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Seroprevalence of Cytomegalovirus Antibodies in Pregnant Women, Benue State, Nigeria

Umeh EU[1*], Onoja TO[1], Aguoru CU[1] and Umeh JC[2]

[1]Department of Biological Sciences, University of Agriculture, Makurdi, Benue State, Nigeria

[2]Department of Agricultural Economics, University of Agriculture, Makurdi, Benue State, Nigeria

[*]**Corresponding author:** Umeh EU, Department of Agricultural Economics, University of Agriculture, Makurdi, Benue State, Nigeria, Tel: 5083347872; E-mail: jceu1@yahoo.com

Abstract

Cytomegalovirus (CMV), a member of the herpes family, belongs to a group of vertically transmitted infections referred to as the TORCH complex including: Toxoplasmosis, Rubella, Cytomegalovirus and Herpes Simplex. Known to be frequently transmitted to developing foetus, it remains one of the leading causes of congenital viral infections. Although the infection has been detected in Nigerian neonates, its awareness is limited particularly in a growing metropolitan city like Makurdi, Nigeria. In this study, the prevalence of CMV antibodies and their association with some socio-demographic factors in pregnant women was evaluated. Pregnant women (N=375; age range=15 to 50 years) attending ante-natal clinic in different hospitals in Makurdi were screened for the infection. Five-ml venous blood was collected from each participant for serological studies, and structured questionnaire was used to obtain socio-demographic data. Serum samples were assayed using enzyme-linked immunosorbent assay (ELISA) technique. The overall prevalence of anti-CMV IgG-antibodies was 93.3% (n=350) and was 3.5% (n=13) for anti-CMV IgM-antibodies. Prevalence of anti-CMV IgG and IgM antibodies was significantly associated with gravidity (PIgG=0.012; PIgM=0.001), while prevalence of anti-CMV IgM only was associated with marital status (P=0.035). The prevalence of anti-CMV IgG antibodies was highest (100%) in older pregnant women aged 41-50 years, but was lowest (85.0%) in younger ones aged 15-20 years. Risk factors for the disease such as history of blood transfusion, scarification, and multiple sexual partners were important, even though not statistically significant (P>0.05). Women of child-bearing age in the growing metropolitan city of Makurdi, Nigeria need to be educated on precautionary measures that will prevent cytomegalovirus infection.

Keywords: Cytomegalovirus; CMV IgG Antibodies; CMV IgM Antibodies; Benue state; Nigeria

Introduction

Human CMV is an enveloped DNA virus and a member of the herpes family that belongs to a group of vertically transmitted infections known as TORCH – Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes simplex. The virus is ubiquitous and the infection it causes is generally asymptomatic. It is a leading cause of disability in children and a common cause of congenital viral infection that results in avoidable conditions such as mental retardation, neurological impairment, and permanent hearing and vision loss. Regarded as the commonest viral infection in pregnancy, it can have serious consequences in pregnant women and in immunocompromised patients, and may even pose a teratogenic danger during pregnancy [1].

CMV infection occurs in many parts of the world irrespective of geographical location and socio-economic group [2,3]. The prevalence of the infection appears to be higher in developing nations than in the developed ones [4] and Africa seems to have the highest prevalence. Nonetheless, high seroprevalence has been reported in some developed nations of the world [5,6]. CMV is frequently transmitted to the developing fetus during pregnancy. Sexual activity and contact with the urine or saliva of young children [7] are other means of transmitting the infection. Infection is lowest at the time of conception but highest during the third trimester of pregnancy [8]. The risk of intrauterine

infection depends on the period of maternal infection during pregnancy. Rate of CMV infection transmission to fetus during pregnancy is higher if the infection is primary than if it were secondary. For primary infection the estimated rate of transmission was between 25% and 75%, but was between 0.2% and 2.0% for secondary infection [9]. Congenital infection in the fetus usually occurs if the mother has a primary infection or a recurrent infection during pregnancy. Maternal infection during the first trimester seems to be associated with adverse effect in the fetus [10]. In Nigeria, previous studies on the seroprevalence of CMV infection in Nigeria had focused on some major cities of the country giving little or no information on the middle-belt region of the country. Given the general unawareness of the infection in pregnancy and the serious consequences it poses to the unborn child, this study was undertaken assess the seroprevalence of this infection in the middle-belt region of Nigeria, and to determine its associated risk factors.

