Tabari Biomedical Student Research Journal

OPEN ACCESS

ORIGINAL: Prevalence of cytomegalovirus infection in hemodialysis patients of Imam Khomeini hospital in Behshahr

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ARTICLE INFO

Submitted: 11 Dec 2024
Accepted: 13 Jan 2025
Published: 24 Feb 2025

Keywords:
Cytomegalovirus, infection, Hemodialysis, IgM and IgG antibodies

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Citation:
Yousefi M, Ahmadipour F, Owrang M. Prevalence of cytomegalovirus infection in hemodialysis patients of Imam Khomeini hospital in Behshahr. Tabari Biomed Stu Res J. 2025;7(1): 1- 10

ABSTRACT

Introduction: Cytomegalovirus (CMV) is one of the most common infection agent among immunocompromised patients, blood acceptors, and acceptors of organ transplantation. This study aimed to consider the prevalence of cytomegalovirus infection in hemodialysis patients.

Material and Methods: In this descriptive (cross-sectional) study, 80 blood samples were collected from hemodialysis patients who referred to Imam Khomeini hospital at Behshahr in 2017-2018. IgM and IgG titration against CMV was determined using a specific kit by ELISA method.

Results: 47 (58.75%) patients were male and 33 (41.25%) patients were female. The mean age of patients was 59.87 ± 14.38 year, while the mean of initial dialysis year for total patients was 92.12 ± 3.91. The mean of dialysis number for all patients was 1.15 ± 0.42 each week. During examination, all patients were positive anti-CMV IgG, while only 4 patients were positive anti-CMV IgM. There was no significant difference in antibodies titration between men and women. Approximately 4.25% of males and 6.06% of females were positive regarding to IgM and 100% of whom were positive for IgG. There was a relationship between the level of education and cigarette smoking with antibodies titrations; however, it was not statistically significant. There was no relationship between the antibody titer and dialysis duration.

Conclusion: Due to the relationship between hemodialysis and being positive anti-CMV IgG, CMV consideration in hemodialysis patients who receive blood products or undergo organ transplants (especially kidney transplant) is necessary.

Introduction

Human cytomegalovirus (CMV) is a widespread infection among human populations that typically remains asymptomatic in immunocompetent individuals [1]. However, following primary infection, the virus establishes lifelong latency within the host. Despite the availability of effective antiviral agents such

as ganciclovir and foscarnet, CMV infection continues to be a major cause of morbidity and mortality among transplant recipients, primarily due to delays in diagnosis and treatment [2]. CMV can cause severe disease in immunocompromised individuals, including blood and blood product recipients, as well as organ transplant recipients [3]. In such patients, latent CMV can reactivate and lead to clinically significant disease manifestations [4].

Although the incidence and severity of CMV-related complications are generally lower in kidney transplant recipients compared to other organ transplant patients, primary CMV infection can still occur in this population. It often presents as symptomatic CMV syndrome, characterized by fever, leukopenia, hepatosplenomegaly, and arthralgia, symptoms that may ultimately reduce patient survival [5].

Upon entering the body, CMV elicits both humoral and cellular immune responses. While both arms of the immune system are crucial for controlling CMV infection, cellular immunity plays a more dominant role in viral clearance [6]. Antibodies against CMV, particularly immunoglobulins, can attenuate disease severity and are effective in prophylaxis; however, the progression of CMV infection in immunosuppressed, seropositive individuals, such as those with immunodeficiency disorders or AIDS, and transplant recipients, highlights the secondary role of humoral immunity in such contexts [7].

Currently, various serological assays allow for the detection of CMV-specific IgM, IgG, and IgA antibodies in the bloodstream during different stages of infection, including primary infection, reactivation, and convalescence. IgM levels typically peak early in the course of infection and decline within 12–16 weeks in asymptomatic cases [8]. However, in symptomatic infections, IgM may persist in the circulation for longer periods. IgG antibodies usually reach peak levels within a month after infection and are predominantly of the IgG1 and IgG3 subclasses [9]. Numerous studies to date have documented the emergence of antibodies against cytomegalovirus (CMV) or an increase in their titers among patients undergoing hemodialysis. Moreover, CMV-related complications such as retinitis, hepatitis, and pneumonitis have also been reported in this patient population [10, 11]. Identified risk factors for primary CMV infection include transfusion of contaminated blood or blood products, transplantation of organs from CMV-positive donors, hemodialysis itself, and the frequency of dialysis sessions [12]. For instance, a previous study reported a case of primary CMV infection attributed to a kidney transplant from an infected donor. In that study, neither the transfusion of frozen red blood cells nor direct transmission between dialysis staff members was found to play a role in the infection's occurrence [12].

