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Seroprevalence of cytomegalovirus (CMV) among pregnant women at a tertiary facility in southern Nigeria

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Abstract

Background: Cytomegalovirus (CMV) also called human cytomegalovirus (HCMV) or human herpesvirus-5 (HHV-5) is an encapsulated double-stranded deoxyribonucleic acid (DNA) virus. It is an opportunistic virus which often remains latent and only become symptomatic in immune-suppressed individuals such as pregnant women, HIV/AIDS patients and other immune weakening disease conditions. It is also estimated to have an 86% global sero-prevalence among reproductive women.

Objectives: To determine the sero-prevalence of CMV infection, investigate the relationship between risk factors and CMV infection and to determine the relationship between obstetric characteristics and CMV infections among pregnant women.

Method: A cross-sectional study among a cross-section of pregnant women receiving ante-natal care in the University of Port Harcourt Teaching Hospital from August 2022 to December 2022. A structured pro forma data sheet was used as interviewer-administered questionnaire by medical personnel to collect data from the study participants. 5ml of blood was collected from each participant and assessed for the presence of anti-CMV IgG using commercial Enzyme-linked Immunosorbent Assay (ELISA). The data were analyzed using Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics (mean, median, frequency percentage and standard deviation), Chi-square test and Fischer's exact test were used appropriately.

Results: Out of 101 respondents, only 24 (24%) were positive for CMV IgG, while 77 (76%) were negative. About 50% of the women were in their 3rd decade of life, while (3) were in the 4th decade of life. All the respondents were married and were Christians. Three quarters of the women [75(74.3%)] had tertiary education, 20 (19.8%) had secondary education, while 6 (5.9%) were Postgraduate students. Based on income, women with income < #50,000 (53.5%) were the most common. The relationship between demographic factors such as age, religion, income, educational level, employment status, marital status and CMV results were statistically insignificant. The relationship between obstetric characteristics and CMV results were not statistically significant, while risk factors for CMV and presence of CMV infection were not statistically significant as well.

Conclusion: The 24% sero-prevalence for CMV at University of Port Harcourt Teaching Hospital was quite low; however it can be reduced to the barest minimum, by encouraging intensive awareness campaigns about the virus and providing free serum testing to all categories of the population, since CMV affects all ages.

Keywords: Cytomegalo virus; Sero-prevalence; Pregnant; Risk factors; Obstetric; Infection

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1. Introduction

Cytomegalovirus (CMV) is an encapsulated double-stranded deoxyribonucleic acid (DNA) virus, which is also called human cytomegalovirus (HCMV) or human herpesvirus-5 (HHV-5) (1). The virus is classified under the viral family name Herpesviridae and further recognized as a member of the beta herpesviridae subfamily (2). It is also among a cluster of vertically transmitted infectious diseases, including Toxoplasmosis, Rubella, Cytomegalovirus and Herpes simplex virus (TORCH)s (3). CMV has the ability to infect several body cells and readily forms inclusions in the nucleus and cytoplasm of infected cells (4,5). CMV shares same characteristics with other herpesviruses including similar genomic and virion attributes, and the ability to initiate latent and persistent infections, via its host-immunity evasive abilities (6). It is an opportunistic virus which often remains latent and only become symptomatic in immune-suppressed individuals such as pregnant women, HIV/AIDS patients and other immune weakening disease conditions (1,7).

According to various serological surveys, the CMV virus has an estimated global prevalence of 40-100% in different population across the world (8). It is also estimated to have an 86% global sero-prevalence among reproductive women (9). The virus had also been implicated as the most common aetiology for congenital viral infection in pregnancy, with a birth prevalence of 0.4-1.3% around the world (1,10-11). In Malaysia, 84% of the pregnant test positive to CMV (12), while 78% were positive for the virus at a tertiary facility in Turkey (13). In Africa, higher rates of CMV among pregnant women had been reported. Chibwe et al (14) reported a 79% seropositive result in Tanzania, while Hamdan et al (15) reported 72% and 96% for pregnant women in South Sudan and Egypt respectively.

High rates of sero-prevalence for CMV had been reported by various studies across various states in Nigeria. In a study conducted by Hamid et al (16), as high as 91% pregnant women were positive for the virus at a tertiary hospital in Kano. Similarly, Akinbami et al (17) documented 97% positive pregnant women in Lagos, 87% was reported by Akele et al (18) in Ekiti state, while Ogbani-Emovon et al (19) reported 92% in Benin City.

