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Seroprevalence of Cytomegalovirus Among Thalassemia Patients in Southern Iran: A Cross-sectional Single-Center Study

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Abstract

Background: Thalassemia, a common autosomal recessive disorder, is associated with complications such as transfusion-transmitted infections. Cytomegalovirus (CMV) is a significant pathogen in immunocompromised individuals, with severe clinical manifestations in thalassemia patients.

Objectives: This study aimed to assess the seroprevalence of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies against CMV in children with thalassemia at the Abu Rayhan Special Diseases Center in Bandar Abbas.

Methods: In this cross-sectional study conducted in 2024, 116 non-thalassemia individuals and 131 patients with thalassemia under 18 years of age who regularly received blood transfusions at the Abu Rayhan Special Diseases Center were included. Enzyme-linked immunosorbent assay (ELISA) was performed to detect IgG and IgM antibodies against CMV. Statistical analyses were performed using SPSS software, and the chi-square test was used to compare the groups.

Results: A total of 131 thalassemia patients, comprising 50.4% males and 49.6% females, were assessed using the ELISA technique. A significant difference was observed in the prevalence of CMV IgG antibodies between the thalassemia and non-thalassemia groups ($P < 0.05$). The prevalence of CMV IgM and CMV IgG antibodies in thalassemia patients was 5.3% and 100%, respectively. Among patients who had received more than 10 transfusions per month, 4.7% were seropositive for CMV IgM antibodies.

Conclusions: Frequent blood transfusions, while indispensable in the management of thalassemia, may inadvertently alter immune responses to CMV. This underscores the importance of vigilant monitoring and targeted interventions to minimize the risk of complications arising from viral reactivation.

Keywords: Cytomegalovirus Infections, Prevalence, Thalassemia, Antibody

1. Background

Thalassemia is an autosomal recessive disorder that disrupts hemoglobin synthesis. The reduced production of beta-globin chains leads to the accumulation of excess alpha-globin chains (1). These excess alpha-globin chains aggregate into tetramers, which interact with red blood cell membranes, resulting in hemolytic anemia (2, 3). This condition has a high prevalence, particularly in the Middle East, with significant rates in Southern Iran and Hormozgan province.

Thalassemia patients are primarily dependent on frequent blood transfusions, a process that can lead to significant complications, including iron overload and

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transfusion-transmitted infections, which contribute to heightened morbidity and mortality rates. Effective screening of donor blood for pathogens, including Hepatitis B, Hepatitis C, Cytomegalovirus (CMV), and human immunodeficiency virus (HIV), is regarded as an essential preventive measure (4). Consequently, thalassemia has emerged as a major genetic disorder and public health challenge, particularly in regions such as Hormozgan province.

Cytomegalovirus, a double-stranded DNA virus within the beta-herpesvirus family, is a significant pathogen in immunocompromised individuals, including patients with thalassemia (5). Clinical manifestations of CMV infection in these patients are often severe and may arise from the reactivation of latent infection or from primary infection. Blood transfusion has been identified as a major route of CMV transmission, particularly in pediatric populations (6, 7).

2. Objectives

This descriptive study aimed to assess the seroprevalence of IgG and IgM antibodies against CMV in children with thalassemia, in comparison with non-thalassemia, at the Pediatric Hospital in Bandar Abbas.

3. Methods

In this cross-sectional study, 131 children with thalassemia under 18 years of age who were receiving regular blood transfusions at the Abu Rayhan Special Diseases Center in 2024 were included. A list of all eligible patients was obtained from the center, and those who voluntarily agreed to participate after providing informed consent were enrolled in the study using a convenience sampling method. In addition, 116 children without any history of underlying diseases, who were hospitalized for various non-infectious conditions at the Pediatric Hospital in Bandar Abbas, were also included for comparison of CMV seroprevalence.

