ACUTE GRAFT VERSUS HOST DISEASE IN HEMATOPOETIC STEM CELL TRANSPLANTATION IN THALASSEMIA: EXPERIENCE OF A MEDICAL COLLEGE HOSPITAL

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Article History: Received: 22.04.2023 **Revised:** 07.06.2023 **Accepted:** 20.07.2023

Abstract

Background: Graft-versus-Host Disease (GVHD) is a condition that may occur after an allogeneic transplant. In GVHD, the donated bone marrow or peripheral blood cells view the recipient's body as foreign and the donated cells/bone marrow attack the body.
Materials and Methods: It is an ambispective study conducted in a tertiary care hospital. All children diagnosed as acute graft versus host disease post-transplant were included in the study.
Results: Acute GVHD was seen in 35 patients (23.48%) who underwent BMT during the study period. Of these 35, fourteen (40%) children who developed aGVHD had undergone matched related BMT while 21(60%) had undergone partially matched related BMT. Mortality as a result of aGVHD was seen in 9 (25.7%) patients. Of these 3(33.33%) deaths due to aGVHD were in matched related donor group while 6 (66.67%) were in the partially matched related donor group.
Conclusion: Although significant improvements have been made, early transplant-related mortality and GVHD remain major obstacles to safe transplantation.

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Conflict of interest: None
Ethical Clearance: MGMC&H/IEC/JPR/2021-418

DOI: 10.31838/ecb/2023.12.3.187

1. Introduction

Graft-versus-Host Disease (GVHD) is a condition that may occur after an allogeneic transplant. In GVHD, the donated bone marrow or peripheral blood cells view the recipient's body as foreign and the donated cells/bone marrow attack the body. Allogeneic hematopoietic stem cell transplant (AHSCT) is an effective treatment for many hematologic and genetic diseases. Patients with hematologic malignancies may derive particular benefit by replacing the patient's bone marrow with the donor; the new immune system can attack tumor cells, known as graft-versus-tumor (GVT). However, donor-derived cells may also recognize recipient organs as foreign and mount an immune attack against the patient's own tissues, known as graft-versus-host disease. GVHD is a major cause of morbidity and mortality even when siblings are matched at the human leukocyte antigen (HLA) locus. GVHD in its chronic form can significantly affect the quality of life of long term survivors following bone marrow transplantation (BMT) and also lead to mortality.[1] Despite decades of research and developments in post-transplant immune-suppressive therapies, GVHD remains a crucial cause of sickness and deaths in AHSC Trecipients, has been classically defined by Billingham in 1966 as a syndrome in which immune-competent donor cells recognize and attack host tissues in an immune compromised recipient. GVHD shows a heterogeneous clinical presentation essentially entail skin, mucosa, liver, lungs, and gastrointestinal tract.

Aims And Objectives

1. To evaluate incidence of aGVHD in Matched related and Mismatched related bone marrow transplantation for Thalassemia

2. Material And Methods

Study design: It involved prospective as well as retrospective type of studies

Study Setting: Department of Pediatric Bone Marrow Transplantation, Mahatma Gandhi Medical College and Hospital, Jaipur

Sample Size: The sizes is the subjects with age group till 18 years undergoing bone marrow transplantation between February 2012 to February 2022

Subjects: Age group till 18 years undergoing Bone Marrow Transplant

Inclusion Criteria: Any child with typical features of acute Graft versus Host Disease (GVHD)

Exclusion criteria: All children with features suggestive of aGVHD but with confirmed diagnosis of other etiologies

3. Results

During our study on "Acute Graft Versus-Host Disease in Hematopoetic Stem Cell Transplantation in Thalassemia", a total of 149 children with thalassemia major underwent bone marrow transplantation. Of these 101 (67.78%) were matched related donor transplants and 48(32.2%) were partially matched donor transplants.

Acute GVHD was seen in 35 patients (23.48%) who underwent BMT during the study period. Of these 35, fourteen (40%) children who developed aGVHD had undergone matched related BMT while 21(60%) had undergone partially matched related BMT.

Acute Skin GVHD was seen in 22(62.85%) of children. Of these, 9(40.9%) belonged to matched related donor group while 13(59.1%) were from partially matched related donor group.

Gut GVHD was seen in 12(34.28%) children who underwent BMT. Of these 4(33.33%) belonged to matched related donor group while 8 (66.67%) were from partially matched related donor group.

Only one case of Lung GVHD was seen and it occurred in a child who underwent matched related donor BMT.

All the patients who developed aGVHD showed engraftment with 100% donor DNA status.

