Original Article

Seroprevalent study of cytomegalovirus infection in the regions of Jharkhand

Anita Sundi, Nilamber Roopa, Piyalee Gupta, Sana Irfan, Tarun Kumar Kar

Department of Microbiology, Virus Research Diagnostic Laboratory, Mahatma Gandhi Memorial Medical College, Jamshedpur, Jharkhand, India

Abstract

Background: The Human Cytomegalovirus (HCMV) is a type of beta herpesvirus widespread in all human populations. It is estimated that up to 80-100% of adults worldwide and most infections are harmless and can cause severe health complications in infants, like hearing loss and developmental issues. Still, immunocompromised individuals can experience serious complications from the virus. Unfortunately, there is limited information on the prevalence of this virus in our country, and no studies have been reported on the rate of CMV transmission yet. **Objectives:** This study aims to evaluate the levels of IgM antibodies against Cytomegalovirus (CMV) in East Singhbhum, West Singhbhum, and Seraikela Kharsawan using an ELISA test. **Methods:** An indirect ELISA test was performed to detect anti-CMV IgM and the period of study was from January'2021 to June'2023. **Results:** The examination tested 55 people for the TORCH profile of CMV parameters from regions of East Singhbhum, West Singhbhum, and Seraikela Kharsawan. Here, 17 people (30.09%) were IgM positive by ELISA. **Conclusions:** The serological data confirms that CMV is not being monitored and recognized in the general population, which limits our study between CMV infection, disease, and clinically diagnosed outcomes. This understanding is crucial for the healthcare and policy sectors. Thus, we recommend implementing a surveillance and mindfulness program for at least one-fourth of the population in Jharkhand and continuing to explore and develop effective vaccines to control CMV infections.

Keywords: Anti-CMV IgM, cytomegalovirus, ELISA, infected babies, seroprevalence

Introduction

Worldwide , the Cytomegalovirus infection is prevailed due to restricted knowledge and even the route of transmission is not known.[1] Worldwide, congenital CMV (cCMV) not only causes long-term suffering in affected families but also imposes a substantial economic burden on health and social care systems.[2] Cytomegalovirus, which enlarges the virus-infected cells,[3] is one of the largest and opportunistic viruses of the herpes family with 240 Kbp nucleotides. The term "Cytomegalic" word first suggested by Goodpasture and Talbert in 1921 and also confirmed that they could be a viral agent. Later, it was isolated from the baby's excretion of urine, and then the term "Cytomegalovirus" was assigned in 1960 by Weller and coworkers. Like all human herpes contagions, cytomegalovirus (CMV) is a common viral infection[4] that establishes a lifelong hidden infection following primary infection that can periodically extinguish with a slipping of contagious contagion.[5] The frequency of natural congenital CMV (cCMV) is more than 3-fold higher in low- and middle-income countries (LMIC) compared with high-income countries.[6] The presence of laboriously replicating CMV during gestation, whether from primary infection, reactivation from quiescence or reinfection, can result in congenital transmission to the fetus.[7]

Address for correspondence: Dr. Nilamber Roopa, Department of Microbiology, Virus Research Diagnostic Laboratory, Mahatma Gandhi Memorial Medical College, Jamshedpur - 831 012, Jharkhand, India.
E-mail: roopaverma1983@gmail.com

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According to research by Gaytant *et al.*,[8] the connection between intrauterine transmission of CMV and fetal, neonatal, or child complaints is not well defined. Viral infections during gestation are a significant global concern that can impact the health of the fetus as congenital and perinatal infections. The incidence of natural congenital infection depends on the epidemiological characteristics (intrauterine growth retardation and prematurity) among the population, especially in maternal CMV seroprevalence. Populations with high seroprevalence have consistently demonstrated high rates of natural CMV infection, as shown by Kenneson *et al.*[9] Perinatal CMV infections were seen in newborns delivered through an infected birth canal or post-natal through infected breast milk or secretions from the mother. Most of the infected infants remain asymptomatic and about 5-10% of infected infants are symptomatic. Sometimes symptomatic infants face early fatality.[10] Congenital CMV infection acquired by the fetus during gestation may lead to various neurological and developmental disabilities such as sensorineural hearing loss, cognitive impairment, and visual impairments.[11]

