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Original article

Seroprevalence of cytomegalovirus infection among pregnant women attending some hospitals in Kadunastate, Nigeria

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ABSTRACT

Background: Cytomegalovirus (CMV) infection especially in pregnancy may cause complications such as congenital infections leading to neurological disabilities in children that result in blindness, neuro-developmental delay, and sensory neural hearing loss. This study was carried out to determine the seroprevalence of cytomegalovirus infection among pregnant women attending antenatal clinics in Yusuf Dan Tsoho and 44 Nigerian Army Reference Hospitals in Kaduna metropolis. **Materials and Methods:** Blood samples were collected from ninety-two pregnant women and screened for CMV IgM antibodies using ELISA. Structured questionnaire was used to obtain data on socio-demographic and risk factors associated with the CMV infection. **Results:** Out of the 92 pregnant women examined, 30 (32.6%) tested positive to CMV IgM antibodies. There was statistically significant association between CMV infection and occupation, previous pregnancy and sharing of cups or utensils. There was no significant association between CMV infection and marital status, gestation age, history of blood transfusion, age and educational level. **Conclusion:** The high prevalence of CMV infection observed in this study indicates that the virus is prevalent in the study area, and it is therefore advisable that routine screening of CMV infection be implemented for all pregnant women in the State.

Introduction

Cytomegalovirus (CMV) is one of the human herpesviruses (HHV) and is designated as HHV type 5 [1]. It belongs to the subfamily Betaherpesvirinae and the family Herpesviridae. Other members of Betaherpesvirinae include HHV types 6 and 7 which share common clinical characteristics with CMV [2]. Cytomegalovirus shares many attributes with other herpesviruses including genome, virion structures and ability to cause latent and persistent infection. It has a double stranded DNA with 162 hexagonal capsomeres surrounded by a lipid layer [3].

Cytomegalovirus (CMV) affects individuals of all ages and can cause latent infection. CMV infection is usually asymptomatic in healthy individuals, however infections in pregnant individuals and immunocompromised individuals can result severe disease [4].

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Maternal cytomegalovirus infection is a common viral infection in perinatal period and a leading cause of congenital infection associated with neurological impairment, permanent hearing and vision loss [5,6]. Cytomegalovirus infection is mainly a problem for certain high risk groups which include unborn babies whose mothers become infected with CMV during pregnancy and children or adults whose immune systems have been weakened by disease or drug treatment such as organ transplant recipients or people infected with HIV [7]. It is a common opportunistic infection among human immunodeficiency virus (HIV) infected individuals, a major source of viral complication among organ transplant recipients and a leading cause of hearing loss, vision loss and mental retardation among congenitally infected children. More children suffer disabilities caused by congenital CMV than by several better known childhood maladies such as Down's syndrome or foetal alcohol syndrome [8].

Cytomegalovirus is spread through close contact with body fluids (e.g. saliva, urine, breast milk cervico-vaginal secretions and semen) of infected individuals, through sexual and non-sexual activities, by vertical transmission from mother to unborn foetus, through organ and stem cell transplantation or via blood transfusion [7,9,10]. Mother to child transmission occurs by three routes which include; transplacental, intra-uterine and breast milk transmission. Pregnant women get infected through sexual contact and contact with secretion of children (urine or saliva) [9]. Intrauterine CMV infection result in neonatal death in approximately 10% of fetuses born by infected mothers [11].

Previous studies have reported seroprevalence rates of CMV ranging between 6.7% [12] and 98.7% [13] among pregnant in different parts of Nigeria. Given the general lack of awareness of the infection in pregnancy and the serious consequences it poses to the unborn child, this study was undertaken to assess the seroprevalence of this infection in some hospitals in Kaduna metropolis, and to determine its associated risk factors.

Materials and methods

Study design and setting

A cross sectional study was carried out amongst pregnant women attending antenatal clinic in selected hospitals within Kaduna metropolis. The hospitals were Yusuf Dan Tsoho Memorial Hospital and 44 Nigerian Army Reference Hospital. The period of sample collection was between August and October, 2012.

Sample size determination

The sample size was determined using the seroprevalence of CMV among pregnant women (98.7%) report Ahmad et al. [13] and the Kish Leisle formula for determination of sample size:

$$N = \frac{Z^2 P (1-P)}{d^2}$$

Where N = sample size

P = seroprevalence of CMV among pregnant women (98.7%)

Z = confidence interval (1.96)

d = allowable error (5%)

$$N = \frac{1.96^2 \times 0.987 \times (1-0.987)}{(0.05)^2}$$

N= 19.72 samples.

