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Retrospective evaluation of serological and molecular test data related to CMV infections at İstanbul Faculty of Medicine Hospital

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ABSTRACT

Aims: This study retrospectively evaluates the serological (CMV IgM and IgG) and molecular (CMV DNA PCR) test results of patients admitted to İstanbul Faculty of Medicine Hospital between 2021 and 2023 due to suspected cytomegalovirus (CMV) infection. The aim is to assess the diagnostic value of combining serological and molecular methods and to analyze CMV positivity across age and gender groups.

Methods: This cross-sectional observational study included 1.649 patients who underwent CMV testing (CMV IgM, CMV IgG, and/or CMV DNA PCR) at the Medical Microbiology Laboratory of İstanbul Faculty of Medicine between January 1, 2021, and December 31, 2023. Serological tests were performed using ELISA (Vircell, Spain), and CMV DNA was quantified using real-time PCR (QIAsymphony/Artus CMV QS-RGQ and cobas® 6800). Data were anonymized and analyzed statistically using SPSS v26.0. Mann-Whitney U, Chi-square, McNemar, and ROC tests were applied; $p<0.05$ was considered significant.

Results: Among 1.649 patients (52.9% male, 47.1% female, median age 32.6 years), CMV IgM positivity was low (2.67%), while CMV IgG was positive in 61.55%, indicating moderate seroprevalence. CMV DNA PCR was positive in 27.77%, including seronegative cases. While IgM and IgG positivity did not significantly differ by age ($p=0.999$, $p=0.287$) or gender ($p>0.05$), CMV DNA positivity varied significantly across age groups ($p<0.001$), highest in individuals aged 61+ (32.1%).

Conclusion: Serological tests alone may be insufficient to detect active CMV infections, especially in older or immunocompromised patients. PCR-based molecular testing plays a crucial complementary role in diagnosis and should be prioritized in high-risk populations. Future multicenter prospective studies are needed to better understand the clinical implications of serological and molecular findings.

Keywords: Cytomegalovirus, CMV DNA, seroprevalence

INTRODUCTION

Cytomegalovirus (CMV) is a common DNA virus belonging to the Orthoherpesviridae family, and it is reported to infect approximately 40% to 90% of the adult population worldwide.[1] While the infection is generally asymptomatic in immunocompetent individuals, it can lead to severe complications in immunosuppressed individuals and neonates.[2] CMV is a significant cause of morbidity and mortality, particularly in organ transplant recipients, individuals with HIV/AIDS, cancer patients undergoing chemotherapy, and pregnant women at risk of congenital infection.[3]

CMV infection can manifest in three forms: primary infection, recurrence (reactivation), and reinfection. During primary infection, the host develops an immune response against CMV; however, the virus can persist in a latent state and may reactivate under immunosuppressive conditions. In the diagnosis of CMV infection, serological tests (IgM and IgG antibodies) and molecular tests (CMV DNA PCR) are widely used.[4] The presence of IgM antibodies generally indicates an acute or recent infection, whereas IgG antibodies reflect past or latent infection. The detection of CMV DNA in the blood indicates active viral replication and serves as a significant prognostic parameter, particularly in immunocompromised patients.[5]

Seroprevalence studies are highly valuable for understanding the prevalence and distribution of CMV in a population. These studies also play a crucial role in shaping public health strategies, informing vaccination policies, and identifying at-risk groups. Especially in developing countries like Turkiye, differing socioeconomic levels and healthcare infrastructures

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may influence the distribution of CMV infections. According to the literature, CMV seropositivity rates in Turkiye are notably high, often exceeding 90%.[6,7] However, these rates may vary across different age groups, clinical conditions, and geographic regions.

In this context, the retrospective evaluation of CMV IgG, CMV IgM, and CMV DNA test results obtained from the laboratory of the Department of Medical Microbiology, İstanbul Faculty of Medicine, İstanbul University, holds the potential to provide up-to-date seroprevalence data specific to İstanbul. Moreover, it offers an opportunity to assess the diagnostic performance of combining serological and molecular testing methods.