The transmission of CMV occurs via close contact with all types of secretions such as saliva, semen, breast milk, urine, vaginal secretions, blood, etc., from an infected individual who has the virus in his or her body fluids (8). Another route of transmission is the vertical transmission from the mother to the baby via the placenta, intra-uterine route or through breast feeding (20). Maternal primary infection is responsible for placenta transmission during pregnancy, intra-uterine occurs during delivery when the woman is exposed to infected secretions (cervical and vaginal), while close contact and breast feeding of the baby by an infected mother would aid the transmission of the virus as well (21). According to presenting signs and symptoms, infants could become symptomatic or not, however about 11% of live births with congenital CMV may present with diseased conditions affecting the central nervous system such as intracranial calcification and microcephaly (5,22). Furthermore, primary maternal CMV infection is chiefly responsible for mother-child transmission and poses a transmission risk of about 24-75% (1,8,23).

Therefore in this study we aimed to determine the sero-prevalence of CMV infection, investigate the relationship between risk factors and CMV infection, and also determine the relationship between obstetric characteristics and CMV infections among pregnant women.

2. Materials and methods

2.1. Study Area

The study was carried out at the University of Port Harcourt Teaching Hospital (UPTH) which is located at Port Harcourt, River state.

2.2. Study Design

A cross-sectional study design was adopted for the study. This entailed the assessment of the seroprevalence of anti-Cytomegalovirus Immunoglobulin G (anti-CMV IgG) among a cross-section of pregnant women receiving ante-natal care in the University of Port Harcourt Teaching Hospital.

2.3. Study Duration

The study was a 4 months study which started from August 2022 and terminated on December 2022.

2.4. Study Population

Inclusion criteria were: Women that were currently pregnant and enrolled with the ante-natal clinic of UPTH during the time of the study.

Exclusion criteria included: Women that were not currently pregnant and also women that were pregnant but not registered with the ante-natal clinic of UPTH but came into the labour ward as unbooked patients.

2.5. Sample Size and Sampling

The sample size was calculated as shown below with the Sample size for proportions formula based on a 93% seroprevalence in Benue state[24]

$$n = Z^2pq/e^2$$

Where n= estimated minimum sample size, Z = the critical value of the normal distribution at a 95% confidence interval (1.96) p= rate of reported seroprevalence of anti-CMV IgG among women (93% = 0.93), q = 1 – p = 0.07, e= margin of error at a 95% confidence interval (5% =0.05).

$$n = (1.96^2)x\ (0.93)(0.07)/0.05^2$$

$$n = 100$$

The systematic random sampling technique was used to select the eligible participants for the study was based on an interval K = N/n, where N= 1716 estimated population, n = 100, estimated sample size. Therefor the sampling interval K = 1716/100 = 17.1. Hence, every 17th individual the met the inclusion criteria was selected for the study. The category of participants included 33 participants each in the first, second and third trimester of Pregnancy.

2.6. Data Collection

A structured pro forma data sheet was used as interviewer-administered questionnaire by medical personnel to collect demographic information, medical diagnoses of chronic conditions and other history about the index pregnancy from the study participants.

2.7. Specimen Collection and Analysis

A 5mL sterile specimen bottle was used to collect 5mL of venous blood using aseptic techniques from each participant. The collected sample were appropriately labeled and stored at -20°C for Cytomegalovirus IgG analysis. The collected specimen was assessed for the presence of anti-CMV IgG using commercial Enzyme-linked Immunosorbent Assay (ELISA) following the manufacturer's instruction.

2.8. Data Analysis

The data collected were entered into a spreadsheet (MS Excel). The data were analyzed using Statistical Package for Social Sciences (SPSS) version 25. The demographic data and medical information will be summarized using descriptive statistics (mean, median, frequency percentage and standard deviation) as appropriate. The distributions of anti-CMV IgG were assessed according to demographic variables and clinical information using the Chi-square test and Fischer's exact test as appropriate. All analyses were done at a 95% confidence interval and a p-value less than 0.05 were considered significant.