Establishing CMV seroprevalences by age and other demographic factors is important for identifying populations of women who are immunocompromised during the gestational period and are at higher risk of severe CMV infection.[12] These findings can inform behavioral interventions aimed at preventing infection in pregnant women[13-17] and help identify the target populations for future CMV vaccines.[17-19]

Since clinical symptoms are usually absent, the only reliable way to estimate the frequency of infection in a population is through laboratory diagnosis. CMV seropositivity is considered to be the best laboratory measure of past infection. This paper mainly focused on screening studies with high maternal CMV seroprevalence and clinical findings in infected patients in the East Singhbhum, West Singhbhum, and Seraikela Kharsawan regions of Jharkhand.

Materials and Methods

Case selection for this study: Cases were selected based on having a medical condition for CMV. Blood samples were received in VRDL, Department of Microbiology, MGM Medical College, Jamshedpur. Ethical committee approval is obtained Ref. no.:MC/870/23 date:19/07/2023.

The IgM ELISA method was used for CMV detection.

Definition of terms

A CMV-infected individual has anti-CMV IgM antibodies in serum which indicates CMV seropositivity and hence those antibodies act as a marker in that individual.

Seroprevalence of Cytomegalovirus is defined as the prevalence rate of CMV positivity in a given population.

Study selection

We categorized CMV seroprevalence studies according to age and sex. Many of the seroprevalence studies examined individual samples who possess complaints either of body swelling, fever, and seizures or without any particular complaint about CMV risk factors.

Assays of IgM antibody to CMV

CMV viruses are host-specific viruses (Human to Human/animal to animal) and the only known reservoir for the host is humans for CMV infection. Various laboratory methods were used to diagnose the infection for CMV such as antibody detection and antigen detection by ELISA, molecular methods by PCR and RT PCR. Among the above assays, the vast and superior performance of the studies used is an enzyme-linked immunosorbent assay (ELISA) to detect CMV-specific IgM. When simply determining whether a person is antibody positive or negative, Nevertheless, the studies done with assays other than the ELISA may to some extent underestimate the true seroprevalence in the population studied.

Seroprevalent studies of Cytomegalovirus Infection in the regions of Jharkhand were tested and diagnosed at the Virus Research Diagnostic Laboratory (VRDL), Department of Microbiology, MGM Medical College, Jamshedpur. The stored frozen serum samples were focused in our review. Fifty-five samples of serum were tested for screening for anti-IgM CMV. Samples were screened using the ELISA technique (NovaTec Immundiagnostica, GmbH, Dia-Pro ELISA kits, Cal Biotech Diagnostic Kits). Each assay was accompanied by the kits containing both the controls (positive and negative). The specificity and sensitivity of the kit were greater than 98% and 91%, respectively. The results were interpreted as negative, indicating that the patient is not undergoing an acute infection by CMV. An equivocal result indicates that the patient should be re-tested after 1-2 weeks from the first testing, and the positive result is indicative of a CMV infection; therefore, the patient should be treated accordingly.

Results

55 samples were tested from January 2021 to June 2023 of which 17 were positives, 1 testing equivocal, and 37 were negatives [see Table 1 and Figure 1]. The highest number of positive cases were in the age group 0-20 years, followed by 20-40 years, and the lowest number would be between the age groups 40-80 years [see Table 2 and Figure 2]. Among the positive cases, (31.25%) 5 were male with ages of 2 years, 1 month, 18 days, 5 years and 17 years, and (70.5%) 12 were females [see Table 3 and Figure 3] with ages of 3 days, 3 months, 19 years, 21 years, 22 years, 25 years, 36 years, 42 years, 58 years, and 76 years, and the highest positivity (7) would be in the month of November 2022, which is followed by August 2022 (4) and October 2022 (2). July 2022, May 2022, and September 2021 had one case. The mean age

was 19 years, with a median of 17 years and a range of 76 years. 30.9% of the samples tested positive for anti-IgM CMV, with a 95% confidence interval of 19.713-21.487. The distribution of CMV complaints was region-wide [see Table 4 and Figure 4].