A total of 92 blood samples were collected to increase statistical precision and minimize error.

Ethical approval

Ethical approval to conduct the study was obtained from the ethical committee of the hospitals from which samples were collected (44 NARHK/G1/300/51).

Inclusion and exclusion criteria

The inclusion criteria were all pregnant women attending the selected hospitals and who consented to be included in the study, while pregnant women who did not consent to be included in the study were excluded.

Data collection

A structured questionnaire was used to obtain socio-demographic data, clinical information and risk factors associated with human cytomegalovirus infection. The questionnaires were administered to consenting participants prior to sample collection

Collection of samples and processing

A total of 92 blood samples were collected (46 from each hospital). Five (5) mL of blood was collected from each participant aseptically by venipuncture using a sterile needle transferred into plain vacutainer bottle. The blood samples were allowed to clot and the sera separated using a sterile micropipette. Aliquots of the sera were dispensed into 2.0 mL cryovials each and stored frozen at -20^{o}C [14].

Detection of CMV IgM antibodies using enzyme linked immunosorbent assay (ELISA)

All samples were screened for CMV IgM antibodies using CMV IgM ELISA kit (Diagnostic Automation, Inc., Calabasas USA) following the manufacturer's instruction. The kit is a qualitative assay with a detection range of positive, negative and cutoffs. It has a specificity of 98% and a sensitivity of 97%. The results were interpreted by reading the optical density (O.D.) of the wells at 450 nm using a microwell reader [14].

Statistical analysis

Chi square ($\chi 2$) was used to analyze the differences in seroprevalence of CMV between the various categories of data. Univariate logistic regression was used to analyze the risk factors. *P* values ≤ 0.05 were considered statistically significant.

Results

Out of the ninety-two samples analyzed, thirty were found to be seropositive for CMV IgM giving a seroprevalence of 32.6% among pregnant women **(Figure 1).**

Pregnant women within the age group 26-30 years had the highest seroprevalence of CMV IgM (46.3%) while the lowest seroprevalence was observed in the age group 36-40 years (0.0%). The seroprevalence of CMV among pregnant woman with respect to occupation showed statistically significant association. Highest seroprevalence of 58.3% was observed among the unemployed and the lowest was observed among the retired (0.0%). Based of educational level, highest seroprevalence of CMV IgM was observed among pregnant woman who had inform education (55.6%) while those who had none had the lowest seroprevalence (0.0%). In respect to marital status, pregnant women who were married had the highest seroprevalence of 37.8% while the lowest seroprevalence (0.0%) was observed among the divorced and widows. The difference observed is not statistically significant at $p \leq 0.05$ **(Table 1).**

Table 2 illustrates the seroprevalence of CMV IgM among pregnant women with respect to clinical information. Pregnant women who are in their second trimester had the highest seroprevalence of 35.6% while the lowest seroprevalence of 26.7% was observed in pregnant women who are in their third trimester. There was no statistically significant association between CMV IgM seropositivity and gestation age (p = 0.6970). With respect to physical challenge, pregnant women with physically challenged children have highest seroprevalence (42.9%) than those with none (30.8%). There was no statistically significant association between CMV IgM seropositivity and having physically challenged child (p = 0.3743).

The seroprevalence of CMV IgM among pregnant women with respect to risk factors is presented in **table (3).** Previous history of blood transfusion was not statistically associated with CMV infection among pregnant women (p = 0.7919). All the pregnant women responded to have only one sexual partner with a seroprevalence rate of 32.6%. In relation to previous pregnancies, pregnant women who have had previous pregnancies of four and above had highest seroprevalence (63.6%) while the lowest seroprevalence was observed among those who had only one previous pregnancy (3.13%). Number of previous pregnancies was significantly associated with risk of CMV infection (OR=3.46; 95%CI = 2.04 - 5.84). Pregnant women who do not work in day care centers had the highest seroprevalence of 32.9% as compared to those who work in day care centers (31.3%). Further analysis based on practice of sharing cups and utensils, revealed that those who do not share cups and utensils had the highest seroprevalence (55.0%) while those who practiced the habit had a seroprevalence of 26.4%.

