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Frequency of Cytomegalovirus Positivity in Patients Undergoing Bone Marrow Transplant for 3 Months Post-Bone Marrow Transplant

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Abstract

Objective: To determine the frequency of cytomegalovirus positivity detected within three months in patients underwent bone marrow transplant

Methodology: A cross-sectional study was conducted at the Department of Pediatric Oncology, Pakistan Institute of Medical Sciences, Islamabad from 1-10-2021 to 1-10-2022. Sixty two children who underwent bone marrow transplantation within 3 months, who met the eligibility requirements were enrolled in the study. Blood sample was taken and sent to the pathology laboratory of hospital for cytomegalovirus (CMV) antibodies. Reports were retrieved and presence or absence of cytomegalovirus. This whole data was noted into proforma while later on entered and analyzed in SPSS version 25.

Results: The mean age of patients was 6.05 ± 1.76 years. There were 36 (58.1%) males and 26 (41.9%) females. All bone marrow were donated by sibling. Family history of cytomegalovirus was positive in 8 (12.9%) cases. A family history of thalassemia was positive in 8 (12.9%) cases. History of receiving blood transfusions before a bone marrow transplant was positive in 62 (100%) children. Out of 62 cases, cytomegalovirus infection was noted in 26 (41.9%) cases.

Conclusion: There are higher chances of cytomegalovirus infection positivity in thalassemia children who underwent bone marrow transplant about 3 months ago.

Key words: Cytomegalovirus, Thalassemia, Bone Marrow Transplant.

Introduction

Reduced production of haemoglobin subunit beta (haemoglobin β-chain), which causes microcytic hypochromic anaemia, and lower levels of haemoglobin-A on haemoglobin analysis, are the hallmarks of β-thalassemia.[1] Early onset anaemia is caused by decreased haemoglobin production, and frequent blood transfusions are needed to maintain haemoglobin levels.[2] With more than 200 million victims worldwide, thalassemia is one of the most prevalent hereditary diseases. African Americans with thalassemia make up 15% of the population. B-thalassemia is one of the most common types and may be observed in more than 4 million infants who are born with genetic abnormalities each year.[3-6]

Patients with -thalassemia major usually experience iron overload when receiving transfusion therapy. When deposited in the liver, spleen, pancreas, heart, kidney, skin, pituitary, and other organs, excessive iron can harm many organs.[7] Myocardiopathy, congestive heart failure, liver cirrhosis, arthritis, endocrine problems like diabetes, and other illnesses are among the side effects of iron overloading in transfusion-dependent patients.[8] Only allogeneic hematopoietic stem cell transplantation via bone marrow transplant can treat the worldwide prevalent single-gene diseases β-thalassemia. With developments in preventive measures, the management of transplant-related problems, and preparative regimens, this method of treating thalassemia has significantly improved over the previous 20 years. Disease-free survival rates for patients of classes 1, 2, and 3 using a risk class-based transplanting strategy are 90%, 84%, and 78%, respectively.[9]

The morbidity and mortality linked to bone marrow transplantation are significantly impacted by cytomegalovirus infection. Infection can result in Cytomegalovirus illness, which affects a variety of organs and can cause pneumonia, gastroenteritis, retinitis, and other conditions. About half of bone marrow transplant recipients will develop a clinically severe infection, which

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usually develop within first 100 days following the transplant, and cytomegalovirus seropositivity is a substantial risk factor.[10] Infection with the cytomegalovirus can manifest as a primary infection, reinfection, or reactivation. The prevalence of cytomegalovirus infection is rising along with the population of immunocompromised people, particularly in transplant patients. Infection with the cytomegalovirus occurs in 30% to 50% of allogeneic bone marrow transplant cases, which is a serious concern.[11]

Rationale of this study is to find the frequency of cytomegalovirus positivity in thalassemia children after bone marrow transplant who belong to local population. Literature stated that there is high risk of developing cytomegalovirus after bone marrow transplant. But the evidence for local population is missing. Therefore, we want to conduct this study to get local data, whether the frequency of cytomegalovirus infection is high or low in thalassemia children belong to local community. So that in future we can apply results of this study and can recommend to screen the thalassemia children for cytomegalovirus positivity after bone marrow transplantation and can plan preventive and therapeutic strategies to improve the outcome and benefits of transplant.

