poor graft function was defined as ANC $\geq 0.5 \times 10^9/L$ but requiring ongoing transfusion support.

Chimerism analysis was performed on days +30, +60, +90 and +180 using STR-PCR. Target was set at $\geq 95\%$ donor chimerism in whole blood and CD3+ fraction.

With respect to complications, acute GVHD (aGVHD) was diagnosed clinically and confirmed by biopsy, when possible. It was graded using modified Glucksberg criteria.⁷ The first-line treatment was methylprednisolone 2mg/kg/day.

Fungal infections were assessed as proven on the basis of positive culture from sterile site or histopathology, and they were considered probable in the presence of radiological evidence, host factors and mycological evidence.

CMV reactivation was defined as CMV viral ≥ 1000 IU/mL. Pre-emptive therapy included valganciclovir 900mg twice daily, and weekly monitoring was done till two consecutive negative PCRs.

Veno-occlusive disease (VOD) was diagnosed using modified Seattle criteria⁸ and was treated with defibrotide 6.25mg/kg every six hours.

Haemorrhagic cystitis was graded by using the Common Terminology Criteria for Adverse Events v5.0⁹ and was managed with hyperhydration, mesna and bladder irrigation.

Data was collection after approval from the institutional ethics review committee from electronic medical records, BMT database, pharmacy records, laboratory information system, and transfusion service records.

The data collected included demographics, disease characteristics, donor characteristics, transplant parameters, and 100-day outcomes. Overall Survival (OS) was taken as the time from transplant to death from any cause, while disease-free survival (DFS) was taken as the time from transplant to death or treatment failure.

Data was analysed using SPSS 26. Continuous variables was expressed as mean $\pm$ standard deviation or median with interquartile range (IQR) based on distribution normality, while categorical variables was expressed as frequencies and percentages. Comparative analysis was done using the chi-square test, while Kaplan-Meier method was used for survival estimation, and log-rank test for group comparisons.

Results

Of the 56 patients, 34(60.6%) were male and 22(39.4%) were female. The overall median age was 19 years (interquartile range: 4-41 years). Among the donors, 38(67.9%) were male and 18(32.1%) were female. Patient characteristics were noted at baseline (Table 1). Stem cells were sourced exclusively from BM in 38(67.9%) patients, followed by 17(30.4%) who received from a combination of BM and PBSC, and 1(1.7%) who received solely from PBSC.

Cyclosporine was used for GVHD prophylaxis in all the

Table-1: Patient characteristics (n=56).

Parameter	Value
Male	34 (60.7%)
Female	22 (39.3%)
Median Age (years)	19 (Range: 4–41)
Sex Mismatch	14 (25%)
Donor Relationship	Brother: 38 (67.9%) Sister: 18 (32.1%)
Average RCC Transfusions	40 units
Average Platelet Transfusions	26 units
Mean Ferritin Level	1650 ng/mL

Table-2: Stem cell dose and engraftment.

Parameter	Value
Stem Cell Source – Bone Marrow Only	38 (67.9%)
Stem Cell Source – BM + PBSC	17 (30.4%)
Mean Total Nucleated Cell (TNC) Dose	$6.8 \times 10^6/kg$
Mean CD34+ Cell Dose	$6.2 \times 10^8/kg$
Neutrophil Engraftment (Mean Days)	12
Platelet Engraftment (Mean Days)	17

Table-3: Survival rates and causes of death.

Parameter	Value
100-Day Overall Survival (OS)	75%
100-Day Disease-Free Survival (DFS)	75%
Mortality within 100 Days	14(25%)
Leading Causes of Death	Sepsis, multi-organ failure, pulmonary Haemorrhage, cardiopulmonary arrest

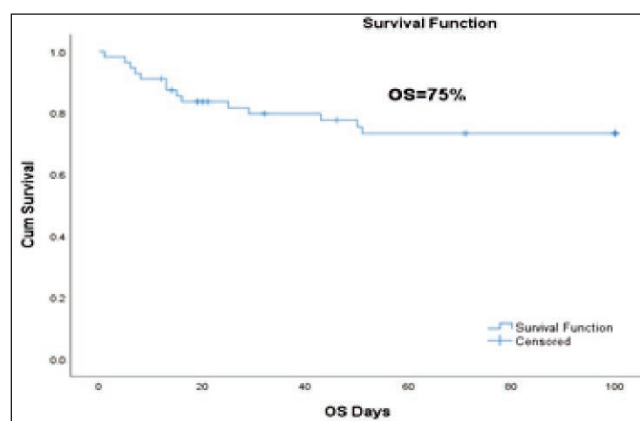


Figure-1: Overall survival.

