

Full Length Research Paper

Seroprevalence and Risk Factors for Cytomegalovirus and Herpes Simplex Virus Infections among Pregnant Women in Irrua, Nigeria

Umelo CC¹, Eifediyi RA^{1,2*}, Jombo SE¹, Oriaifo N¹, Eigbefoh JO^{1,2}

¹Department of Obstetrics and Gynaecology, Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria

²Department of Obstetrics and Gynaecology, College of Medicine, Ambrose Alli University, Ekpoma, Edo State, Nigeria.

Received 14 November, 2017; Accepted 30 November, 2017

Cytomegalovirus (CMV) is the most common congenital infection and viral based mental retardation and hearing deficit in children of developing countries. Herpes simplex virus (HSV) infections are associated with congenital and neonatal herpetic infections. Developing countries have high prevalence and treatment of maternal infection has no beneficial effect on fetal outcome. This study aim to evaluate the seroprevalence, the risk factors for CMV and HSV infections among pregnant women attending the antenatal clinic in ISTH, Irrua. A descriptive cross sectional study conducted among antenatal attendee of Irrua Specialist Teaching Hospital, Irrua. Structured questionnaire was used to gather socio-demographic data. Two TORCHES rapid test kits was used to detect CMV / HSV specific immunoglobulin M antibody (IgM). Seroprevalence of CMV IgM in the study was 1.0%, HSV-1 5.0% and HSV-2 2.7%. Seroprevalence of CMV was observed to increase with maternal age. Being unmarried and of low parity were positively related to the seroprevalence of HSV-1 and 2 (P<0.001). Coinfection with HCV and HIV infection was statistically related to CMV infection (P <0.001). Although seroprevalence of CMV and HSV-1 and 2 was low it was associated with significant adverse pregnancy outcomes. The risk factors identified can aid screening, early diagnosis and treatment.

Keywords: Cytomegalovirus, Herpes Simplex, Antenatal screening, Seroprevalence and Risk factors.

INTRODUCTION

Maternal Cytomegalovirus (CMV) is the most common viral infection in perinatal period and it is the leading cause of congenital cytomegalovirus infection with a permanent hearing, vision loss and neurological impairment (Tabatabaee and Tayyebi, 2009; Cannon et al., 2010).

CMV is also known as Human Herpes Virus 5 (HHV-5) is a member of the family Herpesviridae and subfamily Betaherpes virinae (Hodnka et al., 2007). CMV infection is common and usually asymptomatic in healthy children and adult, but can cause severe disease in newborns and immunocompromised children or adult. CMV is the most common cause of congenital infection,

affecting 0.2-0.4% of all infants, and also viral based mental retardation and hearing deficit in children of developing countries (Kim, 2010). Most infections are asymptomatic but about 15% of adult have mononucleosis-like syndrome characterised by fever, pharyngitis, lymphadenopathy and polyarthritis. Most infections are often recurrent, caused by reactivation of latent virus (especially in immunocompromised patients). Reinfection may also occur due to antigenic diversity of the virus. The risk of seroconversion among susceptible women during pregnancy is from 1-4% (Fowler et al., 1992; Liesnae et al., 2000). Primary Infection, which is transmitted to the fetus in approximately 40% of cases, more often is associated with severe morbidity (Fowler et al., 1992; Liesnae et al., 2000). Congenital CMV infection is the most frequently identified viral cause of mental retardation and is the leading non genetic cause of neurosensory hearing loss which is part of the

*Corresponding Author Email: agbonsreuben@yahoo.com

cytomegalic inclusion disease, a syndrome characterised by low birth weight, microcephaly, intracranial calcifications, chorioretinitis, mental and motor retardation, sensoril neural deficits, hepatosplenomegally, jaundice, haemolytic anaemia and thrombocytopenic purpura.