Blood samples (5 mL) were collected from each participant. Enzyme-linked immunosorbent assay (ELISA) testing was performed using Pishtaz Teb Diagnostics kits (Iran). Control samples and diluted test sera were added to antibody-coated wells. The plates were incubated at 37°C for 30 minutes, and subsequent steps were carried out according to the manufacturer's protocol. After incubation, stop solution was added, and absorbance was measured at 450 nm using an ELISA reader. In the diagnostic kits utilized for this study, values greater than 1.1 were regarded as positive for CMV IgM, while values below 0.09 were categorized as negative. Results within the range of 0.9 to 1.1 were considered suspicious and required further testing for validation. The Pishtaz Teb Diagnostics kit demonstrated a specificity of 99% and a sensitivity of 100% for the ELISA test. Data analysis was performed using SPSS software version 19, and the Chi-square test was employed to evaluate relationships between variables.

4. Results

In this descriptive-analytical and cross-sectional study, 131 pediatric participants were included in the thalassemia group and 116 in the non-thalassemia group. The demographic information of the participants, including general characteristics of the thalassemia and non-thalassemia groups, is summarized in Table 1.

Table 1. Demographic Profile of Participants in Thalassemia and Non-thalassemia Groups [a]

Variables	Values
Thalassemia (N = 131)	
Male	66 (50.4)
Female	65 (49.6)
Age (mean ± SD)	11.49 ± 2.03
Non-thalassemia (N = 116)	
Male	71 (61.2)
Female	45 (38.8)
Age (mean ± SD)	13.24 ± 1.85

[a] Values are expressed as No. (%) unless otherwise indicated.

The results of the ELISA tests (IgM and IgG) for CMV are summarized in Table 2. A total of 131 thalassemia patients were tested using the ELISA method. Cytomegalovirus IgM and IgG antibodies were detected in 5.3% and 100% of the patients, respectively. The data on thalassemia patients, categorized by the frequency of blood transfusions, are shown in Table 3. Among patients who received ≥ 10 blood transfusions per year, 4.7% were seropositive for CMV IgM antibodies. The analysis revealed a statistically significant difference in the prevalence of IgG anti-CMV antibodies between the thalassemia and non-thalassemia groups.

5. Discussion

This cross-sectional, descriptive, analytical study aimed to assess the prevalence of CMV antibodies among thalassemia patients and the general population. The observed 100% prevalence of IgG CMV antibodies in thalassemia patients suggests universal

Table 2. The Result of Cytomegalovirus Enzyme Immunoassay Test for Thalassemia and Non-thalassemia Groups

Variables	Positive; No. (%)	Negative; No. (%)	Mean ± SD	P-Value [a]
IgG status				< 0.001
Thalassemia	131 (100)	0 (0)	153.59 ± 70.05	
Non-thalassemia	85 (73.3)	31 (26.7)	110.54 ± 94.52	
IgM status				0.098
Thalassemia	7 (5.3)	124 (94.7)	0.29 ± 0.30	
Non-thalassemia	6 (5.2)	110 (94.8)	0.09 ± 0.41	

Abbreviations: IgG, immunoglobulin G; IgM, immunoglobulin M.

[a] Independent sample *t*-test, P-value ≤ 0.05 was considered statistically significant.

Table 3. IgG and IgM Status Based on Frequency of Blood Transfusions in Thalassemia Patients

Blood Transfusion	Positive; No. (%)	Negative; No. (%)	Mean ± SD	P-Value [a]
IgG status				< 0.001
≥ 10	129 (100)	0 (0)	153.59 ± 70.05	
< 10	2 (100)	0 (0)	162.35 ± 121.12	
IgM status				< 0.001
≥ 10	6 (4.7)	123 (95.3)	0.30 ± 0.31	
< 10	1 (50)	1 (50)	1.75 ± 2.24	

Abbreviations: IgG, immunoglobulin G; IgM, immunoglobulin M.

[a] Independent sample *t*-test, P-value ≤ 0.05 was considered statistically significant.

exposure to the virus. While a significant difference between the two groups was noted, it is crucial to recognize that a considerable prevalence of IgG CMV antibodies was also observed in healthy children. This finding may reflect the general public health status of the region, indicating that even individuals without underlying conditions are vulnerable to the infection. Moreover, thalassemia patients, due to their frequent blood transfusions, are at an elevated risk of exposure (8, 9).

