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Serological Profile of Patients with Suspected Cytomegalovirus Infection from a Tertiary Care Centre in South India

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ABSTRACT

Introduction: Cytomegalovirus (CMV) is a ubiquitous herpes virus with a wide clinical spectrum, ranging from asymptomatic infection to severe disease in neonates and immunocompromised individuals. In India, CMV seroprevalence is high, with exposure being common in the early-life. Despite serological testing being routinely performed for screening, limited data exists regarding the seroprevalence, especially IgM seropositivity across individuals suspected of CMV infection.
Materials and Methods: This retrospective observational study included consecutive patient samples tested for CMV IgG and/or IgM antibodies. Demographic details, clinical indications, and ward distribution were analysed. Seroprevalence was assessed across age groups and gender.
Results: A total of 309 samples were analyzed. CMV IgG seropositivity was 81.12%, with higher prevalence among adults (88.62%) compared to paediatric patients (68.49%); CMV IgM seropositivity was 13.22%, with higher rates in children (17.97%) than adults (7.89%). Both these findings were statistically significant ($p < 0.05$). Among paediatric patients, IgM positivity was predominantly observed in neonates and infants. In adults, IgM positivity was mainly detected during transplant evaluation and suspected infections. A substantial proportion of IgG-positive cases were identified during pre-transplant screening.
Conclusion: High CMV IgG seroprevalence reflects widespread prior exposure, while IgM positivity indicates recent or active infection. The study findings highlight the importance of CMV screening in high-risk groups, particularly in pre-transplant settings and neonatal care. Though serological testing serves as a useful screening tool, careful clinical correlation is essential for appropriate interpretation and patient management.

Keywords: Human cytomegalovirus, CMV IgG antibodies, CMV IgM antibodies, Seroprevalence

INTRODUCTION

Cytomegalovirus (CMV), a member of the human herpesvirus family, is a double-stranded DNA virus belonging to the beta-herpesvirus subfamily and is an important cause of clinically significant disease. CMV infection manifests across a broad clinical spectrum, ranging from asymptomatic infection in immunocompetent individuals to severe and potentially life-threatening

disease in immunocompromised populations, including transplant recipients with a huge economic burden (1,2).

In immunocompetent hosts, CMV infection is usually asymptomatic but may occasionally present as a nonspecific febrile illness or a mononucleosis-like syndrome characterized by fever, lymphadenopathy, and lymphocytosis (3). Following primary infection, CMV establishes lifelong latency in multiple cell types, including endothelial cells, epithelial cells, smooth muscle cells, and fibroblasts, with persistence in peripheral monocytes facilitating dissemination (4). The host immune response initially involves the production of CMV-specific IgM antibodies, followed by IgG antibodies that persist lifelong; IgG avidity maturation serves as a useful marker for determining the timing of infection (5).

The clinical expression of CMV infection is largely determined by the host immune status (2). In immunocompetent individuals, intermittent viral reactivation is effectively controlled by CMV-specific CD4+ and CD8+ T-cell responses (6). In contrast, immunocompromised individuals—including those with human immunodeficiency virus (HIV) infection and recipients of solid organ or hematopoietic stem cell transplants—are at increased risk of uncontrolled viral replication and CMV disease due to impaired cellular immunity (7,8).

CMV is transmitted via direct contact with infected body fluids, blood transfusion, transplacental transmission, and breast milk (9,10). Globally, CMV seroprevalence in developed countries ranges from 56% to 94% (11,12), while studies from India report higher rates ranging from 83% to 95% (10,13).

In many tertiary care centres, CMV serological testing is frequently performed; however, there is limited region-specific data correlating serological markers (IgG and IgM) with clinical indications and patient characteristics. Understanding these patterns is essential to improve interpretation of serological results, optimize screening strategies, and support evidence-based clinical decision-making in resource-constrained settings.

MATERIALS & METHODS

This is a retrospective observational study conducted at a tertiary care hospital in South India, between June 2022 to May 2023. Institutional Ethics Committee clearance was obtained before initiation of the study (IEC Study Ref No. TH-14/2023) with a waiver of consent as there was no direct contact between patients and the study group. All consecutive samples received for detection of CMV antibodies (IgG/IgM/both) from patients across all age groups and both genders suspected of CMV infection during the study period were included; samples received in duplicate were excluded.