The host defence against CMV infection in immunocompetent individuals combine cellular and humoral immune response which together prevent a severe CMV disease in the vast majority of infections, Antibodies of IgM class are produced immediately after primary infection and may last for several months. IgM can be produced in the secondary infection in some cases. Antibodies of the IgG class are also produced immediately after infection and last for life (Mendelson et al., 2006). Mothers who are CMV seropositive prior to pregnancy can also develop a secondary CMV infection either through reactivation of virus residing at specific sites in the body (primarily salivary glands) or reinfection with a different strain (Adler et al., 2007). Such infections tend to be less severe and are usually asymptomatic for both mother and newborn. Infants born to such mothers can also have sequelae of congenital CMV, but this is far less likely estimated at 0.2% to 2% (Boppana et al., 2001). In cases where maternal CMV infection is suspected, it is important to evaluate the risk of transmission to the foetus and to provide appropriate counselling and guidance to parents.

The diagnosis of primary CMV infection in pregnant women based on symptoms and clinical signs are difficult and unreliable, as infection is usually asymptomatic in 90% of cases and clinical signs if present are non specific. Standard Laboratory Methods for the diagnosis of CMV infection are by isolation of the virus from body fluids, molecular testing for CMV genome by PCR and detection of CMV proteins in infected cells. Serology can also be used. Detection of IgM antibody usually suggests recent infection, this may remain positive for many months after primary CMV infection or be present in the case of viral reactivation (McLver et al., 2005). So, while seroconversion to CMV IgG does confirm primary infection, the presence of CMV IgM and CMV IgG may represent either recent primary infection or reactivation. CMV IgG avidity tests have been used to distinguish recent from distant infection, but the test is not standardized among laboratories. The detection of CMV DNA in amniotic fluid by PCR or culture is generally considered confirmation of intra-uterine infection, however; it may rarely represent a false positive result due to contamination from maternal fluids.

Herpes Simplex Virus (HSV) type 1 and 2, belong to the subfamily Alphaherpesviridae in the Herpesviridae, genus Simplex virus (Jerome and Morrow, 2007). The prevalence of HSV-1 infection is greater than HSV-2 infection in most geographical areas (Chayavichsilp et al., 2009). Herpes simplex virus infections are caused by two strains, HSV-1 and HSV-2. Oro-labial infection is mainly caused by HSV - 1, however, this strain is

responsible for up to 53% of primary genital herpetic infections. Oro-labial herpes has an infection rate of approximately 33% in developing countries and 20% in developed countries (Chayavichsilp et al., 2009). Genital herpes, caused mainly by HSV-2, is the main cause of genital ulcers worldwide (Gupta et al., 2007). Neonatal herpes is an uncommon but serious complication of genital herpes with occurrence rates ranging from 1/3,000 to 1/20,000 live births, resulting in an estimated incidence of 1,500 new cases of neonatal HSV infection annually in the United States (Gupta et al., 2007).

Corneal diseases due to HSV infection are an important cause of blindness. Herpes Simplex Encephalitis (HSE) is one of the most severe central nervous system infection CNS infections, accounting for approximately 10-20% of all encephalitic viral infections of the CNS, in the United States (Whiley et al., 2006). Primary genital HSV-1 or HSV-2 infection in pregnant women can result in abortion, premature labour and congenital and neonatal herpes (Kimberlin and Whitley, 2005). HSV-2 infections in the newborn are particularly severe and frequently involve the CNS (Whiley et al., 2006). Direct contact with infected secretions or mucous membranes or skin with lesions from an asymptomatic or symptomatic patients shedding the virus, is the main mode of transmission of HSV (Jerome and Morrow, 2007; Chayavichsilp et al., 2009). Transmission can also occur by respiratory droplets (Whiley et al., 2006). Genital herpes is transmitted sexually (Jerome and Morrow, 2007). The seroprevalence is higher among women than among men across various populations (Cowan et al., 2004). A very large serologic study in the U.S found that approximately 23% of women had serologic evidence of HSV-2 infection (Xu et al., 2006). Among women with recurrent genital HSV, nearly 75% can expect a recurrence during pregnancy, and about 14% of women will have prodromal symptoms or clinical recurrence at delivery (Sheffield et al., 2005). Transmission of the virus from mother to foetus typically occurs by direct contact with the virus in the genital tract during delivery. The risk of vertical transmission is related to the gestational age at delivery, the presence of maternal antibody to HSV and the route of delivery (Brown et al., 2003). Infection can be classified as disseminated disease (25%), central nervous system disease (30%), or disease limited to the skin, eyes, or mouth (45%). About 30% of infants with disseminated disease and 4% of infants with CNS disease will die from their infection. Long term neurologic sequelae occur in about 20% of survivors (Kimberlin et al., 2001). Neonatal herpes can be acquired at different times: Intrauterine (in-utero) in 5% of cases, peripartum (perinatal) in 85% of cases, and postpartum (postnatal) in 10% of the cases (Drew, 2004; Kimberlin and Whitley, 2005, Miller and Dummer, 2007). To reduce neonatal transmission, it is currently recommended that a cesarean delivery be offered to all women with active genital lesions or