Materials and Methods

Study area

Makurdi is the capital of Benue State, in the meddle-belt of Nigeria. It is located on latitude 7°43'32" N and longitude 8°33'51" E, and has a population between 250,000 and 500,000. Temperature ranges between 23°C and 35°C depending on the time of the year. Farming is the main occupation of the inhabitants; other professions include civil service, business, and petty trading.

CMV IgG	CMV IgM				Total	
	positive		negative			
	Number	**(%)**	**Number**	**(%)**	**Number**	**(%)**
positive	13	-3.5	337	-89.9	350	-93.3
negative	0	0	25	-6.7	25	-6.7
Total	13	0.035	362	-96.5	375	-100
Note: four infection categories were observed: Primary infection cases=IgG$^+$/IgM$^+$ Previously exposed cases=IgG$^+$/IgM$^-$ Recent primary infection cases=IgG$^-$/IgM$^+$ Susceptible persons=IgG$^-$/IgM$^-$						

Table 1: Seroprevalence of anti-CMV IgG and IgM antibodies in pregnant women.

Study population

Cross-sectional data were collected from 375 pregnant women (age range, 15 to 50 years) attending ante-natal clinic at the Federal Medical Centre, Makurdi (a referral health-care facility) and Madonna Hospital, Makurdi (primary health-care facility).

Sampling technique

Consecutive sampling technique was employed in this study. This is a non-probability sampling technique which involves taking every subject who meets the selection criteria over a specified time interval.

Ethical consideration

Ethical approval was obtained from the Research Ethics Committee of Federal Medical Centre Makurdi. Permission for the study was sought from Head of Medical Microbiology Laboratory. Written informed consent was obtained from all participants after detailed explanation of nature and objectives of the study was given to them in English and local languages. The study was at no cost to the participants, while the option to opt out of the study at any time was left open to them without any prejudice.

Inclusion criterion: Consenting pregnant women aged 15-50 years.

Exclusion criterion: Non-consenting pregnant women.

Category	entire group	IgG		IgM	
		Number seropositive	**(%)**	**Number seropositive**	**(%)**
Age					
15 - 20 yr.	20 (100)	17	-85	1	-5
21 - 30 yr.	266 (100)	247	-92.9	10	-3.8
31 - 40 yr.	81 (100)	78	-96.3	2	-2.5
41 - 50 yr.	8 (100)	8	-100	0	0
TOTAL	375 (100)	350	-93.3	13	-3.5
Chi-square value		4.043 (P=.257)		0.737 (P=.865)	

No. of pregnancies					
none	130 (100)	115	-88.5	0	0
once	109 (100)	101	-92.7	5	-4.6
twice	51 (100)	50	-98	0	0
more than twice	85 (100)	84	-98.8	8	-9.4
TOTAL	375 (100)	350	-93.3	13	-3.5
Chi-square value		10.971 (P=.012)		15.886 (P=.001)	
Gestational age					
1st trimester	44 (100)	39	-88.6	1	-2.3
2nd trimest	188 (100)	176	-93.6	7	-3.7
3rd trimester	143 (100)	135	-94.4	5	-3.5
TOTAL	375 (100)	350	-93.3	13	-3.5
Chi-square value		1.849 (P=.397)		0.225 (P=.894)	

Table 2: CMV seroprevalence by age, parity and gestational age.

Sample and data collection

Five-mL blood sample was collected from each consenting pregnant women by venipuncture, transferred into sterile anticoagulant-free sterile bottle, and allowed to clot. The clotted blood sample was centrifuged (3000 rpm, 5 min), and the serum (the supernatant) was transferred into cryovials and stored at -20°C until required for use. Socio-demographic characteristics were obtained with structured questionnaires.

Serologic testing

Samples of serum were tested for CMV-specific IgG and IgM antibodies using IgG and IgM ELISA kit by DIA. PRO Diagnostic Bioprobes (Milan m,./kh/, Italy). All the samples, reagents and calibrators were brought to room temperature an hour before the test. Test was carried out as specified by manufacturers. All samples with optical densities less than 10 U/ml were considered negative and those greater than or equal to 10 U/ml were considered positive.

Statistical analysis

Data were analysed using SPSS version 19 (2010). Pearson chi-square test was used to determine associations between seroprevalence and the socio-demographic variables. Significance was set at 0.05 level.