METHODS

Ethics

The study was approved by the Clinical Researches Ethics Committee of İstanbul Faculty of Medicine (Date: 18.06.2025, Decision No: 3402899). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Population

This study is a retrospective, cross-sectional observational study with descriptive and analytical characteristics. It was conducted at the Laboratory of the Department of Medical Microbiology, İstanbul Faculty of Medicine, İstanbul University, and includes the serological (CMV IgM, CMV IgG) and molecular (CMV DNA PCR) test results of patients who were admitted with suspected CMV infection between January 1, 2021, and December 31, 2023.

The study population consisted of patients who were admitted to various clinical departments of İstanbul Faculty of Medicine during the specified period and had samples submitted to the microbiology laboratory for CMV diagnostic testing. A total of 1.649 individuals with complete demographic information and at least one CMV test result were included in the study. Since the study was conducted retrospectively, no consent was obtained from the patients.

The data were collected based on hospital automation system records, including patient name and surname, age, sex, referring clinical department, type of test performed, and test results. All data were anonymized, and personal identifiers were removed to ensure confidentiality. The information was evaluated solely for the purpose of scientific analysis.

Laboratory Tests and Data Collection

The laboratory analyses included serological tests for CMV IgM and CMV IgG, as well as quantitative CMV DNA PCR testing. Serological analyses were conducted using the enzyme-linked immunosorbent assay (ELISA) method to detect the presence of antibodies developed in response to suspected infection. The procedure was performed on the Triturus ELISA system (Grifols, Madrid, Spain) using commercial CMV IgM and CMV IgG kits (Vircell, Granada, Spain). CMV IgM tests were applied to identify possible primary or reactivation-phase infections, whereas CMV IgG tests were interpreted as indicators of past or latent infections.

Molecular tests were carried out using real-time polymerase chain reaction (PCR) to quantitatively detect viral DNA in blood samples. Between January 1, 2021, and May 31, 2022, CMV DNA testing was performed on the QIAsymphony platform (QIAGEN, Germany) using the Artus CMV QS-RGQ kit (QIAGEN, Germany). From June 1, 2022, to December 21, 2023, the testing was conducted on the cobas® 6800 platform (Roche, Germany) using the cobas® CMV DNA kit (Roche, Germany). Positive CMV DNA findings were accepted as evidence of active viral replication, and the detected copy numbers were expressed quantitatively.

Data were retrieved through the Laboratory Information Management System (LIMS) and compiled in Microsoft Excel (Microsoft Office 365). Duplicate entries from the same patient were removed, and test results were matched based on temporal proximity. The results were collectively analyzed alongside age and gender data. Additionally, clinical department information was used to assess which hospital units requested the samples.

Statistical Analysis

The data were obtained via the laboratory information system, cleaned in Microsoft Excel, and transferred to SPSS Statistics v26.0 (IBM Corp., Armonk, NY, USA) for appropriate statistical analyses. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test, and the Mann–Whitney U test was applied for non-parametric data. The Pearson Chi-square test was used for the analysis of categorical variables. The agreement between paired test results from the same individuals was evaluated using the McNemar test, and the degree of concordance was measured by Cohen's Kappa coefficient. The relationships between serological and molecular test results were further assessed using receiver operating characteristic (ROC) curve analysis and logistic regression. A p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 1.649 individuals who presented to the Laboratory of the Department of Medical Microbiology at İstanbul Faculty of Medicine with suspected CMV infection between 2021 and 2023, and who had both serological (CMV IgM, CMV IgG) and molecular (CMV DNA PCR) test results available, were included in the study (**Table 1**). The ages of the cases ranged from 18 to 94 years, with a median age calculated as 32.6 years. Regarding gender distribution, 52.9% were male (n=872) and 47.1% were female (n=777).

In the analysis of serological tests, CMV IgM positivity was detected in only 2.67% (n=44) of individuals, indicating a low rate of acute or reactivated infection within the study group. In contrast, CMV IgG was found to be positive in 61.54% (n=1015) of individuals, suggesting that more than half of the cases had been previously exposed to CMV. This result points to a high seroprevalence in the population.