prodromal symptoms at delivery. There are several antiviral agents that have been used both for therapy and for prophylaxis in the management of women with genital herpes virus infections, which include acyclovir, penciclovir, valacyclovir and famciclovir. Oral antiviral agents are used in pregnancy to treat genital herpes infections. No increase in drug related foetal abnormalities was ascribed to acyclovir, although long term development outcomes were not evaluated (Stone et al., 2004) Although the American College of Obstetricians and Gynaecologist states that the use of acyclovir to suppress recurrent HSV infection in pregnancy is acceptable, some reports note that there are insufficient data to recommend this prophylaxis (Brown et al., 2003).

Treatment of maternal CMV and HSV infection frequently has no beneficial effect on the foetus, thus recognition of maternal disease and fetal monitoring once disease is recognized are important for all clinicians. Knowledge of this disease will help the clinician appropriately counsel mothers on preventive measures to avoid these infections and will aid in counselling parents on the potential for adverse foetal outcomes when these infections are present. The knowledge of the seroprevalence will also add to the existing knowledge and can contribute to the modification of obstetric practice also serve as baseline for Irrua Specialist Teaching Hospital (ISTH). The basic data concerning CMV and HSV infections during pregnancy is important for health planners and care providers, thus this is the aim of the study to investigate seroprevalence, associated possible risk factors for CMV and HSV infections among pregnant women in ISTH.

The aim of the study is to determine the seroprevalence and the risk factors for CMV and HSV infections amongst pregnant women.

Specific Objectives

1. To determine the seroprevalence of Cytomegalovirus specific IgM antibodies
2. To determine the seroprevalence of Herpes simplex 1 and 2 specific IgM antibodies
3. To evaluate the risk factors for CMV and HSV infections.

MATERIALS AND METHODS

The study was conducted at the obstetrics and gynaecology department of Irrua Specialist Teaching Hospital (ISTH). Due to its strategic location, it serves two of the three senatorial district in Edo state (Edo central and Edo north senatorial districts), South-South, Nigeria and also serves as a major referral centre for Delta, Ondo and Kogi states.

Study Design

This is a cross sectional descriptive study.

Study Population

Pregnant women who booked for antenatal care in ISTH, Irrua and met the inclusion criteria were recruited into the study.

Inclusion Criteria

Pregnant women that registered for antenatal care in our ISTH, Irrua

Exclusion Criteria

Pregnant women who are unbooked and pregnant women who have received any sulphonamide containing intermittent preventive treatment (I.P.T) for malaria prophylaxis.

Ethical Consideration

Approval for the study was obtained from the ethical committee of ISTH through the Head of Department of Obstetrics and Gynaecology. Informed consent was obtained from the subjects before enlistment into the study. Ethical considerations in this study were based on the general ethical principles as applicable to human subjects (CIOMS, 1993). These are respect for persons, beneficence, non-maleficence and justice.