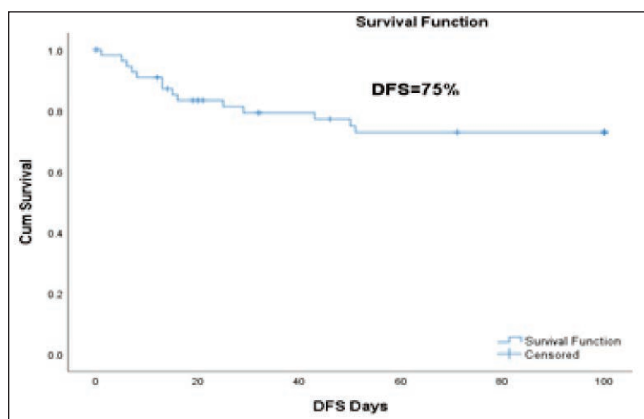


Figure-2: Disease-free survival (DFS).

56(100%) patients, while tacrolimus was administered in 3(5.4%) cases. Amphotericin B was the most commonly used antifungal agent. Neutrophil engraftment and platelet engraftment details were also noted (Table 2).

Fungal infections were observed in 24(42.1%) patients, and CMV reactivation occurred in 18(31.6%). They were all treated with valganciclovir. Acute GVHD was documented in 10(17.5%) patients, with the skin being the most commonly affected site, followed by the gastrointestinal tract. Cyclosporine-induced hypertension was reported in 17(30.4%), and haemorrhagic cystitis occurred in 10(17.9%). VOD/SOS was diagnosed in 4(7.1%) patients. Graft failure was seen in 4(7.1%) patients. Neutropenic sepsis remained the leading cause of transplant-related mortality. In the first 100 days, there were 14(25%) deaths (Table 3), leaving both the 100-day OS (Figure 1) and DFS (Figure 2) to be 42(75%).

Discussion

In the current study, 56 patients with SAA underwent allo-BMT. There were 60.7% male representation, and the median age was 19 years, which was consistent with literature.^{10,11} Stem cell sources included BM alone in 67.9% cases, and a combination of BM and PBSC in 30.4%, closely mirroring earlier proportions.¹² The mean CD34+ cell dose was $6.2 \times 10^8/\text{kg}$ and the mean total nucleated cell (TNC) dose was $6.8 \times 10^6/\text{kg}$, comparable to previously reported averages.¹²

Engraftment outcomes were encouraging, and suggested robust haematological recovery, which aligned with prior observations.¹³ However, complications remained prevalent. Fungal infections were documented in 42.1% of the patients, which were slightly lower than the previously reported 46%,¹⁰ but were still significant. Cyclosporine-induced hypertension affected 30.4% of patients the, exceeding earlier rates of 21%,¹⁴ while aGVHD was observed in 17.5%, comparable to the previously noted

19%.¹⁵

The current study achieved a 100-day OS and DFS rate of 75%, slightly improved from the earlier 73%.^{14,15} The study's resource-limited setting directly impacted outcomes through delayed referrals—leading to advanced disease with high transfusion burden and iron overload—and constrained access to first-line antifungal prophylaxis and molecular diagnostics. These systemic challenges contributed to the observed high rates of fungal infections and graft-related complications. Key lessons for similar centres include the critical importance of implementing strict, affordable infection protocols, investing in training for clinical recognition of early complications, and developing robust referral networks to reduce delays. Ultimately, successful transplantation in constrained environments requires contextualised, systematic adaptations in clinical and supportive care protocols.¹⁶