Given the clinical importance of determining CMV seroprevalence among hemodialysis patients, the present study was designed to assess and compare the levels of CMV-specific serum antibodies in patients attending Imam Khomeini Hospital in Behshahr. In addition to quantifying and comparing serum titers of CMV-specific IgG and IgM antibodies, this investigation examined potential correlations between antibody levels and a range of demographic and lifestyle factors—including age, gender, education level, occupation, quality of life, and geographical location. The findings of this study are expected to contribute substantially to estimating the regional prevalence of CMV infection and enhancing infection control strategies across the province.

Methods

In this descriptive study, blood samples were collected from 80 hemodialysis patients, both male and female, who were referred to Imam Khomeini Hospital in Behshahr. The samples were analyzed for CMV-specific IgG and IgM antibody titers. Participants were randomly selected across different age groups from among the dialysis patients. Prior to sample collection, each participant completed a questionnaire (see attached appendix) containing a series of demographic and

lifestyle-related questions, including age, gender, occupation, educational background, history of specific illnesses, quality and location of residence, history of specific medication use, tobacco use, and more. Once the questionnaire was completed, venous blood samples were collected. All personal data obtained were treated confidentially and securely stored in accordance with ethical guidelines. Following informed consent and the collection of 5 mL of venous blood from each participant, serum levels of IgG and IgM antibodies against CMV were quantified using the indirect ELISA method, employing a commercial ELISA kit (PISHTAZ TEB, Iran).

Statistical Analysis

Data obtained from this study were analyzed using SPSS software (version 22). Continuous variables were summarized using descriptive statistics and presented as mean ± standard deviation (Mean ± SD). The Crosstabs procedure was used to determine frequencies and percentages for categorical variables. Comparisons of means between groups were performed using the Independent t-test, while the Chi-square test was used to compare proportions or frequencies between two groups. A p-value of less than 0.05 was considered statistically significant in all analyses.

Results

In this case-control study, 80 hemodialysis patients aged between 21 and 88 years, who visited Imam Khomeini Hospital in Behshahr during the year 1397 (2018–2019), were assessed for CMV-specific IgG and IgM antibody titers. Additionally, 59 age- and sex-matched healthy individuals were enrolled as the control group. Demographic characteristics of the patients are summarized in Table 1. Of the total patient population, 47 (58.8%) were male and 33 (41.3%) were female. Approximately 91.3% were married, while only 8.8% were single. The mean age of the patients was 59.87 ± 14.38 years. The average number of dialysis sessions per week was 1.15 ± 0.42, and the mean duration of each dialysis session was 3.7 ± 0.37 hours. The average year of dialysis initiation was 1392.12 ± 3.91 (corresponding to 2013–2014). Regarding education level, 30 participants were illiterate, one had primary education, 23 had completed lower secondary school, 18 had a high school diploma, four had an associate degree, and three held a bachelor's degree. Additional variables, such as occupational status, are detailed in Table 1. Serological testing showed that all dialysis patients (100%) were seropositive for CMV-specific IgG. In contrast, 95% were IgM-negative, with only 5% testing IgM-positive. Among the control group, 81.35% were IgG-positive, and only 1.2% were IgM-positive. These differences between the patient and control groups were statistically significant ($p < 0.05$). Subsequently, dialysis patients were stratified by gender to compare various demographic parameters (Table 2). The mean age was 59.82 ± 14.2 years for men and 59.93 ± 15.03 years for women, a difference that was not statistically significant ($p = 0.97$). The average number of dialysis sessions per week was 1.19 ± 0.49 in men and 1.09 ± 0.29 in women, which also did not reach statistical significance ($p = 0.29$). However, a significant difference was found in the mean duration of dialysis sessions: 3.8 ± 0.3 hours for men versus 3.56 ± 0.4 hours for women ($p = 0.003$; Table 2-3). Significant differences were also observed in educational attainment ($p = 0.014$) and employment status ($p < 0.0001$) between male and female patients. No statistically significant difference was noted between the two groups regarding marital status.