Sample Size Determination

The sample size of 402 parturient was calculated using the statistical formula $N = 4z^2pq/d^2$ (John, 2003) and prevalence of CMV 65% and 14% for HSV infection and adjusted by 10 % to make up for attrition.

METHODOLOGY

All parturient who met the inclusion criteria were counseled by the researcher (and the researcher assistance) and informed consents obtained from them and thereafter enrolled into the study. Enrolled women were administered a structured interviewer questionnaire which contained their biodata and socio-demographic characteristics, obstetric history, immunization history, history of current pregnancy and investigations.

A pilot study was done to pretest the questionnaire

before commencement of the study.

Assay Method

CMV and HSV I & II Rapid Test kit was used to carry out the study. It is an immuno-chromatographic assay based on the principle of Gold Immuno-Chromatography assay (GICA) principle. Recombinant antigens of the two viruses and anti-human IgM antibodies to the two viruses were respectively used to detect the specific antibodies in the human serum samples. If CMV and HSV antibody was present in the sample in concentration above detection, a labelled antibody-dye complex was formed. This complex was then captured by antigen immobilized in the Test zone ('T') of the membrane, producing a visible pink –rose colour band on the membrane. The colour intensity depended on the concentration of CMV and HSV antibody in the sample.

A colour band always appeared at the control zone (marked with a "C") in the case of a positive or negative result, however this colour band does not appear in the control zone in an invalid result. It is a protein microarray technology with immunogold based assay that has the capability of serodiagnosis of IgM antibody on the microarray at 0.24 mg/L (Jiang et al., 2008). The sensitivity of this method approaches that of ELISA and it is simple to perform and saves more time (Gutiérrez, 2000). It requires less personnel training and it is less expensive.

About 3-5 millilitres (ml) of peripheral venous blood was collected aseptically by venopuncture in a sterile dry test tube with no anticoagulant from each pregnant woman.

The blood samples were kept at room temperature, then centrifuged and sera collected. The sera were tested for CMV and HSV specific IgM class of antibodies by Two Link Torch Rapid Test method. The test was performed with commercially available kits purchased from ATLAS LINK, No.811 Zeyang plaza, No.166 Fushi Road, Shijingshan Dist., Beijing 100043, China and the manufacturer's instructions was followed strictly. The serum could be refrigerated at 2-8 degrees Centigrade if it is not tested the serum is not tested immediately.

The sealed foil pouch bag was opened, the cassette taken out and put on the table, about 2-3 drops of serum specimen (80-120uml) were dropped into each hole (total 5) and result read after 15 minutes but within 30 minutes.

Interpretation of Results

Negative: Only one coloured line appear on the control region, no apparent line in the test region.

Positive: In addition to a coloured control line, a coloured line will also appear on the test region.

Invalid: A total absence of coloured line in both (T) and (C) regions or no coloured line appears on the control (C) region.

Data Analysis

Data obtained from the study, were analysed using the IBM Statistical Package for social Sciences (SPSS) version 16.0 software. The social class classification of the women were assessed using the occupation of the husband and the educational level of the woman (Olusanya et al., 1985).

RESULTS

A total of 402 regnant women were screened for the presence of CMV and Herpes 1 and 2 specific IgM antibodies. The highest age of the participant was 43 years while the lowest age was 15 years and the mean age (SD) of the participant was 27.7±5.51. The seroprevalence of CMV was 1% while Herpes simplex type1 and type 2 were 5.0 and 2.7% respectively.

Age as a risk factor for CMV and Herpes typ1 and 2 infections was considered in this study and classified into five groups. The seroprevalence of CMV was observed to decrease with decreasing age.