When placed alongside prior investigations, the current findings align with general patterns in the literature regarding transplantation outcomes for aplastic anaemia patients.¹⁷ For instance, Bacigalupo et al. reported median engraftment times of 15 days for neutrophils and 21 days for platelets, closely matching the 12- and 17-day averages observed in the current cohort.¹⁸ Additionally, Marsh et al. in 2020 and Gupta et al. in 2018 emphasised that GVHD and primary infections, such as candidiasis, remain persistent challenges in post-transplant care.¹⁹⁻²¹

Overall, trends in engraftment timing, complication frequency and survival rates show minimal variation across studies, which can be because of differences in patient populations and transplant strategies.^{22,23} Importantly, earlier research has highlighted the impact of graft failure on treatment outcomes in haematological diseases, a concern reaffirmed by the current data, which identified graft failure as a major contributor to transplant-related mortality.²⁴

Taken together, the findings from the current study are consistent with the broader literature on allo-BMT in patients with aplastic anaemia, under scoring the continuing need for research and refinement of transplant protocols to improve patient outcomes, particularly in regions with limited resources—where systemic challenges can reverse progress despite clinical advances.²⁵

The current study has several limitations, including its retrospective, single-centre design and the relatively short follow-up period, affecting the generalisability of the findings. Also, there was no control group that restricted direct comparative analysis of conditioning regimens or supportive care strategies.

Conclusion

Allo-BMT was found to be a viable curative treatment for severe aplastic anaemia even in resource-limited settings. The 100-day OS and DFS rate was 75%, with timely engraftment and sustained haematological recovery. However, frequent complications, such as fungal infections, GVHD and graft failure, highlighted the critical need for enhanced infection control and supportive protocols.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