A total of 319 samples were received for testing of CMV IgG, IgM, or both antibodies during the study period. Among these, ten duplicate samples were excluded from the study. Out of the remaining 309 samples, as per the clinician's request, 196 were tested for CMV IgG antibodies, 242 were tested for CMV IgM antibodies, and 129 were tested for both antibodies using the Chemiluminescent microparticle immunoassay (CMIA) methodology in the Microbiology Laboratory.

Laboratory data was collected from the laboratory information system and laboratory registers. Patient related information was obtained from the medical records department through in-patient/out-patient charts which included patient demographics and indications for testing.

The study group was divided into different categories based on their age- neonates from 0 day to 28 days, infants from 29 days to 1 year of age, children between 1 year of age to 5 years of age and children more than 5 years of age. Adults were further divided into three groups- those between 18 years to 30 years, 30 years to 50 years, and those more than 50 years of age.

Based on the risk factors and indications for testing, the study group was further divided

into different groups. Data regarding the indications for testing was available for 172 patients for whom IgG was tested and 213 patients for whom IgM was tested. The various groups included- congenital disorders (which included children with genetic disorders such as Primary Hemophagocytic lymphohistiocytosis, Down's syndrome, etc.), growth disorders in children (such as intrauterine growth restriction, microcephaly, etc.), hepatobiliary symptoms (such as hepatitis, cholestasis, jaundice, etc.), infectious etiology (which included patients showing features such as sepsis, pneumonitis, etc. in whom CMV infection was suspected), malignancy (immunosuppressed patients who were diagnosed with cancer), neurological symptoms (such as seizures, hydrocephalus, etc.), pregnancy (as part of antenatal screening) and the transplant group (which included patients undergoing solid organ or hematopoietic stem cell transplant). 23 patients who could not be classified into any of the above categories were classified into the miscellaneous category. Some of the patients who had an overlap between two categories such as those with underlying malignancy as well as showing signs of infection were categorized into the relevant group based on the major indication at the time of testing.

Statistical Analysis

All quantitative variables were summarized by frequency and percentages. The distribution of demographic variables was compared against CMV IgM results and CMV IgG results by frequency and percentages. Chi-square test was performed wherever applicable, p value <0.05 was considered as statistically significant. Statistical comparison was not possible for selected variables due to insufficient observations per cell. The analysis was performed by using R, version 4.2.1 (R core team,2023, Vienna, Austria).

RESULT

Gender and Age wise distribution:

Among the 309 patients, there was a balanced distribution of samples between the genders, with 154 samples from male patients (49.84%) and 155 samples from female patients (50.16%). Majority of the samples received were from infants (23.30%) and middle-aged adults (22.65%). (Table 1)

Table 1: Sub-grouping of patients in the study group (N=309)

Age wise distribution	Female n	Male n	Total count n (%)
0-28 days	17	30	47 (15.21%)
29 days- 1 years	26	46	72 (23.30%)
>1 year- 5 years	5	9	14 (4.53%)
> 5 year - 18 years	15	12	27 (8.73%)
> 18 years - 30 years	41	15	56 (18.12%)
> 30 years – 50 years	39	31	70 (22.65%)
> 50 years	12	11	23 (6.79%)
Total	155	154	309 (100%)

Ward-wise distribution:

A higher proportion of the samples were from patients admitted in the Intensive Care Units (ICUs) (25.57%) and the Nephrology department (24.92%). (Figure 1)

