

## Cytomegalovirus (CMV) IgM antibodies among HIV-infected patients at a teaching hospital in Port Harcourt, Nigeria

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### Abstract

Cytomegalovirus (CMV) is an important pathogen in HIV (Human Immunodeficiency Virus) patients, as it could drive accelerated disease progression leading to increased morbidity and mortality in the population. This cross-sectional study analyzed plasma samples from 93 HIV positive participants in the Rivers State University Teaching Hospital, Port Harcourt, Nigeria, to investigate the magnitude and associated factors of cytomegalovirus (CMV) infection. Plasma samples were screened serologically for the presence of specific CMV IgM antibodies using microwell ELISA kits. Demographic and behavioural risk factors were collected by the use of a structured questionnaire. Chi-square test was used to assess the statistical significance of different demographic and behavioural risk factors to CMV acquisition. Of the 93 subjects 3(3.2%) were seropositive for CMV IgM antibody. No statistical association existed between the prevalence of CMV IgM antibodies and the socio-demographic factors studied. Higher prevalence of CMV IgM antibody was found in age group 21-40 years (3.2%), female sex (3.9%), single marital status (6.0%), tertiary education (10.0%), students (6.7%) and Christians (3.7%). The observation from this study necessitates the need for serological evaluation in all HIV patients for CMV IgM antibodies for early diagnosis and preventive strategies.

**Keywords:** Antibodies; CMV; IgM; ELISA

### 1. Introduction

Cytomegalovirus (CMV) is member is a member of the family Herpesviridae and subfamily Betaherpesvirinae. In healthy persons, infection with this virus is largely asymptomatic whereas it poses significant threat to pregnant and immunocompromised individuals (Gianella & Letendre, 2016). The virus is endemic globally but more predominant in developing countries particularly in areas of low socio-economic conditions (Ellis et al., 2019). Its seroprevalence in the general population ranges from 50% to 90% and increases to 75% to 90% in HIV-infected individuals (Sert et al., 2019). Its principal route of transmission is through transfusion of blood, infected body fluids, sexual contact, during delivery and organ transplant. Sexual transmission appears to be the most common route of infection in adults, though CMV can also be spread through oropharyngeal secretions, urine, breast milk and blood (Akinbami et al., 2010).

The CMV can ordinarily be contained by the cellular immune response and hence often categorized as a self-limiting infection in healthy individuals. However, the CMV in immunosuppressed individuals as in case of HIV infection carries a risk of high morbidity and mortality (Boulougoura & Sereti, 2016). It establishes latent state following primary infection, reactivating when there are changes in immune status as a result of immunosuppression.

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The presence of detectable CMV viremia increases with decreasing CD4+T-cell count, with a reported prevalence ranging from 23-55% in persons who are HIV-positive and have CD4+ T-cell counts  $\leq 100$  cells/ $\mu$ l (Moore et al., 2019; Jabbari et al., 2021). CMV is associated with more-rapid HIV disease progression, more AIDS-related events, and a wide range of serious end-organ diseases (Effros, 2016; Sachithanandham et al., 2014). HIV-infected individuals are almost universally coinfecting with CMV. In people with HIV infection, it can present with a wide array of complications such as gastrointestinal tract ulceration, hepatitis, encephalitis, retinitis, leukopenia and respiratory infections (Udeze et al., 2018).

Cytomegalovirus is mainly a concern for certain high-risk groups including unborn babies whose mothers become infected with CMV during pregnancy (Schleiss, 2010). In most people with a fully functional immune system, the initial infection with CMV may cause a mild flu like illness and later the virus remains dormant. CMV infection usually does not cause symptoms and mainly affects the salivary glands, kidneys, and other organs. However, viral replication can occur in immunocompromised patients and may contribute to the damage to organs and their functions.

A crucial part of immune system defense against CMV is the development of CMV specific antibodies. The first type of antibody to develop in response to CMV is IgM, which develops within a few days following primary infection. Because of the non-specificity of clinical symptoms caused by CMV infection, laboratory examination is the main basis for the diagnosis of CMV infection. The most two widely used clinical methods are CMV virus replication and serum immunological methods including the detection of CMV IgG, CMV IgM and CMV antigen PP65 (Mangare et al., 2018). The anti-CMV-IgM antibody is often used as a marker of active viral infection while the IgG antibody is indicative of previous infection (Zhao et al., 2020).

The need for this study is strengthened by the fact that because both viruses (HIV and CMV) are immunosuppressive, hence, a synergistic effect could drive accelerated disease progression. A thorough understanding of the epidemiologic impact of CMV is hampered by the variation of burden between countries, within countries, and within subpopulations (Zuhair et al., 2019; Fowler et al., 2022). Therefore, there is a need to highlight seroprevalence and transmission in specific populations affected by CMV to meet the future health challenges. This study was aimed at determining the prevalence of Cytomegalovirus in HIV patients at Rivers State University Teaching Hospital as well as identifying risk factors for CMV acquisition.