Analysis of the data based on the marital status, showed that majority of the studied subjects were married (90.8%), there is a significant association between Herpes simplex type and marital status ($\chi^2=12.297$, $df=3$, $p=0.006$). The seroprevalence of Herpes 2 was highest among separated pregnant women (9.2%). Of the 402 pregnant women studied, 163(40.5%) were primigravida/nullipara, 219 (54.5%) were multipara, while 20 (5.0%) were grandmultipara. Seroprevalence of CMV, Herpes 1 and Herpes type 2 were noted to be lowest amongst the grandmultipara meanwhile, there was a significant association between CMV and herpes seroprevalence and parity in this study. However, the distribution of the participants according to their educational status showed that 29 (7.2%) of them had no formal education, 97(24.1%) had a secondary level of education, while 185 (46.0%) had a tertiary level of education.

A total number of 93 (23.1%) of the pregnant women were in their first trimester, 249 (61.9%) in the second trimester and 60 (14.9%) in the third trimester. The seroprevalence of Herpes simplex type 2 were highest (5.0%) in the third trimester. Some of the studied subjects (11.7%) reported past pregnancy losses, majority (53.2%) occurred around the 12th week of gestation and the least occurrence was at about 20 weeks of gestation. Further analysis of the data based on the history of congenital malformation showed that of the total number studied, 6 (1.5%) reported previous

Table 1. Sociodemographic Information

VARIABLES	N=402	(%)
AGE		
15-19	31	7.7
20-24	88	21.9
25-29	146	36.3
30-34	93	23.1
>34	44	10.9
MARRITAL STATUS		
SINGLE	24	6.0
MARRIED	365	90.8
SEPARATED	11	2.7
DIVORCED	2	0.5
PARITY		
PRIMIGRAVIDA/NULLIPARA	163	40.5
MULTIPARA	219	54.5
GRAND MULTIPARA	20	5.0
OCCUPATION OF CLIENT		
UNSKILLED	145	36.1
SEMI SKILLED	144	35.8
SKILLED	113	28.1
HUSBAND OCCUPATION		
UNSKILLED	96	23.9
SEMI SKILLED	169	42.0
SKILLED	137	34.1
RELIGION		
CHRISTIANITY	311	77.4
ISLAM	88	21.9
AFRICAN TRADITION	3	0.7
EDUCATIONAL STATUS		
NO FORMAL EDUCATION	29	7.2
PRIMARY LEVEL OF EDUCATION	91	22.6
SECONDARY LEVEL OF EDUCATION	97	24.1
TERTIARY LEVEL OF EDUCATION	185	46.0

Mean age \pm SD= 27.74 \pm 5.51

Table 2. Indicators in Past Obstetric History among Women with HSV And CMV Seropositivity (N=402)

PAST OBSTETRIC HISTORY	YES		NO	
	n	(%)	n	(%)
SPONTANEOUS MISCARRIAGE(S)	47	(11.7)	355	(88.3)
PREVIOUS FETAL DEATH	5	(1.2)	386	(98.8)
PREVIOUSLY CONGENITAL MALFORMED BABY	6	(1.5)	396	(98.5)
PRETERM DELIVERY	21	(5.2)	381	(94.8)
INTRA UTERINE GROWTH RETARDATION	8	(2.0)	394	(98.0)
BLOOD TRANSFUSION IN PREGNANCY.	3	(0.7)	399	(99.3)

Table 3. Frequency Distribution of the Result Outcome of Routine Antenatal Investigations done in Index Pregnancy of the Participants

INVESTIGATIONS	N=402	(%)
RETROVIRAL DISEASE STATUS		
POSITIVE	12	3.0
NEGATIVE	390	97.0
GENOTYPE		
AA	295	73.4
AS	95	23.6
SS	6	1.5
OTHERS	6	1.5
V.D.R.L RESULT		
POSITIVE	8	2.0
NEGATIVE	394	98.0
HBsAg		
POSITIVE	5	1.2
NEGATIVE	397	98.8
HCV		
POSITIVE	6	1.5
NEGATIVE	396	98.5