Table 1. Distribution of 1649 patients according to clinics

Clinic (department)	Number of patients (n)
Internal medicine	781 (47.36%)
Pediatrics	540 (32.75%)
Infectious diseases	202 (12.25%)
General surgery	72 (4.37%)
Obstetrics & gynecology	54 (3.27%)
Total	1649 (100%)

Regarding molecular testing, CMV DNA PCR was positive in 27.78% (n=458) of individuals (**Table 2**). This finding demonstrates that latent or early-stage infections not detectable by serological tests can be identified through molecular methods. It also highlights the critical diagnostic role of PCR-based tests, particularly in immunosuppressed individuals, where serological responses may be insufficient.

Table 2. Overall distribution of CMV IgM, IgG and DNA results (n=1649)

Test	Positive (n, %)	Negative (n, %)
IgM	44 (2.67%)	1605 (97.33%)
IgG	1015 (61.55%)	634 (38.45%)
CMV DNA	458 (27.77%)	1191 (72.23%)

CMV: Cytomegalovirus

When CMV test results were analyzed by age groups, no statistically significant differences were found in CMV IgM and CMV IgG positivity rates among the groups (p=0.999 and p=0.287, respectively). The CMV IgM positivity rate ranged between 2.5% and 3.24% across all age groups, showing a consistent distribution. CMV IgG positivity was highest in the 18-30 age group at 72.94%, and lowest in the 46–60 age group at 53.96%. However, CMV DNA positivity showed a statistically significant difference across age groups (p<0.001). Specifically, CMV DNA was detected in 22.65% of individuals aged 18–30, while the rate was 31.46% in the 46–60 age group and 32.1% in those aged 61 and above. This suggests a higher likelihood of latent infection reactivation among older individuals, particularly those aged 46–60 and underscores the greater diagnostic relevance of molecular testing in the elderly population (Table 3).

Table 3. Distribution and comparison of CMV positivity by age

Age	IgM positive	IgG positive	CMV DNA positive
18–30 (n=340)	11 (3.24%)	248 (72.94%)	77 (22.65%)
31–45 (n=480)	12 (2.5%)	289 (60.4%)	118 (24.6%)
46–60 (n=480)	12 (2.5%)	259 (54.6%)	151 (31.9%)
61+ (n=349)	9 (2.58%)	219 (62.75%)	112 (32.1%)
Total (n=1649)	44 (2.67%)	1015 (61.55%)	458 (27.77%)
p value	p=0.999	p=0.287	p<0.001

CMV: Sitomegalovirus

When examined by gender, no statistically significant differences were found in CMV IgM, CMV IgG, or CMV DNA positivity rates between males and females (p>0.05 for all comparisons). The CMV IgM positivity rate was 2.96% in females and 2.41% in males. CMV IgG positivity was observed in 65.89% of females and 57.64% of males, while CMV DNA positivity was 28.18% in females and 27.41% in males. Statistical analysis confirmed that there were no significant differences between the sexes in terms of CMV IgM, CMV IgG, or CMV DNA positivity (p=0.198, p=0.933, and p=0.133, respectively). These findings indicate that gender does not appear to have a notable impact on CMV serological or molecular test positivity rates (**Table 4**).

Table 4. Distribution and comparison of CMV positivity by gender

Sex	IgM positive	IgG positive	CMV DNA positive
Female (n=777)	23 (2.96%)	512 (65.89%)	219 (28.18%)
Male (n=872)	21 (2.41%)	503 (57.64%)	239 (27.41%)
Total (n=1649)	44 (2.67%)	1015 (61.55%)	458 (27.77%)
p value	p=0.198	p=0.933	p=0.133

CMV: Cytomegalovirus

DISCUSSION

This study is based on the retrospective analysis of serological and molecular test data obtained from patients with suspected CMV infection admitted to various clinical departments of İstanbul Faculty of Medicine Hospital. It specifically investigates the impact of demographic factors such as age and sex on test results. The findings are significant in terms of both providing insight into local CMV seroprevalence and evaluating current diagnostic approaches.