Table 1. Seroprevalence of CMV IgM among Pregnant Women with respect to Socio-demographic Factors

	No. examined	**No. of positive**	**Seroprevalence (%)**	***p*-value**
Age				
16 – 20	10	2	20.0	0.1139
21 – 25	20	1	5.0	
26 – 30	41	19	46.3	
31 – 35	19	8	42.1	
36 – 40	2	0	0.0	
Total	92	30	32.6	
Occupation				
Civil servant	10	4	40.0	0.0221*
Self employed	51	12	23.5	
Unemployed	24	14	58.3	
Retired	7	0	0.0	
Total	92	30	32.6	
Educational level				
Primary	28	6	21.4	0.1375
Secondary	11	2	18.2	
Tertiary	2	0	0.0	
Informal	42	17	40.5	
None	9	5	55.6	
Total	92	30	32.6	
Marital status				
Single	11	1	9.0	0.0856
Married	74	28	37.8	
Widow	0	0	0.0	
Divorce	7	0	0.0	
Total	92	30	32.6	

* The difference observed is statistically significant at $p \leq 0.05$. Chi square was used to analyze the differences.

Table 2. Seroprevalence of CMV IgM among Pregnant Women with respect to Clinical Information.

Clinical Information	**No. examined**	**No. of positive**	**Seroprevalence (%)**	***p*-value**
Any physically challenged child				
Yes	14	6	42.9	0.3743
No	78	24	30.8	
Total	92	30	32.6	
Gestation age (month)				
1 – 3	3	1	33.3	0.6970
4 – 6	59	21	35.6	
7 – 9	30	8	26.7	
Total	92	30	32.6	

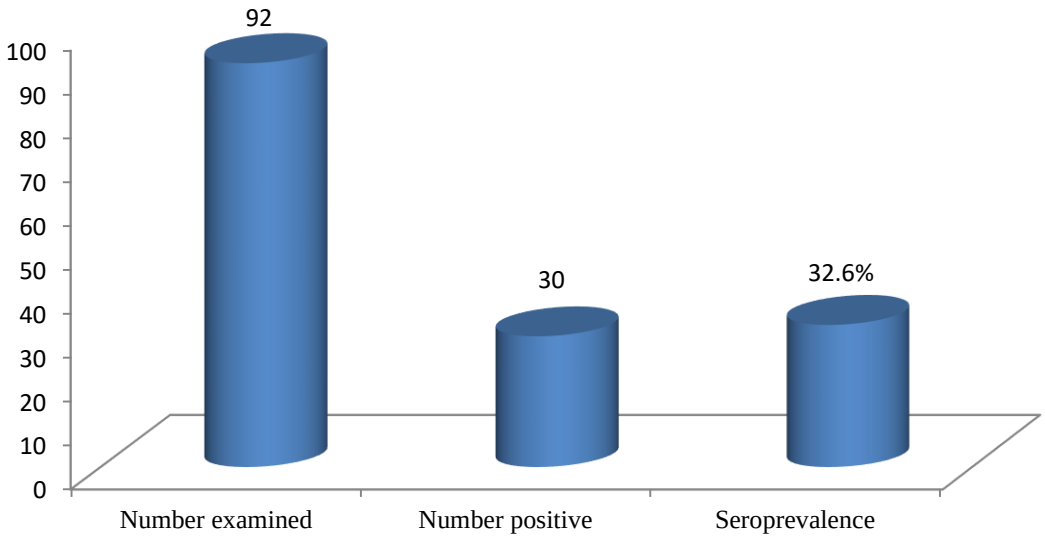
Chi square was used to analyze the differences.

Table 3. Seroprevalence of CMV IgM among Pregnant Women with respect to Risk Factors

Risk Factors	No. examined	No. positive	Seroprevalence (%)	OR (95% CI)	*p*-value
History of blood transfusion					
Yes	32	11	34.4	1.13(0.46-2.81)	0.7919
No	60	19	31.7		
Total	92	30	32.6		
No. of previous pregnancies					
None	5	0	0.0	3.46(2.04-5.84)	0.0000*
One	32	1	3.13		
Two	10	2	20.0		
Three	23	13	56.5		
Four and above	22	14	63.6		
Total	92	30	32.6		
Worked as a daycare worker					
Yes	16	5	31.3	0.93(0.29-2.96)	0.8985
No	76	25	32.9		
Total	92	30	32.6		
Knowledge on Cytomegalovirus					
Yes	5	1	20.0	2.00(0.21-18.72)	0.5435
No	87	29	33.3		
Total	92	30	32.6		
Washing of hands after diapers change					
Yes	25	6	24.4	1.77(0.62-5.03)	0.2854
No	67	24	35.8		
Total	92	30	32.6		
Sharing cups or other utensils					
Yes	72	19	26.4	0.29(0.11-0.82)	0.0190*
No	20	11	55.0		
Total	92	30	32.6		

* The difference observed is statistically significant at $p \leq 0.05$. Univariate logistic regression was used to calculate the Odd Ratio (OR) and 95% Confidence Interval (CI).