Comparison of IgG titers between male and female patients revealed that 100% of participants in both groups were IgG-positive, with no significant difference. Similarly, no significant sex-based difference was observed in IgM positivity. Specifically, 4.25% (n = 2) of men and 6.06% (n = 2) of women were IgM-positive, while 95.74% (n = 45) of men and 93.93% (n = 31) of women tested negative.

Demographic comparisons between patients with IgM-positive and IgM-negative status are shown in Table 3. Most parameters did not differ significantly between the two groups.

However, the mean year of dialysis initiation was significantly different (p = 0.001), with patients in the IgM-negative group having started dialysis earlier than those in the IgM-positive group.

Table 1. Comparison of Demographic Parameters in the Studied Patients

Parameters	Results
Number of patients	80
Gender	
– Male	47 (58.8%)
– Female	33 (41.3%)
Age (years)	59.87 ± 14.38
Dialysis sessions/week	1.15 ± 0.42
Duration of each dialysis session (hours)	3.7 ± 0.37
Year of dialysis initiation	1992.12 ± 3.91
Educational level (n)	
– Illiterate	30 (38%)
– Primary school	1 (1.3%)
– Secondary school	23 (29.1%)
– High school diploma	18 (22.8%)
– Associate degree	4 (5.1%)
– Bachelor's degree	3 (3.8%)
Occupational status	
– Unemployed	19 (23.8%)
– Retired	16 (20%)
– Disabled	4 (5.1%)
– Laborer	1 (1.3%)
– Driver	3 (3.8%)
– Self-employed	6 (7.5%)
– Housewife	27 (33.8%)
– Employee	2 (2.5%)
– Educator	2 (2.5%)
Marital status	
– Single	7 (8.8%)
– Married	73 (91.3%)

Parameters	Male (n = 46)	Female (n = 33)	p-value
Dialysis sessions/week	1.15 ± 0.45	1.09 ± 0.29	0.29
Dialysis duration (hours)	3.8 ± 0.3	3.56 ± 0.4	0.003
Year of dialysis initiation	1992.08 ± 3.92	1992.18 ± 3.95	0.91
Educational level (n)			0.014
– Illiterate	10	20	
– Primary school	1	0	
– Secondary school	15	8	
– High school diploma	14	4	
– Associate degree	3	1	
– Bachelor's degree	3	0	
Occupational status (n)			<0.0001
– Unemployed	13	6	
– Retired	16	0	
– Disabled	4	0	
– Laborer	1	0	
– Driver	3	0	
– Self-employed	6	0	
– Housewife	0	27	
– Employee	2	0	
– Educator	2	0	
Marital status (n)			0.37
– Married	44	29	
– Single	3	4	

Table 2. Comparison of Demographic Parameters Between Male and Female Patients

Table 3. Comparison of Demographic Parameters Between IgM-Positive and IgM-Negative Patients

Parameters	IgM-Positive (n = 4)	IgM-Negative (n = 76)	p-value
Age (years)	58.25 ± 12.91	59.96 ± 14.52	0.81
Dialysis sessions/week	1.0 ± 0.0	1.15 ± 0.43	0.47
Dialysis duration (hours)	4.0 ± 0.0	3.68 ± 0.37	0.10
Year of dialysis initiation	1985.75 ± 7.93	1992.46 ± 3.36	0.001
Educational level (n, %)			0.84
– Illiterate	1 (25%)	29 (38.66%)	
– Primary school	0	1 (1.33%)	
– Secondary school	1 (25%)	22 (29.33%)	
– High school diploma	2 (50%)	16 (21.33%)	
– Associate degree	0	4 (5.33%)	
– Bachelor's degree	0	3 (4%)	
Occupational status (n, %)			0.81
– Unemployed	0	19 (25.33%)	
– Retired	2 (50%)	14 (17.33%)	
– Disabled	0	4 (5.33%)	
– Laborer	0	1 (1.33%)	
– Driver	0	3 (4%)	
– Self-employed	0	6 (8%)	
– Housewife	2 (50%)	25 (33.33%)	
– Employee	0	2 (2.66%)	
– Educator	0	2 (2.66%)	
Marital status (n, %)			0.52
– Single	0	7 (9.21%)	
– Married	4 (100%)	69 (90.78%)	