Table 4. Past Obstetric Performance With Cmv & Hsv Serology

	CMV		Statistical significance	HERPES 1		Statistical significance	HERPES 2		Statistical significance
	+VE	-VE		+VE	-VE		+VE	-VE	
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
HISTORY OF SPONTANEOUS MISCARRIAGE(S)									
YES	0 (0)	47 (100.0)	χ^2 1.535	1 (2.1)	46 (97.9)	χ^2 0.913	1 (2.1)	46 (97.9)	χ^2 0.074
NO	4 (1.1)	351 (98.9)	df 1 p 0.465	19 (5.4)	336 (94.6)	df 1 p 0.339	10 (2.8)	345 (97.2)	df 1 p 0.785
HISTORY OF PREVIOUS FETAL DEATH									
YES	0 (0)	16 (100.0)	χ^2 1.167	0 (0)	16 (100.0)	χ^2 0.872	0 (0)	16 (100.0)	χ^2 0.469
NO	4 (1.1)	382 (99.0)	df 1 p 0.682	20 (5.2)	366 (94.8)	df 1 p 0.350	11 (2.8)	375 (97.2)	df 1 p 0.494
ANY HISTORY OF PREVIOUSLY CONGENITALLY MALFORMED BABY									
YES	0 (0)	6 (100.0)	χ^2 0.061	0 (0)	6 (100.0)	χ^2 0.319	0 (0)	6 (100.0)	χ^2 0.171
NO	4 (1.1)	392 (99.0)	df 1 p 0.805	20 (5.1)	376 (94.9)	df 1 p 0.572	11 (2.8)	385 (97.2)	df 1 p 0.679
HISTORY OF PRETERM DELIVERY									
YES	0 (0)	21 (100.0)	χ^2 0.223	0 (0)	21 (100.0)	χ^2 1.160	1 (4.8)	20 (95.2)	χ^2 0.342
NO	4 (1.1)	377 (99.0)	df 1 p 0.637	20 (5.2)	361 (94.8)	df 1 p 0.281	10 (2.6)	371 (97.4)	df 1 p 0.559

Table 4. Continued

ANY HISTORY OF UTERINE RETARDATION	PREVIOUS OF INTRA UTERINE GROWTH	0 (0)	8 (100.0)	χ^2 0.082	1 (12.5)	7 (87.5)	χ^2 0.978	1 (12.5)	7 (87.5)	χ^2 2.924
YES										
NO		4 (1.1)	390 (99.0)	df 1 p 0.775	19 (4.8)	375 (95.2)	df 1 p 0.323	10 (2.5)	384 (97.5)	df 1 p 0.087
PREVIOUS HISTORY OF TRANSFUSION	HISTORY OF BLOOD	0 (0)	3 (100.0)	χ^2 0.030	0 (0)	3 (100.0)	χ^2 0.158	0 (0)	3 (100.0)	χ^2 0.085
YES										
NO		4 (1.0)	395 (98.0)	df 1 p 0.862	20 (5.0)	379 (95.0)	df 1 p 0.691	11 (2.8)	388 (97.2)	df 1 p 0.771

Table 5. CMV and HSV Serology with other Viral Infection Screened during the Antenatal Period

	CMV		Statistical significance	HERPES 1		Statistical significance	HERPES 2		Statistical significance
	+VE	-VE		+VE	-VE		+VE	-VE	
	n(%)	n(%)		n(%)	n(%)		N(%)	n(%)	
RETROVIRAL DISEASE STATUS									
POSITIVE	3(25.0)	9(75.0)	χ^2 72.353	0(0)	12(100.0)	χ^2 0.648	1(8.3)	11(91.7)	χ^2 1.459
NEGATIVE	1(0.3)	389(99.7)	df 1 p 0.000	20(5.1)	370(94.9)	df 1 p 0.421	10(2.6)	380(97.4)	df 1 p 0.228
V.D.R.L RESULT									
POSITIVE	0(0)	8(100.0)	χ^2 0.082	0(0)	8(100.0)	χ^2 0.427	0(0)	8(100.0)	χ^2 0.230
NEGATIVE	4(1.0)	390(99.0)	df 1 p 0.775	20(5.1)	374(94.9)	df 1 p 0.513	11(2.8)	383(97.2)	df 1 p 0.632
HBsAg									
POSITIVE	0(0)	5(100.0)	χ^2 0.051	0(0)	5(100.0)	χ^2 0.265	0(0)	5(100.0)	χ^2 0.142
NEGATIVE	4(1.0)	393(99.0)	df 1 p 0.822	20(5.0)	377(95.0)	df 1 p 0.607	11(2.8)	386(97.2)	df 1 p 0.706
HCV									
POSITIVE	1(16.7)	5(83.3)	χ^2 15.185	0(0)	6(100.0)	χ^2 0.319	0(0)	6(100.0)	χ^2 0.171
NEGATIVE	3(0.8)	393(99.2)	df 1 p 0.000	20(5.1)	376(94.9)	df 1 p 0.572	11(2.8)	385(97.2)	df 1 p 0.679