3. Results

Out of 101 respondents, only 24 (24%) were positive for CMV IgG while 77 (76%) were negative for CMV IgG. This is illustrated in Figure 1. Table 1 shows the demography of the respondents. About half of the women (50) were in their 3rd decade of life while (3) were in the 4th decade of life. All the respondents were married and were Christians. Three quarters of the women [75(74.3%)] had tertiary education, 20 (19.8%) had secondary education, while 6 (5.9%) were Postgraduate students. Based on income, women with income < #50,000 (53.5%) was the most common, while income > #150,000 (4%) was the least occurring.

Table 2 shows the demographic distribution of CMV among the respondents. The relationship between demographic factors such as age, religion, income, educational level, employment status, marital status and CMV results were

statistically insignificant. Overall, fewer respondents had the presence of the infection and vice versa. Table 3 reveals the relationship between obstetric characteristics and CMV results as not statistically significant. However, the risk of contracting CMV is increased with the obstetric factors, aside induced abortion which played negligible role in the contraction of the virus. Gestational age increased the likelihood of contracting CMV by 3 times. Increased number of pregnancies, deliveries, number of abortions and previous history of abortions can increase the likelihood of CMV by 1 fold rise.

Table 4 reveals that the relationships between risk factors for CMV and presence of CMV infection were not statistically significant. It also depicts that impaired immunologic states and systemic conditions such as hypertension diabetes mellitus, HIV and hepatitis have increased the likelihood of women contracting CMV by 5, 7, 1 and 1 time(s) respectively. However, history of blood transfusion and past surgery are less likely associated with the contraction of the virus (values are < 1). Furthermore, the absence of screening and sterility can increase the likelihood of contraction of the virus.

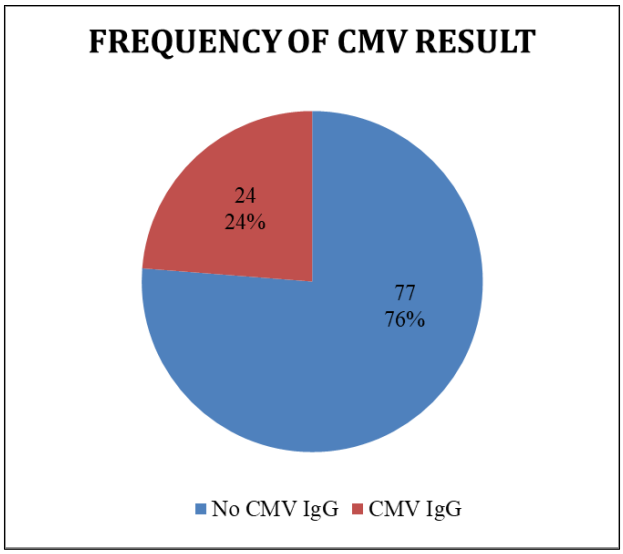

Figure 1 Prevalence of CMV in the Study Population (n=101)

Table 1 Demography of Study Population (n=101)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
20 – 30	48	47.5
31 – 40	50	49.5
>40	3	3.0
Marital Status		
Single	0	0
Married	101	100.0
Separated	0	0
Widowed	0	0
Religion		
Christianity	101	19.8
Islam	0	0.0

Others	0	0.0
Educational status		
Secondary	20	19.8
Tertiary	75	74.3
Post Graduate	6	5.9
Income		
<50,000	54	53.5
50,000 – 99,999	29	28.7
100,000 – 149,999	14	13.9
≥150, 000	4	4.0

Table 2 Demographic Distribution of CMV (n=101)

Variable	Present	Not Present	Total	Chi-square	P-value
Age Group (years)					
20 – 30	11(22.9)	37(77.1)	48(100.0)	0.172	0.918
31 – 40	12(24.0)	38(76.6)	50(100.0)		
>40	1(33.3)	2(66.7)	3(100.0)		
Marital Status					
Married	24(23.8)	77(76.2)	101(100.0)	-	-
Religion					
Christianity	24(23.8)	77(76.2)	101(100.0)	-	-
Educational status					
Secondary	6(30.0)	14(70.0)	20(100.0)	0.977	0.613
Tertiary	16(21.6)	59(78.7)	75(100.0)		
Post Graduate	2(33.3)	4(66.0)	6(100.0)		
Employment					
Student	2(20.0)	8980.0)	10(100.0)	4.327	0.503
Public Servant	4(33.3)	8(66.7)	12(100.0)		
Not Employed	3(13.0)	20(87.0)	23(100.0)		
Teacher	4(40.0)	6(60.0)	10(100.0)		
Civil Servant	2(15.4)	11(84.0)	13(100.0)		
F(Others)	9(27.3)	24(72.7)	33(100.0)		
Income					
<#50,000	14(25.9)	40(74.1)	54(100.0)	1.431	0.698
#50,000 – 99,999	7(24.1)	22(75.9)	29(100.0)		
#100,000 – 149,999	3(21.4)	11(78.6)	14(100.0)		
≥#150,000	0(0.00)	4(100.0)	4(100.0)		