Discussion

This study investigated the titers of anti-CMV IgG and IgM antibodies in hemodialysis patients attending Imam Khomeini Hospital in Behshahr. Our findings revealed that all patients (100%) were seropositive for CMV-specific IgG, while only 5.1% tested positive for IgM. These results align closely with those reported in previous research. For instance, Aminzadeh et al. (2005) evaluated anti-CMV antibody titers in patients undergoing chronic hemodialysis at Shahid Labbafinejad Hospital

in 2002, finding that 91% of patients were IgG-positive and 20.4% were IgM-positive [13].

In another study, Tarabadi et al. (2001) compared CMV-specific IgG and IgM titers between healthy individuals and 128 kidney transplant candidates receiving maintenance hemodialysis [9]. Their results showed that 86% of healthy individuals and 89.8% of dialysis patients were IgG-positive, with no statistically significant difference, suggesting widespread CMV exposure within the general population. However, CMV-specific IgM was detected in 0.4% of healthy individuals and 2.3% of dialysis patients, a statistically significant difference. The authors suggested that these findings may reflect primary CMV infections or reactivation of latent virus in immunosuppressed individuals, possibly due to blood transfusion.

In a subsequent study, Tarabadi et al. (2002) examined CMV-specific IgG and IgM titers, as well as serum β2-microglobulin levels, in both hemodialysis patients and blood donors [9]. They found IgG seropositivity rates of 90% in healthy individuals and 89.8% in dialysis patients, with no significant difference between groups. However, IgM positivity was significantly higher in the patient group (2.3%) compared to healthy controls (0.2%). Moreover, β2-microglobulin levels were markedly elevated in the hemodialysis group, likely reflecting impaired immune function. The absence of a significant difference in IgG seropositivity further supports the notion of CMV's broad prevalence in the population.

Aminzadeh et al. (2005) also reported no significant correlation between dialysis frequency and antibody titers, a finding consistent with our study [13]. In contrast, Abbas et al. (1996) reported a significant association between dialysis frequency and antibody titers [10]. These discrepancies may be attributable to differences in sample size and study design. Similarly, our study did not find any correlation between the duration of each dialysis session and antibody titers, mirroring results reported by Aminzadeh et al. [13]. We also observed no significant association between CMV antibody titers and patients' educational level or occupational status, in agreement with previous findings [13]. However, a statistically significant relationship was observed between the time of dialysis initiation (i.e., duration of dialysis history) and antibody titers, with results comparable to those of Aminzadeh et al., who also reported a significant positive correlation between dialysis duration and antibody levels [13]. In contrast, no significant associations were found between antibody titers and patient age or the duration of each dialysis session. Numerous studies have assessed CMV-specific IgG and IgM titers in hemodialysis patients, examining their correlation with variables such as age, gender, and dialysis duration, often yielding contradictory results. For example, Ikram et al. (1981) conducted a multicenter study on CMV infection across several dialysis units [14]. Their analysis of 983 patients and 238 healthcare workers showed significantly higher CMV antibody titers in patients compared to staff. Titers were also higher in women and increased with age. Moreover, among healthcare workers, CMV antibody levels were higher in Black individuals compared to White individuals, although no association was found with social status or dialysis duration.

In a case report by Kim et al. (2011), CMV infection was identified in a dialysis patient without any prior history of HIV or other comorbidities [6]. Another study by Rasic et al. (1999) assessed antibody titers for CMV, herpes simplex virus (HSV), and Epstein-Barr virus (EBV) in a group of patient's post-dialysis [15]. They reported IgG seropositivity rates of 100% for CMV and 95% for HSV, with no significant correlations between antibody titers and variables such as sex, age, dialysis duration, or number of prior transplants. Similarly, Spisni et al. (1992) reported that 67% of hemodialysis patients were IgG-seropositive for CMV [4]. More recently, Kowalczyk et al. (2015) analyzed CMV-specific IgG and IgM titers in 162 healthy individuals and 162 hemodialysis patients from 2010 to 2011 [11]. They found