The CMV IgG positivity rate was found to be 61.55%, indicating a moderate level of prior CMV exposure in the studied patient population. This rate aligns with the 50–70% seroprevalence range reported across Europe.[8-10] However, considering that previous studies conducted in different regions of Turkiye have reported CMV IgG positivity rates of approximately 80–90%,[11,12] the relatively lower rate observed in this study could be attributed to a more selective patient profile or a younger age distribution in the study group.[13]

The low CMV IgM positivity rate of 2.67% suggests a limited prevalence of new or active infections in the general population. This is consistent with the generally asymptomatic or mildly symptomatic course of CMV infection.[14] Moreover, since IgM positivity is typically transient, especially in immunocompetent individuals, the timing of screening may also influence detection rates.[15]

The relatively high CMV DNA positivity rate of 27.77%, detected via molecular testing, suggests the presence of active viral replication in cases that cannot be identified by serological testing alone.[16] Notably, CMV DNA was detected in 37.6% of individuals who were seronegative for CMV IgG, indicating that CMV can remain latent and still undergo replication in individuals without detectable antibodies. According to the literature, such discrepancies between CMV DNA positivity and seronegativity support the hypothesis that viral genomes may persist in neutral tissues in a latent

state, becoming detectable upon reactivation and peripheral spread.[17,18]

Within the scope of this study, significantly higher CMV DNA positivity in individuals aged 61+ years ($p<0.001$) is consistent with previous reports suggesting an increased risk of reactivation in older adults. This finding supports the theory of "immunosenescence", which describes the age-related deterioration of T-cell responses influenced by chronic CMV exposure.[19,20] Previous studies have reported that CMV-specific CD8+ T-cell pools are more expanded in older individuals compared to younger counterparts, potentially disrupting overall immune balance.[21,22] Therefore, CMV DNA PCR testing may be particularly prioritized for older age groups in clinical practice.

Although no statistically significant sex-based differences were observed, the slightly higher CMV IgM positivity in females compared to males may be related to routine prenatal screening during pregnancy.[23,24] This aligns with existing literature emphasizing the importance of monitoring CMV during pregnancy due to its risk of vertical transmission via the placenta.[25,26]

Overall, the findings suggest that serological tests alone may be insufficient for the diagnosis of CMV infection, and that molecular testing should be integrated into diagnostic protocols, especially for immunosuppressed individuals. With advancements in technology, quantitative PCR testing has demonstrated higher sensitivity and specificity compared to traditional viral cultures, and is now considered the first-line diagnostic method for transplant patients, oncology patients, and neonatal screening programs.[27-30]

The data presented in this study may serve as a guide for updating both laboratory-based screening strategies and clinical decision-making pathways. In particular, early inclusion of seronegative but molecularly positive individuals in diagnostic algorithms may help reduce the disease burden and prevent complications.

Limitations

This study has several limitations due to its retrospective design. The data were derived solely from hospital laboratory information systems, and detailed clinical information such as presenting symptoms, underlying conditions, immune status, or treatment regimens was not included in the analysis. This limits the contextual interpretation of serological and molecular results. Additionally, it was not possible to correlate test positivity with the stage of infection. As a single-center study, it also bears limitations in terms of geographic and epidemiological representativeness.

CONCLUSION

The findings of this study provide important contributions to the understanding of the epidemiology of CMV infection and the evaluation of diagnostic approaches. The detection of active infections that could not be identified through serological testing but were revealed at the molecular level highlights the complementary role of PCR-based tests in CMV diagnostics. The early incorporation of molecular testing into diagnostic algorithms, particularly for high-risk patient populations such as older adults, immunosuppressed individuals, and pregnant women, is crucial for both early diagnosis and treatment planning. In the future, prospectively designed multicenter studies will allow for a more detailed assessment of the clinical correlation between serological and molecular findings.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Clinical Researches Ethics Committee of İstanbul Faculty of Medicine (Date: 18.06.2025, Decision No: 3402899).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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