*Statistically significant (P < 0.05)

Table 3 Distribution of CMV by Obstetric Characteristics (n=101)

Variable	Present n (%)	Not Present n (%)	Total n (%)	Chi-square (p-value)	OR (95% C.I)
Gestational Age (wks)					
0 – 13	3(50.0)	3(50.0)	6(100.0)	2.424	3.524 (0.662 – 18.758)
14 - 42	21(22.1)	74(77.9)	95(100.0)	(0.119)	
No of Pregnancies					
0 – 2	21(25.6)	61(74.4)	82(100.0)	0.821	1.836 (0.486 – 6.936)
>2	3(15.8)	16(84.2)	19(100.0)	(0.365)	
No of deliveries					
0 – 2	23(24.0)	73(76.0)	96(100.0)	0.041	1.260 (0.134 – 11.848)
>2	1(20.0)	4(80.0)	5(100.0)	(0.839)	
No of abortions					
0 – 2	23(24.2)	72(75.6)	95(100.0)	0.177	1.597 (0.177 – 14.383)
>2	1(16.7)	5(83.3)	6(100.0)	(0.674)	
Sexual Partners					
1	14(25.9)	40(74.1)	54(100.0)	0.300	1.295 (0.513 – 3.271)
>1	10(21.3)	37(78.7)	47(100.0)	(0.584)	
Had abortions					
Y	10(25.0)	30(75.0)	40(100.0)	0.056	1.119 (0.441 – 2.841)
N	14(23.0)	47(77.0)	61(100.0)	(0.813)	
Induced Abortions					
Y	4(21.4)	15(78.9)	19(100.0)	0.095	0.827 (0.296 – 2.780)
N	20(24.4)	62(75.6)	82(100.0)	(0.758)	
Congenital Deformities					
Y					
N	24(23.8)	77(76.2)	101(100.0)		-

*Statistically significant (P < 0.05)

Table 4 Distribution of CMV by Risk Factors (n=101)

Variable	Present	Not Present	Total	Chi-square (p-value)	OR (95% C.I)
Blood Transfusion					
Y	3(17.6)	14(82.4)	17(100.0)	0.422	0.643(0.168 – 2.458)
N	21(25.0)	63(75.0)	84(100.0)	(0.576)	
Past Surgery					
Y	6(17.6)	28(82.4)	34(100.0)	1.058	0.583(0.207 – 1.641)

N	18(26.9)	49(73.1)	67(100.0)	(0.304)	
Organ Transplant					
Y					-
N	24(23.8)	77(76.2)	101(100.0)	-	
Hypertension					
Y	3(60.0)	2(40.0)	5(100.0)	3.813	5.357(0.839 – 34.189)
N	21(21.9)	75(78.1)	96(100.0)	(0.051)	
Diabetes Mellitus					
Y	0(0.0)	1(100.0)	1(100.0)	0.315	7.316(1.179 – 1.469)
N	24(24.1)	76(76.0)	100(100.0)	(0.575)	
HIV					
Y	0(0.0)	4(100.0)	4(100.0)	1.298	1.329(1.185 – 1.489)
N	24(24.7)	73(75.3)	97(100.0)	(0.255)	
Tuberculosis					
Y					-
N	24(23.8)	77(76.2)	101(100.0)	-	
Hepatitis					
Y	1(25.0)	3(75.0)	4(100.0)	0.004	1.072(0.106 – 10.816)
N	23(23.7)	74(76.3)	97(100.0)	(0.953)	
Cancer					
Y				-	-
N	24(23.8)	77(76.2)	101(100.0)		

*Statistically significant (P < 0.05)