significantly higher IgG titers in dialysis patients compared to controls, 90.7% versus 81.9%, respectively. Among men, 87.9% were IgG-positive, compared to 96.3% of women, though this gender-based difference was not statistically significant. Notably, a positive correlation between age and IgG titers was observed in both groups. IgM positivity was reported in only 1.9% of dialysis patients and 0.6% of healthy individuals. The authors concluded that both advancing age and hemodialysis are potential predictors of CMV seropositivity. In another case report, CMV infection was diagnosed in a 77-year-old man with end-stage renal disease (ESRD) undergoing hemodialysis [16]. Moreover, a separate study involving 52 hemodialysis patients reported an IgM seropositivity rate of 15.4% for CMV [2].

In summary, our findings support the growing body of evidence indicating high CMV seroprevalence among hemodialysis patients, consistent with the notion that hemodialysis and immune suppression may contribute to both primary infection and viral reactivation. Although some demographic and clinical variables did not show consistent associations with antibody titers, the relationship between dialysis history and CMV immunity warrants further exploration in larger, longitudinal studies. Understanding these associations is essential for improving infection control strategies and patient outcomes in dialysis settings. In a study conducted by Abu-Yazd and colleagues (2008), anti-CMV IgG and IgM antibody titers were evaluated in 100 patients with renal impairment undergoing hemodialysis between 2007 and 2008. Their findings indicated that 98% of patients were IgG-positive, while 11% tested positive for IgM. Moreover, the diagnostic value of IgG and IgM serology was compared against PCR results. IgM antibodies demonstrated low sensitivity (30%) but high specificity (97%), whereas IgG antibodies exhibited high sensitivity (93%) but lacked specificity (0%). Based on these results, the authors concluded that the diagnostic utility of CMV-specific IgG and IgM antibody testing is dependent on the stage of infection and disease activity [17]. In another study by Valizadeh (1999), CMV infection was assessed in 28 kidney transplant recipients at Taleghani Hospital in Tehran [18]. Using ELISA, the researchers found that 78.5% of patients had active CMV infection. All transplant recipients were seropositive for CMV-specific antibodies prior to transplantation. However, due to the small sample size, no statistically significant associations were observed between active infection, graft rejection, or Rh blood group. Similarly, Fallahi et al. (2009) evaluated the prevalence of active CMV infection among 923 kidney transplant recipients using PCR and indirect immunofluorescence techniques [1]. Their results revealed a CMV infection prevalence of 7.7% by PCR and 35% by immunofluorescence. No significant associations were found between CMV positivity and age or sex. However, a statistically significant seasonal variation was observed, suggesting that the timing of sample collection may influence detection rates. This seasonal pattern underscores the importance of timely and accurate diagnosis of active CMV infection, including screening for latent infection and monitoring its potential reactivation around the time of transplantation, which could inform therapeutic decision-making.

Taken together, previous studies and the present investigation suggest that CMV infection is highly prevalent among both kidney transplant recipients and hemodialysis patients. In fact, CMV may be considered one of the most common viral infections following renal transplantation or maintenance dialysis. While comprehensive epidemiological studies focusing on CMV prevalence among hemodialysis patients in northern Iran are limited, the findings of this study provide compelling evidence for the widespread presence of CMV infection in this region. Specifically, our results demonstrate a 100% seropositivity rate for CMV-specific IgG among hemodialysis patients from northern Iran.

Conclusion

Considering these findings, along with two critical risk factors for CMV transmission in Iran, population density and socioeconomic conditions, it is plausible that CMV antibody prevalence is also rising among healthy individuals in the general population. Therefore, based on the present data, the incidence of active CMV infection among Iranian hemodialysis patients appears to be substantial. Vigilant monitoring and effective management of CMV infection in this vulnerable patient population are thus of paramount importance.

Acknowledgments

This research was supported by the Faculty of Basic Sciences, Department of Biology, Islamic Azad University, Sari Branch. The authors would like to express their sincere gratitude to all members of the Biology Department at Islamic Azad University, Sari Branch, for their valuable contributions and support.

Authorship

all authors meet the ICMJE authorship criteria.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Funding

The authors received no financial support for this article's research, authorship, and publication.

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