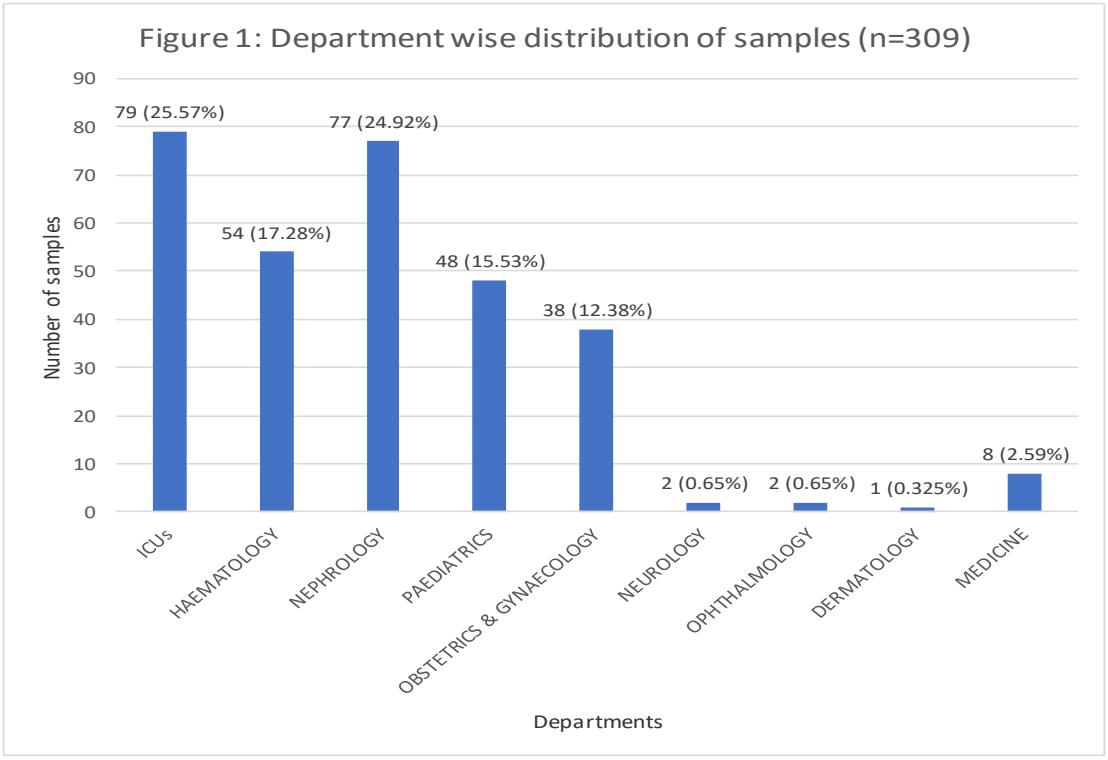

Figure 1: Ward-wise distribution of samples (N=309)

Seroprevalence:

The positivity of CMV IgG among the adult and paediatric patients was 87.90% and 69.44%, while the positivity of CMV IgM among the adult and paediatric patients was 7.96% and 17.83% respectively. Combined IgG and IgM positivity in adult patients was 6.82% and paediatric groups was 7.14%. (Table 2)

Table 2: Distribution of CMV serological testing and seropositivity among study participants (N = 309)

Parameter	Category	Total n (%)	Positive n (%)	Negative n (%)
Testing Pattern	IgG only	67 (21.68)	—	—
	IgM only	113 (36.57)	—	—
	Both IgG & IgM	129 (41.75)	—	—
	Tested for IgG (±IgM)	196 (63.43)	—	—
	Tested for IgM (±IgG)	242 (78.32)	—	—
CMV IgG	Overall	196 (63.43)	159 (81.12)	37 (18.88)
	Adults	124 (63.27) *	109 (87.90)	15 (12.10)
	Paediatric	72 (36.73) *	50 (69.44)	22 (30.56)
CMV IgM	Overall	242 (78.32)	32 (13.22)	210 (86.78)
	Adults	113 (46.69) *	9 (7.96)	104 (92.04)
	Paediatric	129 (53.30) *	23 (17.83)	106 (82.17)
CMV IgG and IgM combined	Overall	130 (42.07)	9 (6.92)	13 (10.00)
	Adults	88 (67.69)	6 (6.82)	6 (6.82)
	Paediatric	42 (32.31)	3 (7.14)	7 (16.67)

* Percentages for adult and paediatric subgroups are calculated within the respective IgG or IgM tested populations.