history of congenital malformation, congenital cataract represented 50%, limb deformity was 33.3% while the least was microcephaly 1 (16.7%). Analysis of the result based on the symptom showed a very strong association between CMV and retroviral disease and hepatitis C virus (HCV)($p < 0.001$ and $p < 0.001$ respectively).

DISCUSSION

Microbial agents such as CMV and HSV are important causes of infections during pregnancy. These infections

often lead to mild or asymptomatic infection in the mother (Karabulut et al., 2011) However, the infection during pregnancy may result in serious congenital abnormalities, intra-uterine growth retardation and may cause foetal death (Robertson et al., 2003). Any patient infected with CMV and HSV infections, mainly two types of antibodies are produced against the infecting organisms (Molhotra and Bhardwaj, 1991). These are of immunoglobulin M (IgM) and immunoglobulin G (IgG) types. By the way of measuring the antibody in mother's blood, we can identify the type of infection. When IgM antibody is present, it invariably suggests acute or recent

infection and the presence of IgG antibody suggests past or present active infection (Turbadkar et al., 2003; Arif et al., 2003). In the present study, the seroprevalence of CMV and HSV infections were determined.

The seroprevalence for CMV IgM was 1%. This is in keeping with 1.2% reported from Turkey, 1% by Uyar et al. 2008, 0.9% from Bangladesh, (Nabi et al, 2012), however, this is higher than 0.4% from Italy, 0.09%(Gurgose et al., 2006) from Croatia (96%) (Gomwalk and Ahmad, 1989), but lower than 2.5% from Western Sudan (Paschale et al., 2012) 8% from Kenya (Vilibik-Cavlek et al., 2011). This result agrees with the report of Ludwig and Hengel, 2009 who asserted that the seroprevalence of CMV differs between countries and regions. The low prevalence rate of CMV in this study compared to the rest of the studies in African countries, could be due to diverse HIV infections (which is an important coinfections with CMV (Uyarl et al., 2008) diverse socio-demographics, diverse cultures, population behaviour, child care, breast feeding and sexual activity (Zakayo and Anthony, 2014). There was a strong significant association noted in this study between religion and CMV. The highest prevalence with respect to the religion was among pregnant women who belong to African religion tradition; this could be due to the exposure to multiple sexual partners permitted by the religion through its polygamous family setting. There was a strong association between HIV and CMV infections. This is in concert to previous studies that observed HIV infections as an important coinfections with CMV (Nabi et al., 2012). There is no significant association between age, marital status, parity, occupation, educational status and CMV infection. However, from the analysis, younger age group, women who are married and women with low educational status were found to be of higher risk for CMV infection. These risk factors were similar to those found by previous studies (Ludwig et al., 2009). These factors increased susceptibility to acquisition of CMV infection, perhaps through the direct contact with contagious secretions from their own children or poor hygiene practiced by these women (Peckham et al., 1989). In addition, in these settings most women are usually married based on customs of most African settings with high number of children.