Table 1 and Figure 1 indicate the total number of cases in the past three consecutive years with their positivity, negativity, and equivocal reports.

Table 2 and Figure 2 indicate the IgM Status of CMV in the different age groups and the positive rates are high between 0-20 years.

Table 3 and Figure 3 indicate the total positivity rate and their positivity in sex-wise distribution. The CMV positivity rate is high in females when compared to males.

Table 4 and Figure 4 indicate the total no of cases in the region-wide distribution over three consecutive years.

Discussion

The normal immune system controls primary infection, reinfection, or reactivation. Generally, Cytomegalovirus (CMV) is asymptomatic. However, it becomes an important pathogen in immature or immunocompromised individuals, such as in pregnant females or unborn children. Several vaccines against CMV are currently in clinical trials that aim to induce immunity in seronegative individuals and/or boost the immunity of those with prior natural infection seropositive.[20]

Table 1: Reporting CMV seroprevalence study

Year	Total no cases	Positivity	Negative	Equivocal
2021	17	1	16	0
2022	37	16	20	1
2023	1	0	1	0

Table 2: IgM status in the different age groups

Age distribution in years	CMV positivity rates (%)
0-20	10
20-40	4
40-60	2
60-80	1

Table 3: CMV positivity in sex-wise distribution

Gender	No of Positive Cases
Total Positive	17
Male Positivity	7
Female Positivity	12

Table 4: Region-wide distribution of CMV

Regions	2021	2022	2023
East Singhbhum	16	33	1
West Singhbhum	0	2	0
Seraikela Kharsawan	1	2	0
Total Cases	17	37	1