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## 2. Material and methods

### 2.1. Data Collection and Ethical Consideration

Consent was obtained from participants after carefully explaining the concept of the study to them. Detailed history and information on socio-demographics and risk factors (including religion, level of education, marital status, age, sex) associated with CMV acquisition were obtained using a structured questionnaire.

### 2.2. Determination of anti-CMV IgM status

This is a cross sectional study that was carried out amongst HIV-1 infected persons attending the Rivers State University Teaching Hospital (RSUTH) in Port Harcourt, Nigeria. Plasma samples were examined for anti-CMV immunoglobulin M (IgM) antibodies at the Virus & Genomics Research Unit, Department of Microbiology, University of Port Harcourt, Choba, Rivers State, Nigeria using commercial IgM ELISA kit. Anti-CMV IgM antibodies were detected in serum using a commercial indirect enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. Participant specimens, standards, and procedural controls, provided by the manufacturer, were run simultaneously. The test was qualitative IgM ELISA, in which positive results signified an acute infection.

### 2.3. Data analysis

Chi-square test was used to test associations between demographic and behavioral risk factors and the CMV serostatus of study participants.  $P \leq 0.05$  was considered statistically significant.

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## 3. Results

The Table 1 below shows the rate of seropositivity of CMV IgM antibody according to age, sex, occupation and religion. In relation to age, only two groups out of four groups were reactive. The age group of 21-40 years with 2(3.2%) and 1(3.8%) in the age group of 41-60 years were seropositive. The other age group 9-20 and 61-80 years showed no presence of CMV IgM antibody.

As shown in Table 1, the females have higher seropositivity rate of CMV IgM antibody of 2(3.9%) than that of the males which is 1(2.3%). In relation to marital status, the rate of seropositivity of CMV IgM antibody revealed that 2(6.0%) were in the singles category which is higher than married having 1(2.0%) seropositivity. The “others” marital status showed no presence of CMV IgM antibody.

As shown in Table 1, those with tertiary educational background (10.0%) had the highest seropositivity. This was followed by those with no formal educational background (6.7%). Other educational background showed no presence of CMV IgM antibody. In terms of occupation and religion, students (6.7%) and especially Christians (3.7%) recorded more prevalence than their respective counterparts (Table 1). However, these differences were not statistically associated ( $p>0.05$ ).

**Table 1** The Socio-Demographic characteristics and CMV IgM Seropositivity

| Socio-Demographic Characteristics | Categories       | No. Tested (%)   | No. of Positive for CMV IgM (%) | p-value |
|-----------------------------------|------------------|------------------|---------------------------------|---------|
| Age (Years)                       | 9-20             | 3(3.2)           | 0(0.0)                          | 0.97    |
|                                   | 21-40            | 62(66.6)         | 2(3.2)                          |         |
|                                   | 41-60            | 26(27.9)         | 1(3.8)                          |         |
|                                   | 61-80            | 2(2.1)           | 0(0.0)                          |         |
| Sex                               | Males            | 42(45.1)         | 1(2.3)                          | 0.67    |
|                                   | Females          | 51(54.8)         | 2(3.9)                          |         |
| Marital Status                    | Singles          | 33(35.4)         | 2(6.0)                          | 0.49    |
|                                   | Married          | 50(53.7)         | 1(2.0)                          |         |
|                                   | Others           | 10(10.7)         | 0(0.0)                          |         |
| Education                         | None             | 15(16.1)         | 1(6.7)                          | 0.14    |
|                                   | Primary          | 34(36.5)         | 0(0.0)                          |         |
|                                   | Secondary        | 24(25.8)         | 0(0.0)                          |         |
|                                   | Tertiary         | 20(21.5)         | 2(10.0)                         |         |
| Occupation                        | Students         | 30(32.2)         | 2(6.7)                          | 0.59    |
|                                   | Unemployed       | 20(21.5)         | 1(5.0)                          |         |
|                                   | Civil Servants   | 17(18.2)         | 0(0.0)                          |         |
|                                   | Traders/Business | 18(19.3)         | 0(0.0)                          |         |
|                                   | Artisans         | 8(8.6)           | 0(0.0)                          |         |
| Religion                          | Christians       | 81(87.0)         | 3(3.7)                          | 0.49    |
|                                   | Islam            | 12(12.9)         | 0(0.0)                          |         |
| Total                             |                  | <b>93(100.0)</b> | <b>3(3.2)</b>                   |         |

#### 4. Discussion

The early detection and intervention of opportunistic viruses such as CMV among PLWH are very crucial for delaying HIV disease progression (Sachithanandham et al., 2014). The seroprevalence of CMV infection among participants in this study was determined through detection of IgM antibodies. This study reported that 3.2% of the HIV seropositive patients were anti-CMV IgM seropositive indicating current infection or reinfection/reactivation of cytomegalovirus. This is consistent with a previous study by Mahjoob et al. (2019) among 92 HIV positive samples, which showed a similar prevalence (3.2%) with the result of this present investigation. However, several other earlier studies reported higher prevalence when compared with the current study. Fowotade et al. (2015) had reported 11.1% anti-CMV IgM

seroprevalence whilst Zhao et al. (2020) and Mangare et al. (2018) reported a 10.4% prevalence respectively. Adeiza et al. (2016) and Kiros et al. (2021) also reported IgM antibody prevalence of 13.2% and 12.4% respectively in a similar study. Results of one study reports CMV IgM antibody seroprevalence to be 8.4%-9% among HIV-infected Thai children (Schoenfisch et al., 2011).