4. Discussion

African continent had been reported to show high CMV prevalence among pregnant women (25). In this study the prevalence of CMV was 24%, with 24 pregnant women tested positive to the CMV antibody (CMV IgG). However, 77 (76%) of them tested negative for the virus. The prevalence is comparatively lower to the 79, 92, 94, 97 and 98% reported by Babayo et al (26), Ogbani-Emovon et al (19), Yeroh et al (8), Akinbami et al (17) and Odebisi-Omokanye et al (2) respectively across various states in Nigeria. The lower prevalence in this study could be attributed to the low or absence of other co-morbid infections such as HIV, tuberculosis and hepatitis in the study population. Another factor could be due to the increased awareness about the CMV virus during the antenatal sessions and the execution of hygienic practices from the women.

The demography of the study population showed that higher percentages (49.5%) of the pregnant women were in the age bracket of 31-40, closely followed by 20-30 years with 47.5%, which explains that most parous women are within these age brackets. Similarly, the highest level of education by most women was tertiary education, followed by secondary and the least being postgraduate. The financial status also depicted that majority of the women earned < #50,000 income, however only 14 (25%) of the women who earned <50,000 were CMV positive. Thus, contradicting the statement by Goderis et al (5) that the prevalence of CMV is inversely related to the socioeconomic level of the population in developing countries such as Brazil, Nigeria and other sub-Saharan nations. However, there was no significant relationship ($p<0.05$) established between demographic factors in this study and the CMV infection. This is in accordance with Akinbami et al (17) who also reported no significant relationship between demographic factors and CMV prevalence. Similarly, Yeroh et al (8) reported no significant relationship between ages, religion, marriage,

educational status and CMV infection as correlated in this study as well; he however noticed a significant relationship between employment status and CMV infection among the women in Kaduna state.

In this study, obstetric factors showed that 21 women in gestational age of 14 weeks and above were CMV positive, while only 3 women whose pregnancies were < 14 weeks had CMV infection. Furthermore, pregnant women with 0-2 number of pregnancies, number of deliveries and number of abortions respectively, all had higher CMV prevalence as against pregnant women with >2 of these factors respectively. Interestingly, 25% of pregnant women with only 1 sexual partner had CMV infection when compared to the 21% who had more than >1 sexual partners in the past. Other obstetric factors such as history of spontaneous abortion, induced abortion and congenital deformities were also documented in this study. However, these obstetrics factors and CMV infection in this study showed no significant relationship. These revealed that obstetric factors did not play a pivotal role in the transmission of CMV among the study population. This correlated with the findings of Akele et al (18) who reported no significant relationship between number of pregnancies, gestational age and CMV infection in a study done at a tertiary centre in Ekiti state. Likewise, Aliyu et al (6) reported no significant relationship between gestational age and CMV infection in a study conducted in Kaduna state.

The relationship between risk factors and CMV infection was also investigated in this study. Risk factors assessed were: organ transplant, blood transfusion history, past surgery, and co-morbidities such as diabetes, hypertension, cancer, HIV, hepatitis and tuberculosis. For blood transfusion, only 3 out of the 17 women who had received blood transfusion in the past, tested positive for CMV, only 6 out of 34 women with past surgical history had CMV infection, while none of the women had undergone any organ transplantation in the past. Furthermore, there was no significant relationship between these 3 risk factors and CMV infection in this study. The lack of association between blood transfusion, past surgery and the CMV infection may be explained by the fact that proper blood screening is usually done before blood transfusion and surgical instruments for surgeries are usually sterile, hence the risk of CMV transmission is reduced. This finding is in agreement with Akinbami et al (17), Akende et al (27) and Yeroh et al (8), who in their separate studies reported that past history of blood transfusion is not a significant factor for CMV infection. Although there was no observed significant relationship between hypertension, diabetes, HIV, hepatitis, tuberculosis and cancer with CMV infections in this study, there was however increased likelihood of CMV infection occurring among women who are hypertensive, diabetic, HIV positive or hepatitis positive.

5. Conclusion

The 24% seroprevalence for CMV at University of Port Harcourt Teaching Hospital was quite low, however it can be reduced to the barest minimum, by encouraging intensive awareness campaigns about the virus and providing free serum testing to all categories of the population, since CMV affects all ages.

Compliance with ethical standards

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All the senior registrars, registrars and house officers of the obstetric and gynaecology department and also the entire staff of the medical microbiology laboratory.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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