- Young NS. Aplastic anaemia. *N Engl J Med* 2018;379:1643-56. doi: 10.1056/NEJMra1413485.
- 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 Haematol* 2016;172:187-207. doi: 10.1111/bjh.13853.
- Bacigalupo A. How I treat acquired aplastic anaemia. *Blood* 2017;129:1428-36. doi: 10.1182/blood-2016-08-693924.
- Marsh JC, Ball SE, Cavenagh J, Darbyshire P, Dokal I, Gordon-Smith EC, et al. Guidelines for the diagnosis and management of aplastic anaemia. *Br J Haematol* 2009;147:43-70. doi: 10.1111/j.1365-2141.2009.07842.x.
- Bacigalupo A. Treatment of acquired severe aplastic anaemia. *Semin Hematol* 2020;57:77-81. doi: 10.1053/j.seminhematol.2020.04.001.
- Dufour C, Veys P, Carraro E. How we manage aplastic anaemia in children and adolescents. *Br J Haematol* 2017;177:855-66. doi: 10.1111/bjh.14612.
- Przepiorka D, Weisdorf D, Martin P, Klingemann HG, Beatty P, Hows J, et al. 1994 Consensus Conference on Acute GVHD Grading. *Bone Marrow Transplant*. 1995;15:825-828.
- Shulman HM, Hinterberger W. Hepatic veno-occlusive disease—liver toxicity syndrome after bone marrow transplantation. *Bone Marrow Transplant*. 1992;10:197-214.
- National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. Bethesda (MD): National Cancer Institute; 2017.
- ElGohary G, El Fakih R, de Latour R, Risitano A, Marsh J, Schrezenmeier H, et al. Haploidentical hematopoietic stem cell transplantation in aplastic anaemia: a systematic review and meta-analysis of clinical outcome on behalf of the Severe Aplastic Anaemia Working Party of the European Society for Blood and Marrow Transplantation. *Bone Marrow Transplant* 2020;55:1906-17. doi: 10.1038/s41409-020-0893-1.
- Bacigalupo A, Socié G, Schrezenmeier H, Tichelli A, Locasciulli A, Fuehrer M, et al. Bone marrow versus peripheral blood as the stem cell source for sibling transplants in acquired aplastic anaemia: survival advantage for bone marrow in all age groups. *Haematologica* 2015;100:e409-11. doi: 10.3324/haematol.2015.127753.
- Gupta V, Eapen M, Brazauskas R, Carreras J, Aljurf M, Gale RP, et al. Impact of age on outcomes after bone marrow transplantation for acquired aplastic anaemia using HLA-matched sibling donors. *Haematologica* 2018;103:1312-9. doi: 10.3324/haematol.2018.189241.
- Zhang MX, Wang Q, Wang XQ. Hematopoietic stem-cell transplantation versus immunosuppressive therapy in patients with adult acquired severe aplastic anaemia: a cost-effectiveness analysis. *Int J Gen Med* 2021;14:3529-37. doi: 10.2147/IJGM.S313698.
- Zhang LL, Yu X, Fang LW, Pan H, Liang Q, Zhao JY, et al. A real-world study of 176 cases with aplastic anaemia treated in outpatient settings. *Zhonghua Xue Ye Xue Za Zhi* 2021;42:58-62.
- Sridhara S, Nair R, Stanek M. Severe aplastic anaemia after receiving SARS-CoV-2 Moderna mRNA vaccination. *J Hematol* 2022;11:34-37. doi: 10.14740/jh1046.
- Fattizzo B, Pasquale R, Croci GA, Pettine L, Cassanello G, Barcellini W. Aplastic anaemia after SARS-CoV-2 infection or vaccines: case series and literature review. *Blood Transfus* 2023;21:567-74. doi: 10.2450/BT.2023.0185-23.
- Brzeźniakiewicz-Janus K, Rupa-Matysek J, Hoppe A, Gil L. The impact of clonal haematopoiesis on outcomes in patients with aplastic anaemia. *Acta Haematol Pol* 2021;52:543-51. doi: 10.5603/AHP.a2021.0088.
- Onishi Y, Mori T, Yamazaki H, Hiramoto N, Zaimoku Y, Kanaya M, et al. Comparison of haploidentical stem cell transplantation with post-transplantation cyclophosphamide versus umbilical cord blood transplantation in adult patients with aplastic anaemia. *Transplant Cell Ther* 2023;29:766.e1-766.e9. doi: 10.1016/j.jtct.2023.08.022.
- Iftikhar R, Mahmood SK, Ghafoor T, Satti HS, Shahbaz N, Khan MA, et al. Single-agent cyclosporine for graft-versus-host disease prevention in patients with acquired aplastic anaemia receiving fludarabine-based conditioning. *Biol Blood Marrow Transplant* 2020;26:2245-51. doi: 10.1016/j.bbmt.2020.08.020.
- Arora S, Thakkar D, Upasana K, Yadav A, Rastogi N, Sharma PS, et al. Incidence, risk factors, characteristics, and outcome of chronic graft-versus-host disease in children undergoing haploidentical peripheral blood stem cell transplant with post-transplant cyclophosphamide. *J Pediatr Hematol Oncol* 2024;46:e44-50. doi: 10.1097/MPH.0000000000002716.
- Gómez-Almaguer D, Gómez-De León A, Colunga-Peña PR, Cantú-Rodríguez OG, Gutierrez-Aguirre CH, Ruíz-Argüelles G. Outpatient allogeneic hematopoietic stem-cell transplantation: a review. *Ther Adv Hematol* 2022;13:20406207221080739. doi: 10.1177/20406207221080739.
- Seval GC, Bozdogan SC, Toprak SK, Yuksel MK, Topcuoglu P, Arslan O, et al. Allogeneic hematopoietic stem cell transplantation for primary myelofibrosis: a 20-year experience in a single centre. *Balkan Med J* 2023;40:197-204. doi: 10.4274/balkanmedj.galenos.2022.2022-10-48.
- Marsh JCW, Bacigalupo A, Schrezenmeier H, Tichelli A, Risitano AM, Passweg JR, et al. Prospective study of rabbit anti-thymocyte globulin and cyclosporine for aplastic anaemia from the EBMT Severe Aplastic Anaemia Working Party. *Blood Adv* 2020;4:4133-44. doi: 10.1182/bloodadvances.2020002005.
- Passweg JR, Perez WS, Eapen M, Camitta BM, Gluckman E, Hinterberger W, et al. Bone marrow transplants from mismatched related and unrelated donors for severe aplastic anaemia. *Bone Marrow Transplant* 2017;52:522-7. doi: 10.1038/bmt.2016.333.

Author Contribution:

SS: Concept and design.

UA: Drafting and final approval.

HMN: Data analysis.

AA & MF: Revisiting critically.

MA: Drafting.