In another study, a prevalence of 3.1% was recorded by Ojide et al. (2012) in Benin and 19.5% by Akinbami et al. (2010) in Lagos both in Nigeria. Equally, lower prevalence values of 2.3% and 2.8% were obtained by Schoenfisch et al. (2011) and Grønborg et al. (2018) in another related study in the USA and Guinea Bissau respectively. Also, Mhandire et al. (2019) reported a 2.9% prevalence in Zimbabwe while Abubakar and Adamu (2021) recorded a 7.1% IgM seropositivity.

Other varying figures was reported in general population in Nigeria. Okonko et al. (2023) reported 20.4% among females in Buguma, Rivers State. Odebisi-Omokanye et al. (2017), reported 24.9% among women in Ilorin. Additionally, Okonko et al. (2022) reported 25.6% in Port Harcourt, Nigeria. These figures were higher than the finding of this present study. The variation in seroprevalence of CMV IgM observed may probably be due to epidemiological and methodological differences. It could also be inferred that there has been a decline in prevalence as earlier studies recorded increased prevalence values. This finding suggests continued surveillance studies to monitor the trend of this infection.

The association between the age distribution and cytomegalovirus infection among HIV patients in this study showed that there was no statistically significant association ( $p=0.97$ ) between the cytomegalovirus infection and the age distribution among the HIV patients. This in line with the research carried out in Infectious disease hospital, Kano state by Musa et al. (2014), as well as those of Denué et al. (2014). The CMV IgM age-specific seroprevalence was highest in the 21–40years age group in the HIV-positive patients. The higher CMV IgM seroprevalence in the younger age groups of HIV-positive patients in this study may be related to the higher burden of HIV infection and force of sexual transmission in the younger age group.

However, CMV infection (shown by IgM) was higher in females than males although the difference was not statistically significant ( $p> 0.05$ ). Similar studies by Ojide et al. (2013) and Fowotade et al. (2015) on HIV-infected individuals also did not record any significant association between both CMV-specific IgM and IgG antibodies and gender of the patients. The significantly higher rate of acute/active infection among females in this study suggests more exposure of females to factors that lead to re-activation or infection of CMV in the study locality.

Also, there was no statistical association ( $p=0.49$ ) in the distribution of anti-CMV IgM antibody among the different marital groups. There was an IgM prevalence of 90.9% among the singles. This observation is similar to that of Edward et al. (2015) in Kafanchan, Kaduna State, Nigeria. In contrast to our study, Okonko et al. (2023) reported a higher prevalence among the married in Buguma, Rivers State, Nigeria.

This study revealed that patients with tertiary educational background (10.0%) had the highest seropositivity. This was followed by those with no formal educational background (6.7%). This observation supports previous studies in Nigeria. Bawa et al. (2019) reported a strong correlation between CMV seropositivity and higher education. Okonko et al. (2023) reported that participants with tertiary education had a higher seropositivity (25.0%) than their counterparts. Odebisi-Omokanye et al. (2017) had similar observation and tertiary-educated participants in Ilorin, Nigeria had higher CMV IgM seropositivity.

The present study did not support studies by Okonko et al. (2023) and Bawa et al. (2019) which stated that CMV seropositivity substantially correlates with employment. CMV antibody was found only among students and unemployed patients in this current study. In consonance with the present study, Ndako et al. (2016) identified a higher CMV seropositivity among farmers and the unemployed. However, the study disputes that of Edward et al. (2015), who reported higher seropositivity among farmers in Kafanchan, Kaduna State, Nigeria. It also disputes the finding of Odebisi-Omokanye et al. (2017) in Ilorin, Nigeria, who reported a higher seropositivity among businesswomen.

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## 5. Conclusion

Our findings show low seroprevalence of CMV IgM antibodies in HIV-infected patients presenting at the Rivers State University Teaching Hospital (RSUTH). There was also no significant association of sex/gender in acquisition of CMV. Thus, transmission of CMV infection is not attributed to any given sex. All patients have equal chance of infection provided they are exposed to CMV. This study highlights the need for an expanded study in different parts of the country

to ascertain the severity of the problem. This will help in better management of the HIV cases by early diagnosis of CMV IgM antibodies in the patients

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## Compliance of ethical standards

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### *Disclosure of conflict of interest*

The authors have declared that no competing interests exist.

### *Statement of ethical approval*

All authors declare that all experiments have been examined and approved by the University of Port Harcourt Research Ethics committee. Therefore, the study is performed following the ethical standards laid down in the 1964 Declaration of Helsinki.

### *Statement of informed consent*

All authors declare that informed consent was obtained from all individual participants included in the study.

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