On comparison of CMV IgG and IgM seropositivity across the different age groups, CMV IgG positivity was noted to increase with increasing age. (Table 3) On further comparison, across adult and paediatric age groups, CMV IgG positivity was noted to be higher in adults. In contrast, CMV IgM positivity was mainly seen in the paediatric age group; both these findings were statistically significant. (Table 4)

Table 3: Seropositivity of CMV IgG and IgM based on different age groups

Age Group	CMV IgG Results (n=196)		CMV IgM Results (n=242)	
	Positive n (%)	Negative n (%)	Positive n (%)	Negative n (%)
0 - 28 days	4(40%)	6(60%)	5(11.36%)	39(88.64%)
29 days - 18 years	46(73.02%)	17(26.98%)	18(21.43%)	66(78.57%)
> 18 years	109(88.62%)	14(11.38%)	9(7.89%)	105(92.11%)

Table 4: Comparison of Seropositivity of CMV IgG and IgM between adult and paediatric patients

Age Group	CMV IgG Results (n=196)		CMV IgM Results (n=242)	
	Positive n (%)	Negative n (%)	Positive n (%)	Negative n (%)
Paediatric	50(68.49%)	23(31.51%)	23(17.97%)	105(82.03%)
Adult	109(88.62%)	14(11.38%)	9(7.89%)	105(92.11%)
p-value*	0.0005		0.021	

* p-value by Chi-square test

On gender-wise comparison, CMV IgG positivity was noted to be high among both genders when compared to CMV IgM positivity. (Table 5)

Table 5: Seropositivity of CMV IgG and IgM across gender in the adult population

Gender	CMV IgG Results (n=196)		CMV IgM Results (n=242)	
	Positive, n (%)	Negative, n (%)	Positive, n (%)	Negative, n (%)
Female	62(88.57%)	8(11.43%)	6(8.11%)	68(91.89%)
Male	47(87.04%)	7(12.96%)	3(7.5%)	37(92.5%)

On comparison of CMV IgG and IgM seropositivity across the different specialties, the distribution of CMV IgG positivity was higher from Nephrology and Hematology units; CMV IgM positivity was higher among samples from ICUs. (Table 5)

Table 6: Ward-wise seropositivity of CMV IgG and IgM

Department	CMV IgG (n=196)		CMV IgM (n=242)	
	Positive n (%)	Negative n (%)	Positive n (%)	Negative n (%)
Dermatology	1(0.51%)	0(0%)	0(0%)	1(0.41%)
Haematology	41(20.92%)	6(3.06%)	3(1.24%)	26(10.74%)
Intensive Care Units	16(8.16%)	13(6.63%)	14(5.79%)	51(21.07%)
Medicine	6(3.06%)	0(0%)	0(0%)	5(2.07%)
Nephrology	59(30.10%)	6(3.06%)	5(2.07%)	65(26.86%)
Neurology	1(0.51%)	0(0%)	1(0.41%)	1(0.41%)
Obstetrics & Gynaecology	20(10.20%)	7(3.57%)	2(0.83%)	29(11.98%)
Ophthalmology	1(0.51%)	1(0.51%)	0(0%)	1(0.41%)
Paediatrics	14(7.14%)	4(2.04%)	7(2.89%)	31(12.81%)

Majority of the IgG positives (47.09%) were from patients in the transplantation workup group while most of the IgM positives were from patients in the transplantation group and with an underlying infectious etiology (3.29% in each group). (Table 6)

Table 7: Seroprevalence of CMV IgG and IgM with indications for testing

Indications	CMV IgG (n=172)		CMV IgM (n=213)	
	Negative n (%)	Positive n (%)	Negative n (%)	Positive n (%)
Congenital disorders	3 (1.74%)	3 (1.74%)	5 (2.35%)	3 (1.41%)
Growth disorders	1 (0.58%)	9 (5.23%)	20 (9.39%)	4 (1.88%)
Hepatobiliary disorders	2 (1.16%)	5 (2.91%)	17 (7.98%)	3 (1.41%)
Infectious etiology	7 (4.07%)	12 (6.98%)	26 (12.21%)	7 (3.29%)
Malignancy	0 (0%)	2 (1.16%)	2 (0.94%)	0 (0%)
Miscellaneous	5 (2.91%)	6 (3.49%)	15 (7.04%)	4 (1.88%)
Neurological	1 (0.58%)	1 (0.58%)	4 (1.88%)	0 (0%)
Pregnancy	6 (3.49%)	18 (10.47%)	27 (12.68%)	2 (0.94%)
Transplant	10 (5.81%)	81 (47.09%)	67 (31.46%)	7 (3.29%)

DISCUSSION

The present study was undertaken to determine the serological profile of CMV infection and its associated clinical characteristics among patients presenting to a tertiary care centre. Consecutive samples from patients undergoing CMV IgG and/or IgM testing were included. The study population showed an almost equal gender distribution, with samples obtained from multiple hospital units, including intensive care units (ICUs), paediatrics, nephrology, and haematology, with the highest proportion from ICUs, followed by nephrology units.