The prevalence of IgM CMV antibodies in thalassemia patients was found to be 5.3%, a rate similar to that observed in non-thalassemia children. In thalassemia patients, splenectomy, iron overload, and frequent blood transfusions are the main causes of immune deficiency in these individuals (10). This suggests that the immune response in thalassemia patients may be impaired, preventing sufficient production of IgM antibodies in response to acute CMV infection. Additionally, the frequent blood transfusions received by these patients could lead to continuous exposure to CMV antigens, potentially resulting in immune tolerance and reduced ability to generate IgM antibodies. In contrast, Nigro et al. found that the overall rate of CMV infection in thalassemia patients was similar to that in healthy individuals, although the incidence was higher in the patient group. Notably, changes in CMV antibody titers were not observed concurrently with changes in antibodies to other viruses (such as HSV, VZV, and EBV), suggesting that CMV in these patients is more likely due to the reactivation of latent virus rather than new infection (11). Our findings align with those of Nigro et al., but the reduced IgM antibody response in our cohort, likely due to immune tolerance induced by repeated blood transfusions, may explain the lower prevalence of IgM antibodies. However, active CMV infections, whether clinical or subclinical, remain prevalent in this population. To further understand the mechanisms behind these observations, we recommend the use of advanced serological techniques or polymerase chain reaction (PCR) to accurately differentiate between CMV reactivation and new primary infections in future studies (11).

Immune dysregulation in thalassemia, resulting from factors such as iron overload, splenectomy, and chronic blood transfusions, has been well documented and is often associated with alterations in immunoglobulin profiles, including elevated IgG levels. Passive transfer of donor-derived IgG through transfused blood components may also contribute to transient CMV IgG seropositivity without indicating

active infection or long-term immunity. Furthermore, repeated antigenic exposure due to chronic transfusions may stimulate memory B-cell activation, leading to enhanced IgG production. Collectively, these mechanisms provide a biologically plausible explanation for the higher IgG levels observed in thalassemia patients, although the extent and persistence of such alterations may vary across different studies (12-15).

The findings of this study indicate that the prevalence of IgM antibodies is significantly higher in thalassemia patients who receive more frequent blood transfusions compared to those receiving less than 10 transfusions per month. This difference can be attributed to the increased risk of exposure to viruses in individuals receiving more frequent transfusions.

However, when comparing IgM antibody levels, the results show that patients with less frequent blood transfusions exhibit significantly higher levels of IgM antibodies. This observation suggests differences in the immune status between the two groups. In patients with transfusion-dependent thalassemia, immune dysregulation together with repeated exposure to blood products has been linked to an increased risk of transfusion-transmitted CMV infection. Although preventive measures such as leukoreduction and the use of CMV-seronegative blood components have significantly reduced this risk, the possibility of CMV reactivation or viremia remains biologically plausible (16, 17).

Conversely, patients receiving fewer transfusions experience fewer recurrent infections, allowing them to generate a stronger IgM antibody response and a more active immune defense against new infections. Ultimately, the immune response to CMV appears to be more pronounced in thalassemia patients with less frequent transfusions compared to those undergoing regular transfusions. These findings align with the results of Alsayab et al.'s and Moghimi et al.'s study (8, 18).

This study was conducted as a single-center, cross-sectional investigation among children under 18 years of age in Hormozgan province, southern Iran. The relatively small sample size limits the generalizability of the findings and may affect the statistical power of the analysis. Furthermore, the very small number of participants with ≤ 10 transfusions (only two cases) resulted in an imbalance between subgroups, thereby reducing the robustness of the statistical comparisons. These findings should be interpreted within the constraints of the study's sample size and design. While the single-center design limits the generalizability of the findings, the results still provide valuable insights into the seroprevalence of CMV among thalassemia patients in southern Iran.

5.1. Conclusions

Frequent blood transfusions, while indispensable in the management of thalassemia, inadvertently alter immune responses to CMV. This underscores the importance of vigilant monitoring and targeted interventions to minimize the risk of complications arising from viral reactivation.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design: M. M. and S. A.; Analysis and interpretation of data: H. A. and T. A.; Drafting of the manuscript: M. T. and M. M.; Critical revision of the manuscript for important intellectual content: S. H.; Statistical analysis: H. A., S. A., and M. M.

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