Mortality as a result of aGVHD was seen in 9 (25.7%) patients. Of these 3(33.33%) deaths due to aGVHD were in matched related donor group while 6 (66.67%) were in the partially matched related donor group.

Of the 9deaths due to GVHD, 8 (88.88%) were due to gut GVHD and 6(75%) of these had undergone partially matched related donor BMT.

Table 1

Total transplants	Matched related donor		Haploidentical donor	
N=149	Number	Percentage	Number	Percentage
	101	67.78	48	32.22
aGVHD= 35	14	40	21	60

Table 2

Type of gvhd	Matched related donor		Haploidentical donor	
	Number	Percentage	Number	Percentage
SKIN (n=22)	9	40.9	13	59.1
GUT (n=12)	4	33.33	8	66.67
LUNG (n=1)	1	100		

Table 3

Mortality due to aGVHD		Matched related donor		Haploidentical donor	
Number	Percentage	Number	Percentage	Number	Percentage
9	25.7	3	33.33	6	66.67

4. Discussion

Hemoglobinopathies are treated with allogeneic HSCT; following conditioning to get beyond the immunological barrier, allogeneic stem cells are employed as a means of re-inserting the genes required for healthy hematopoietic, which corrects the underlying genetic abnormality. Allogeneic HSCT is essentially allogeneic stem cell gene therapy in the treatment of various disorders. Acute graft-versus-host disease (GVHD) is still the second-leading cause of morbidity and mortality after hematopoietic cell transplantation (HCT). Acute GVHD is the term historically used to describe GVHD that occurs within the first 100 days after allogeneic BMT. Though this timeline is not always precise, chronic GVHD is defined as GVHD that develops more than 100 days after a BMT. GVHD prevention has made hyper acute GVHD, a severe fulminant form of acute GVHD that commonly results in death, extremely rare. In our study aGVHD was seen in 23.48% patients. In the study by Park B et al[2] the cumulative incidence of aGVHD was 36.4%. The skin, gastrointestinal system, and liver are the three primary organ systems affected by the clinicopathological condition known as acute GVHD. Any one of these organs, alone or in combination, may be impacted. Acute GVHD manifests in the first 100 days, often 2 to 6 weeks after allogeneic BMT. Acute GVH reaction targets a variety of host cells, including skin and mucosal epithelial cells, hair follicle cells, bile ducts, liver, crypt cells, airways, mucous membranes, bone marrow, and immune system cells. As per type of transplant, we discovered that 54.29% of cases belong to a matched related donor, whereas 45.71% of cases belong to a partially matched related donor. In a study by Yesilipek M A 2022[3] Thalassemia-free survival TFS rates were noticeably higher following transplants from matched unrelated donors. In order to improve results for Thalassemia patients who have a matched donor, HSCT is advised before the age of seven. Swaminathan VV et al 2022 [4] in their study had 76% as matched related donor.

In our study according to organ involvement, 65.71% had skin GVHD followed by 25.71% with gut GVHD. Only one patient had Lung GVHD in our study. These findings were in concordance with the study undertaken by Gokera H et al 2000[5] who observed that the skin, gastrointestinal tract and Liver were the major target organs of acute GVHD. Chandy in 2011[6] observed that the incidence of acute mucocutaneous GVHD was 26.3%**.**

Grade of GVHD

The clinical staging and grading of acute GVHD integrate the stage of each affected organ. The overall clinical grade of acute GVHD is used to evaluate the effectiveness of the prophylactic or treatment and has a significant impact on survival following BMT. GVHD is categorized into severity levels I through IV. The concordance for the diagnostic and grading between the doctors presents one challenge in grading. This emphasizes the significance of additional research and adjustments to the grading criteria when new data become available.

Of the 35 patients who developed aGVHD, mortality was seen in 9 (25.7%). GVHD as a cause of transplant related mortality in our centre was 6%. The EBMT group has reported a mortality incidence of 25% patients with aGVHD[7]. In a study by Natasha Ali et al the mortality due to aGVHD was 9%.[8]

5. Conclusion

Graft-versus-host disease (GVHD) is a major cause of morbidity and mortality after allogeneic hematopoietic stem-cell transplantation, and it is the subject of much ongoing research. Despite considerable advances in our understanding of the pathophysiology, diagnosis, and predisposing factors for both acute and chronic forms of the disease, a standardized therapeutic strategy is still lacking.

Allogeneic hematopoietic stem cell transplantation can be curative for a variety of malignant and nonmalignant conditions. Although significant improvements have been made, early transplant-related mortality and GVHD remain major obstacles to safe transplantation. Newly and less damaging

nonmyeloablative allogeneic stem cell transplantation viewpoint seems to be promising with possible supremacy

6. References

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