Figure 1. Overall seroprevalence of CMV IgM among pregnant women attending some hospitals in Kaduna Metropolis



Discussion

CMV IgM seroprevalence rate of 32.6% was obtained in this study among pregnant women, which indicates that the seroprevalence of CMV infection among pregnant women in Kaduna metropolis is high. This implies that almost one third of the pregnant women have recent active infection or viral reactivation. Even though CMV infection or reactivation during pregnancy is mostly asymptomatic; it could result to fetal infection and congenital CMV syndromes [15]. The reason for the high seroprevalence of CMV infection might be due poor hygienic practices and depreciating socioeconomic standard which might play important role in increasing the rate of CMV infection. This rate is lower than the CMV seroprevalence rates of 98.7% and 84.2% reported among pregnant women in Sokoto State and Bida, Niger State by **Ahmad et al.** [13] and **Okwori et al.** [16] respectively. However, the observed seroprevalence of CMV IgM in this study is higher than 8.1%, 6.7%, 8.2% and 24.9% seroprevalence rates of CMV IgM reported by **Maingi et al.** [9], **Habeeb et al.** [12], **Zenebe et al.** [17] and **Odebisi-Omokanye et al.** [18] among pregnant women in Thika, Kenya; Kano, Nigeria; Hawassa, Southern Ethiopia and Kwara, Nigeria respectively. The observed variation could be as a result of differences in cultural behavior of the study subjects.

Pregnant women within the age group 26 - 30 years had the highest seroprevalence of CMV IgM. The high rate among this age group could be explained by increase sexual activities common to this age group as the virus can be sexually transmitted. This agrees with the findings of **Yeroh et al.** [7], where pregnant women within age group 25 - 29 years had the highest seroprevalence. However, contrary to this finding, highest seroprevalence of CMV IgM was reported among pregnant women aged 18 – 28 years by **Habeeb et al.** [12].

The present study showed a statistically significant association between CMV infection in pregnant women and occupation, with higher seroprevalence among pregnant women who were unemployed. Similar finding was reported by **Hamid et al.** [19], who also observed higher seroprevalence among the unemployed. This might be due to inability to afford better and healthy living conditions which decreases exposure to the virus as a result of low socioeconomic status.

Seroprevalence of CMV in relation to educational status was higher among subjects who had no any form of education. This might be attributed to the fact that illiterate women are at higher risk of CMV infection due to contact with contagious secretions from their own children and poor hygienic practice. This is in keeping with the findings of **Yeroh et al.** [7].

Analysis of the results based on gestation age revealed the highest seroprevalence among pregnant women who were at their second trimester. This might be due to the fact that most pregnant women report for antenatal clinics in their second trimester than in the first and third trimester. Highest CMV seroprevalence among pregnant women in second trimester was also reported by **Odebisi-Omokanye et al.** [18]

In this study, number of previous pregnancies was identified as a risk factor associated with CMV infection. However, history of blood transfusion and lack of washing of hand after diaper change were not statistically associated with risk of CMV infection. This result is not in agree with the finding of **Matos et al.** [20] who reported blood transfusion as a risk factor for CMV infection. Improper handling diaper have been identified as a potential risk factors for CMV infection [19].

Seroprevalence of CMV IgM was significantly higher among pregnant women who had more than four previous pregnancies (63.6%). Similar observation of higher CMV seroprevalence among pregnant women with more than four previous pregnancies was reported by **Hamid et al.** [19]. This is contrary to the findings of **Maingi et al.** [9] who reported least IgM seroprevalence (0.0%) among pregnant women with more than four parities.

There was a significant association between number of previous pregnancies and CMV seroprevalence. The highest seroprevalence was observed among pregnant women who have had pregnancies from four and above. This agrees with the findings of **Ahmad et al.** [13]. This might be because the more the number of children, the higher the probability of being seropositive. High parity has been reported to be significantly associated with a higher risk of CMV infection in pregnant women [21].

Higher seroprevalence of CMV IgM with respect to knowledge of CMV was observed among those who had no knowledge of CMV, which could be attributable to ignorance of the mode of spread and prevention of CMV. This is similar to the findings of **Mujtaba et al.** [22].

Conclusion

The seroprevalence of 32.6% obtained in this study shows that CMV is highly associated with pregnant women within Kaduna metropolis. Occupation and number of previous pregnancies were statistically associated with CMV infection. Risk factors of CMV infection among pregnant women identified in this study was number of previous pregnancies.

Conflict of interest

Not declared.

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