Methodology

A cross-sectional study was conducted at the Department of Pediatric Oncology, Pakistan Institute of Medical Sciences, Islamabad from 1-10-2021 to 1-10-2022. Non-Probability, consecutive sampling technique was used. A sample size of 62 cases was calculated with a 95% confidence level, 12.5% margin of error and percentage of cytomegalovirus positive i.e. 50%[10] after bone marrow transplantation in thalassemia children

Inclusion criteria: Children of age 3-10 years, either gender, who underwent bone marrow transplant about 3 months ago for thalassemia.

Exclusion criteria: Patients with the following history were excluded, i.e. who were taking steroids before surgery or antibiotics therapy for cytomegalovirus, patients positive for cytomegalovirus infection before transplant as confirmed on polymerase chain reaction of blood sample, chronic kidney disease (creatinine>1.8mg/dl), and congenital heart disease, hepatitis or HIV.

Ninety three children fulfilled the selection criteria were enrolled in the study from OPD of Thalassemia center. Informed consent was obtained. Their demographic data including age, gender, weight, history of blood transfusions, duration form transplant, were noted. Blood sample was taken by using 5cc disposable syringe and converted to collection tubes and sent to the laboratory of the hospital for assessment of presence or absence of cytomegalovirus through polymerase chain reaction. All blood samples were sent to the pathology laboratory of hospital. Reports were retrieved and presence or absence of cytomegalovirus infection was noted. Children who were found to be positive for cytomegalovirus infection were managed as per standard protocols of the hospital. This whole data was noted into proforma while later on entered and analyzed in SPSS version 25.

The collected data was analysed statistically by using SPSS version 21. Age, weight, duration of transplant, duration from transplant, number of blood transfusions before bone marrow transplant, were quantitative variables that were provided as mean and standard deviation. The frequency and percentage were calculated of certain qualitative characteristics, such as gender, parent's education, occupation, personal hygiene of child, family history of cytomegalovirus, and history of cytomegalovirus in siblings.

Results

The mean age of patients was 6.05 ± 1.76 years. There were 36 (58.1%) males and 26 (41.9%) females. The male to female ratio was 1.4: 1. The mean weight of child was 13.99 ± 3.42 kg. Out of 62 cases, bone marrow was donate by sibling in 62 (100%) cases. The mean duration of bone marrow transplant was 89.03 ± 16.54 minutes. The mean duration from transplant until current presentation was 41.13 ± 6.62 days. Baseline features of patients is described in Table I

Table I: Baseline features of patients

	N(%)
Gender	
Male	36 (58.1%)
Female	26 (41.9%)
Weight of child (kg)	13.99 ± 3.42
Bone marrow donor	
Received from Sibling	62 (100%)
Duration of transplant (min)	89.03 ± 16.54
Days from transplant	41.13 ± 6.62

Socioeconomic status	
Low	22 (35.5%)
Middle	22 (35.5%)
High	18 (29.0%)
Parents education	
Illiterate	20 (32.3%)
Under matric	15 (21.5%)
Graduate	27 (46.2%)
Mothers' occupation	
House wife	39 (62.9%)
Maid	9 (14.5%)
Job	14 (22.6%)
Personal hygiene of child	
Good	21 (33.9%)
Average	26 (41.9%)
Poor	15 (24.2%)
Family history of thalassemia	
Positive	8 (12.9%)
Negative	54 (87.1%)
Use of corticosteroids	
Yes	43 (69.3%)
No	19 (30.6%)
Reason to use corticosteroids after transplant	
Graft versus host disease	37 (59.7%)
Auto-immune hemolytic anemia	15 (24.2%)
Idiopathic thrombocytopenia	6 (9.7%)
Autoimmune hepatitis	3 (4.8%)
Nephrotic syndrome	1 (1.6%)
Blood transfusions before transplant	
Yes	62 (100%)
No	0 (0.0%)
Irradiated blood transfusions after transplant	
Yes	62 (100%)
No	0 (0.0%)

Out of 62 cases, cytomegalovirus infection was noted in 26 (41.9%) cases. Figure 1

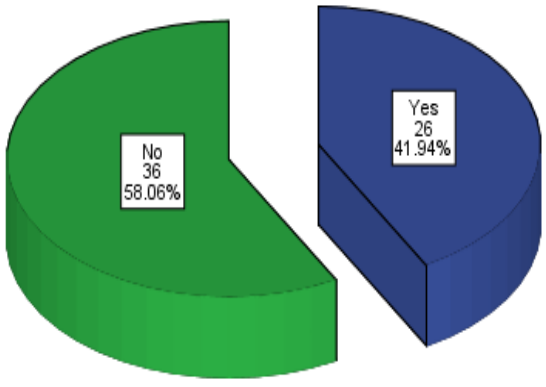

Figure 1. Distribution of cytomegalovirus in children after bone marrow transplant