Results

The seroprevalence of CMV-specific IgG and IgM antibodies for the 375 women enrolled in this study were 93.3% (350/375) for IgG seropositivity (IgG$^+$) and 3.5% (13/375) for IgM (IgM$^+$) seropositivity. As shown in Table 1, 3.5% of the pregnant women who were IgG$^+$/IgM$^+$ were classified as having primary CMV infection, 89% who were IgG$^+$/IgM$^-$ as having had previous exposure of the infection, and 6.7% who were IgG$^-$/IgM$^-$ were classified as susceptible. None of the study population was IgG$^-$/IgM$^+$ indicating that none of them (0%) had recent primary infection.

Characteristics	Entire group(%)	IgG		IgM	
		Seropositive Number	(%)	Seropositive Number	(%)
Marital Status					
married	374(100)	349	-93.3	12	-3.2
widowed	1(100)	1	-100	1	-100
TOTAL	375	350	-93.3	13	-3.5
Chi-square value		0.072 (P=0.933)		27.921 (P=0.035)	
History of miscarriage					
yes	88 (100)	81	-94.2	5	-5.7
no	287 (100)	268	-93.4	8	-2.8
TOTAL	375	350	-93.3	13	-3.5
Chi-square value		0.004 (P=0.556)		1.686 (P=0.165)	
No of Miscarriages					
once	54(100)	49	-90.7	3	-5.6
more than once	31(100)	31	-100	2	-6.5
TOTAL	85(100)	80	-94.1	5	-5.9
Chi-square value		3.050 (P=0.096)		0.029 (P=0.605)	

Table 3: CMV seroprevalence by marital status, history of miscarriage and number of times miscarried.

As shown in Table 2, seroprevalence increased from 85.0% in the youngest age group to 100.0% in the oldest age group for IgG, but these differences in seroprevalence according to age group were not statistically significant. A similar result was obtained for anti-CMV IgM seroprevalence (P>0.05). CMV seroprevalence (for both IgG and IgM antibodies) was higher in multiparous pregnant women than in those who had never been pregnant.

Nonetheless, seroprevalence increased with increase in number of earlier pregnancies. In the same way, gestational age was not significantly associated with CMV seroprevalence for both IgG and IgM antibodies, even though prevalence was least in those who were in the first trimester of pregnancy

Seroprevalence of anti-CMV IgG antibodies was not significantly associated with marital status of the pregnant women (Table 3). On the contrary, the occurrence of anti-CMV IgM antibodies was significantly associated marital status. Neither history of miscarriage nor the number of times miscarriage occurred showed any relationship with seroprevalence of anti-CMV antibodies.

Characteristics	Entire group(%)	IgG		IgM	
		Seropositive Number	(%)	Seropositive Number	(%)
Educational Level					
informal	7(100)	7	-100	1	-14.3
primary school	25(100)	24	-96	0	0
secondary school	152(100)	143	-94.1	5	-3.3
tertiary education	191(100)	176	-92.1	7	-3.7
Total	375(100)	350	-93.3	13	-3.5
chi-square value		1.354(P=0.716)		3.383(P=0.336)	
Occupation					
civil service	33(100)	29	87.9	1	3.0)
business	152(100)	144	94.7)	4	2.6)
Health worker	16(100)	16	100.0)	1	6.3)
student	112(100)	105	93.8)	4	3.6)
unemployed	62(100)	56	90.3)	3	4.8)
Total	375(100)	350	93.3)	13	3.5)
chi-square value		4.136 (P=0.388)		1.058 (P=0.901)	
Type of House					
one-room apartment	49(100)	47	-95.9	1	-2
one-bedroom flat	133(100)	126	-94.7	5	-3.8
two-bedroom flat	148(100)	135	-91.2	7	-4.7
more than two-bedroom flat	45(100)	42	-93.3	0	0
TOTAL	375	350	-93.3	13	-3.5
Chi-square value		2.013 (P=0.570)		2.653 (P=0.448)	

Table 4: CMV seroprevalence by some socio-demographic factors.

Table 4 shows the relationship between seroprevalence of anti-CMV antibodies and some socio-demographic characteristics. Even though most of the subjects screened had tertiary education, there was no statistically significant difference between them and those with lower levels of education. Likewise, seroprevalence did not differ significantly between the different occupational groups and type of residential house owned by the subjects.