CMV IgG seropositivity was found to be higher with advancing age and these results were found to be statistically significant. The overall CMV IgG seropositivity was 81.12%, with higher prevalence among adults (88.62%) compared to the paediatric population (68.49%), consistent with the global estimate of approximately 83% (14). Among children, the highest seroprevalence was observed beyond one month of age, suggesting early exposure. Similar findings have been reported in a South Indian paediatric population (13).

A substantial proportion of CMV IgG–positive cases were observed among patients in nephrology units with chronic kidney disease undergoing pre-transplant evaluation. CMV remains the most common opportunistic infection following renal transplantation, particularly within the first six months post-transplant (15). Current guidelines recommend CMV IgG testing during pre-transplant evaluation, as IgM-based assays have lower specificity and may yield false-positive results; repeat testing is advised when donor or recipient serostatus is negative (16).

The overall CMV IgM seropositivity was 13.22%, comparable to reports among blood donors (17). Among adults, IgM seropositivity was 7.89%, aligning with previous studies (18,11). IgM seropositivity was found to be higher (17.97%) in the pediatric age group and was statistically significant, indicating that primary infection is more common in this age group. Though the prevalence of congenital CMV infection ranges from 0.2% to 5.4% globally as per systematic review analysis (19), the study revealed 11.36% IgM seropositivity among the neonates in the study group probably attributable to the data being reported from a single tertiary care centre.

In this study, the IgM seropositivity was 7.5% in the adult male population and 8.11% in the adult female population and IgG seropositivity was high in both genders. In India, the reported incidence of congenital CMV is approximately 2.1%, reflecting the high maternal seroprevalence (20). Although intrauterine growth restriction (IUGR) is noted in a subset of IgM-positive infants, it remains a nonspecific finding (19). In contrast, studies among blood donors in India demonstrate high IgG seropositivity with minimal IgM detection (21). There is no published literature on the IgM seropositivity in the adult male population (3).

In adults, CMV IgM positivity was primarily detected during transplant evaluation, antenatal screening, or investigation of suspected infection or reactivation. None of the women with adverse obstetric history demonstrated IgM positivity, although IgG positivity was observed in some cases.

Pre-transplant screening constituted the largest group tested and accounted for the majority of CMV IgG–positive cases. CMV remains a major cause of morbidity following solid organ transplantation (16). In high-risk settings, antiviral prophylaxis is recommended. Serological assays have limited utility in diagnosing post-transplant CMV disease, for which nucleic acid amplification tests and antigenemia assays are preferred (16, 22).

In this study, CMV IgM positivity was predominantly observed among transplant recipients and patients evaluated for infectious etiologies. CMV reactivation in critically ill patients has been associated with prolonged ICU stay (9). CMV end-organ disease in immunocompromised

individuals includes pneumonitis, colitis, hepatitis, esophagitis, retinitis, and encephalitis (9).

The major strength of this study is its sample size and the reporting of seroprevalence among male population which is lacking in the published database. Limitations include study being conducted at a single tertiary care centre and the lack of CMV viral load data. In addition to serology, CMV viral load estimation is recommended in symptomatic patients, transplant recipients, and neonates to confirm active infection and guide management (23).

CONCLUSION

This study demonstrates a high seroprevalence of CMV IgG, indicating widespread prior exposure in the study population, with significantly higher rates among adults. CMV IgM positivity, suggestive of recent or active infection, was more frequently observed in paediatric patients and individuals undergoing transplant evaluation. The findings highlight the importance of CMV screening in high-risk groups, particularly in pre-transplant settings and neonatal care. While serological assays provide valuable epidemiological and screening information, their limitations in distinguishing active infection necessitate the use of molecular diagnostic methods such as CMV viral load estimation. Integration of serology with nucleic acid testing is essential for accurate diagnosis, risk stratification, and timely management, especially in immunocompromised and vulnerable populations.

Declaration by Authors

Ethical Approval: This study was approved by the Institutional Ethics Committee, (IEC Study Ref No. TH-14/2023).

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Conflict of Interest: The authors declare no conflict of interest.

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