Discussion

One of the most prevalent genetic disorders in the world is beta thalassemia. The beta globin chain genes have been reported to have more than 200 distinct mutations. Notably, the most prevalent beta-thalassaemia mutations have been broken down by location and ethnicity. For a cost-effective molecular diagnosis of thalassaemia mutations, it is crucial to identify region- and ethnicity-specific commonest mutations.[12]

Thalassemia sufferers' lives have gotten better in terms of length and quality in industrialised nations. Heart disease, chronic liver hepatitis, which can progress to cirrhosis and, infrequently, hepatocellular carcinoma, endocrine issues, stunted growth, osteoporosis, thrombophilia, and pseudoxanthoma elasticum are among the complications that are still frequent. Thanks to the development of novel oral iron chelators and imaging techniques, the incidence of problems is declining in younger patient cohorts who have received transfusions of virus-screened blood.[13]

Nevertheless, high-risk individuals continue to experience higher transplant-related mortality. Due to an advanced stage of the disease, myeloablative bone marrow transplant in adult patients is currently characterised by increased transplant-related toxicity. The transplant-related mortality in these high-risk patients is still significant despite the fact that this novel method of transplanting adult patients with a reduced-dose intensity conditioning regimen has improved thalassemia-free survival. [14]

It is typical for stem cell transplant recipients to experience bone marrow suppression. A fatal post-transplant complication is graft failure. The reasons of bone marrow suppression and graft failure have been identified as cytomegalovirus, Epstein-Barr virus, human herpesvirus-6, and adenovirus. Pancytopenia, hypoplasia of the bone marrow, the presence of a virus while ruling out graft versus host illness, rejection, and relapse should all be considered in the diagnosis of viral-associated graft failure. [15, 16] In our study, we observed Cytomegalovirus in about 41.9% cases after bone marrow transplant, when children presented for regular check-up within 3 months of procedure.

A member of the beta-herpes virinae subfamily is the cytomegalovirus. The cytomegalovirus, which is 150–200 nm in size and has a linear double-stranded DNA molecule in its nucleocapsid, is the largest herpes virus. The distinctive expansion of infected cells with outwardly positioned intranuclear inclusion bodies caused by

cytomegalovirus tends to result in protracted latent infection. Numerous different types of bodily cells, including epithelial, haematopoietic, and connective tissue cells, are susceptible to cytomegalovirus infection.[17]

The incidence of Cytomegalovirus infection after transplantation has decreased, and the incidence of invasive Cytomegalovirus end-organ illnesses has declined from 30% to 5% in recent years as a result of the preventative administration of antiviral medications to patients following stem cell transplant.[18, 19] Despite rigorous therapy utilising antiviral drugs and adjuvant medicines, mortality attributable to deadly Cytomegalovirus disease is still as high as 45–60% in recipients of stem cell transplants; Cytomegalovirus pneumonia and encephalitis are particularly devastating.[20-22] After a bone marrow transplant, the CMV was found in 5% of individuals in another investigation.[23]

However, Shmueli et al. discovered that the incidence of Cytomegalovirus infection in Haploidentical Stem Cell Transplantation was 66.7% after undergoing preemptive medication.[24] In addition, Vallejo et al. discovered that in allogenic stem cell transplants, the rate of Cytomegalovirus infection was 60% following preventive medication.[25] Instances of Cytomegalovirus reactivation after allogenic stem cell transplantation among Cytomegalovirus-seropositive patients can reach up to 80% in patients without Cytomegalovirus prophylaxis and depending on the transplant environment.[25, 26]

In our study, nearly 70% children who developed cytomegalovirus had history of using corticosteroids. Corticosteroids were used to due nephrotic syndrome, hemolytic anemia and idiopathic thrombocytopenia. Another well-known element that influences cytomegalovirus infection is steroids. However, a study found that steroids had no effect on the prevalence of cytomegalovirus infection in high-risk patients. By contrast, steroid administration significantly increased the incidence of cytomegalovirus infection in patients with intermediate risk for cytomegalovirus.[27]

Conclusion

There are higher chances of cytomegalovirus infection positivity in thalassemia children who underwent bone marrow transplant about 3 months ago. Now we have get local magnitudes and found the frequency of cytomegalovirus high. Now in future, we can apply results of this study and recommend to screen the bone marrow transplant patients for cytomegalovirus on regular intervals in order to detect and cure it timely, instead after dysfunction of other multiple organs.

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