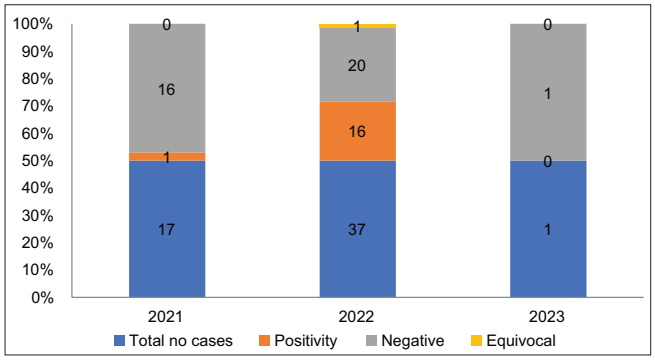

Figure 1: Reporting CMV seroprevalence study

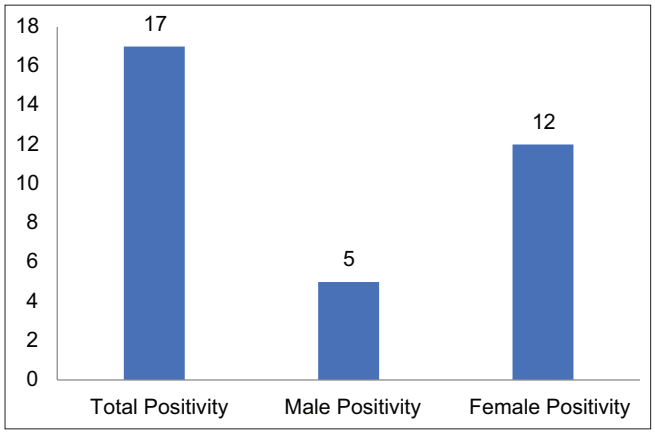

Figure 3: CMV positivity in sex-wise distribution

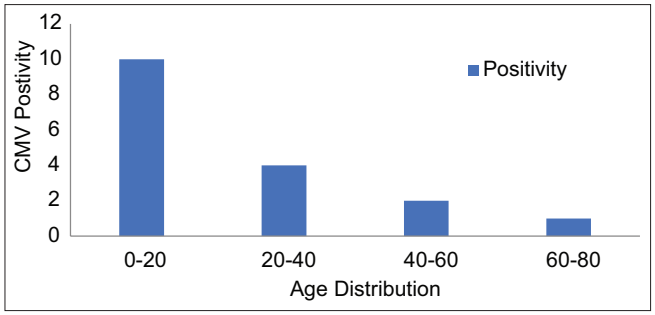

Figure 2: CMV IgM status in the different age groups

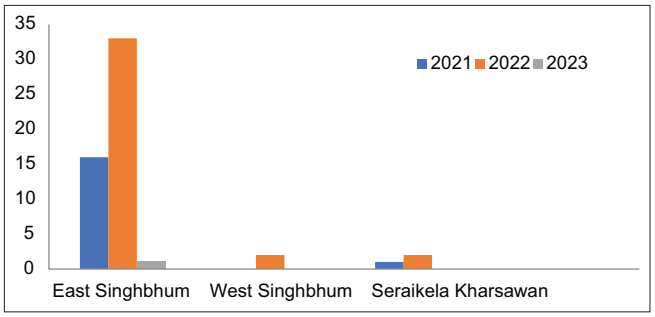

Figure 4: Region-wide distribution of CMV

According to Wang *et al*.,[21] CMV IgM antibodies also act as a marker for transmission. CMV infection during the gestational period leads to hearing loss and developmental issues; if the risk is maximum, it leads to mortality. When using IgM as a diagnostic method, the prevalence ranges were found to be high compared to IgG methods. This is because IgM production occurs first after CMV infection, while IgG levels take a few weeks to increase and remain present throughout a person's life. Therefore, IgM outcomes are more likely to indicate new and active infections, while IgG indicates the total number of patients with past histories of CMV infection.

Our review has 55 TORCH cases, out of which 17 samples tested positive for anti-IgM CMV. A similar study conducted in New Delhi by Kothari *et al*.[22] found no positive cases of anti-IgM CMV among the 200 blood units tested. However, 95% of the blood donors tested positive for IgG antibodies, indicating past exposure to the infection. Other studies conducted in India, including those,[23-25] showed similar prevalence rates for IgG antibodies but remained inconclusive for anti-IgM CMV. In contrast to Western literature, which reports seroprevalence rates ranging from 38% to 75% among voluntary blood donors,[26] Galea *et al*.[27] found high seroprevalence rates in India and other developing countries. Similarly, in advanced countries like the USA, Staras *et al*.[28] found a seroprevalence rate of 58.9% for CMV infection among individuals aged 6 years or more in their study conducted in 2006.

There was no statistically significant association between CMV seroprevalence with age, gender, education, family member, and residency groups in this previous study.[29] When interpreting IgM data in this Systemic Literature Review (SLR), it is important to consider the limitations of IgM studies. There is variability between IgM diagnostic assays, which means the assays are not identical and may be less reliable than evaluations for anti-CMV IgG.[30] Additionally, there is a risk that CMV IgM assays may be affected by antibody cross-reactivity, such as Epstein-Barr infection.[31]

Conclusion

Recent studies are necessary to examine the CMV seroprevalence among critical demographics and nations, considering that individuals are more vulnerable to CMV by age, and developed countries usually have lower rates.[13] To improve clinical recommendations, such as increasing surveillance programs, protocol-making decisions, and vaccine development, conducting thorough research on the prevalence of CMV in developing regions is crucial.

Identifying primary CMV infection requires identifying low CMV IgG avidity. Thorough epidemiologic studies are necessary to enhance our knowledge of CMV among the population through social and health awareness programmes and also to guide public health initiatives to reduce the disease burden. All newborns should be properly examined, especially for auditory and ocular complications.

Until a suitable vaccine is developed, it is recommended that women of reproductive age who plan to become pregnant should have their CMV serologic status evaluated. They should also be informed about the ways CMV can be transmitted and the risks of acquiring CMV from the children in their care.

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Conflicts of interest

There are no conflicts of interest.

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