As shown in Table 5, none of the bloodletting risk factors (or practices) investigated was significantly associated with anti-CMV IgG/IgM antibodies.

Characteristics	Entire group (%)	IgG		IgM	
		Seropositive Number	(%)	Seropositive Number	(%)
Blood transfusion					
yes	26(100)	26	-100	2	-7.7
no	349(100)	324	-92.8	11	-3.2
TOTAL	375 (100)	350	-93.3	13	-3.5
Chi-square value		1.995 (P=0.156)		1.491 (P=0.225)	

Time after Transfusion					
< a year	11(100)	11	-100	2	-18.2
> one year	15(100)	15	-100	0	0
TOTAL	26(100)	26	-100	2	-7.7
Chi-square value		-*		2.955 (P=0.169)	
Intravenous Drug Use					
yes	13(100)	13	-100	2	-15.4
no	362 (100)	337	-93.1	11	-3
TOTAL	375(100)	350	-93.3	13	-3.5
Chi-square value		0.962 (P=0.402)		5.716 (P=0.070)	
Sharing needles					
no	13(100)	13	-100	2	-84.6
TOTAL	13(100)	13	(100)	13	-100
Chi-square**					
Tattoo					
yes	29(100)	28	-96.6	0	0
no	346(100)	322	-93.1	13	-3.8
TOTAL	375	350	-93.3	13	-3.5
Chi-square value		0.523 (P=0.405)		1.129 (P=0.345)	
Scarification					
yes	41(100)	40	-97.6	2	-4.9
no	334(100)	310	-92.8	11	-3.3
TOTAL	375(100)	350	-93.3	13	-3.5
Chi-square value		1.322 (P=0.215)		0.274 (P=0.426)	

*No statistics are computed because CMV IgG is a constant

**No statistics are computed because Sharing Needles is a constant

Table 5: CMV seroprevalence by some risk factors.

Discussion

The results of this study have shown that most of the pregnant women screened have been infected with CMV, while only few had primary CMV infection. This result is consistent with reports from other parts of the world including Nigeria [2,3] in which a high seroprevalence of anti-CMV IgG antibodies and low anti-CMV IgM antibodies (indicating recent CMV infection) in pregnant women was reported and reported low anti-CMV antibodies as in this study [11]. On the other hand, results of studies from developed parts of the world reported low prevalence of anti-CMV IgG antibodies in pregnant women [12-14]. However, higher seroprevalence of anti-CMV IgG antibodies have been reported in Germany [5] and northern Italy) [6]. Primary CMV infection is critical because primary CMV infection is a significant risk factor for vertical transmission of CMV infection to newborn babies with its entire associated clinical conditions.

As portrayed in this study, age was not significantly associated with CMV infection, but the increase in seroprevalence with age could be attributed to weakening of the immune system with increase in age as suggested by Redwan et al. [2].

Although not statistically significant, occupation, parity, place and type of residence appeared to have shown group variations in seroprevalence. In addition, such factors as miscarriage, tattoo, scarification, blood transfusion intravenous drug use and increase in number of partners seemed to be predisposing the women to CMV infection: infection seroprevalence was highest in those who indulged in bloodletting practices and in those who had history of blood transfusion [15-19].

Out of 375 women, 25 have never been exposed to CMV, indicating that these women are susceptible to CMV infection, and are at risk of coming in contact with the virus for the first time during pregnancy (primary infection). The likelihood of giving birth to congenitally infected infants is therefore high. Preventive measures which includes strict hygienic practice should be adhered to in order to avoid primary infection during pregnancy [20-23]. The high seroprevalence may be the result of ignorance about the infection, poor hygiene, inadequate health care facilities and low socio-economic level [24].

In Makurdi, few people are aware of CMV disease, and as a result of this, little or no control measures are put in place by either governmental agencies or non-government organizations to curb the infection [25,26]. In more developed parts of the world, several intervention measures that would reduce the incidence of CMV infections are being executed. We recommend that such intervention measures (e.g., minimising close contact with possible sources of infection, maintaining good hygiene especially during pregnancy, use of prophylactic drugs in susceptible individuals, use of anti-viral drugs in treatment of acute cases of the infection) be adopted in areas where the prevalence of the infection is high as in Makurdi, Benue State. Awareness on the dangerous consequences of CMV to the newborn baby should be created [27].

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