There is a lot of debate concerning maternal age and CMV infection, however, most studies including this study have shown younger women to be at higher risk of CMV infection, while others reports are contrary (Hamdan et al., 2011). Socioeconomic status has been shown to be a risk factor for CMV infection (Kramer et al., 2006) but this was contrary to this study where no significant association was found between education and occupation.

Further analysis with educational status in this study, showed higher prevalence with women with low educational status. This agrees with a previous report that showed that illiterate women are at higher risk of

CMV due to contact with contagious secretions from their own children and poor hygiene practice (Schoub et al., 1993). There is no significant association between CMV and blood transfusion. This disagrees with the report of Matos et al., 2010 where blood transfusion was shown to be a risk factor for transmission of CMV infection. The reason for this disagreement could be as a result of the disproportionate size of women who were transfused to those who were not transfused but enrolled in the study. No significant association was observed between CMV and miscarriages, IUGR, congenital malformation and preterm delivery in this study. This could be due to limited sample size.

Herpes simplex (HSV) is a common sexually transmitted infection, and the prevalence of this infection has increased significantly over the last two decades in many developed and developing countries. The seroprevalence of Herpes Simplex IgM virus in this study is 5.0%, this obtained seroprevalence is in keeping to 5.9% reported by Obeid 2007. This shows that active HSV 1 infection is high in this environment. This could be due to the general public's low level of accurate knowledge on mode of transmission of Herpes which might be due to low mass education campaigns, lack of routine screening of the largest population, presence of other risk factor, like lack of condom use, history of STI, HIV infection, socioeconomic status, duration of HSV in the source partner and duration of relationship. There is a strong association between marital status and Herpes Simplex 1 virus, it is high among single pregnant women and divorced women. The possible explanation for this could be due to vulnerability of the group to multiple sexual partners. Besides marital status, other sociodemographic variables were not significantly associated with Herpes simplex type 1 virus seroprevalence. However, further analysis with respect to the age of the participant showed a high prevalence rate among women of older age group 30-34 and \geq 34years. From the analysis of occupation, it was noted that there was a decreasing prevalence from participants with unskilled to skilled occupation. The high prevalence agrees with previous studies that reported low socioeconomic status, frequency of sexual contacts, duration of HSV in the source partner and duration of relationship as risk factors (Obeid, 2007).

Further analysis into the religion, reported highest prevalence rate among women who practice African traditional religion. It could be due to multiple sexual partners associated with polygamous family setting known for African tradition. There was no significant association between Herpes Simplex 1, RVD, foetal death, congenital malformation, preterm delivery and IUGR. This might be due to limited sample size use in the study. Herpes simplex virus (HSV) is transmitted by intimate contact with someone who is shedding the virus. HSV type 1 (HSV-1), which is excreted mainly orally, is usually acquired during childhood from a parent, but may also be acquired later in life from a

partner through intimate, e.g sexual contact.

HSV type 2 (HSV-2) is excreted mainly genitally and is predominantly acquired through sexual activity. The seroprevalence of Herpes simplex virus type 2 in this study is 2.7%, this is similar with 3.6% reported by Turbadkar et al. 2003, 3.33% by Gumber et al. 2008 but higher than other previous studies 1.8% (Nahmias et al., 1996), 1.69%, but far lower than 8.66% by Surpam et al. 2006. Though there was no significant association between age and Herpes simplex type 2 in this current study, the prevalence was observed to increase with age, being highest among pregnant women of ≥ 34 years age group. This finding is in agreement with previous studies which reported rising prevalence of HSV infection with age, reaching the maximum around 40 years. This appears to be related to the number of sexual partners. There is no significant association between marital status, occupation and educational status of the subjects and Herpes 2 ($p > 0.05$), but analysis of marital status, showed the highest prevalence amongst the women that have separated from their marriages. This could be explained by the fact that currently in our society, due to westernization of our culture, there are no more traditional methods of taking care of such women, hence they are left to fend for themselves in all things including sex. Some of them have multiple sexual partners with attendant increased exposure to sexually transmitted infections. "Primary and secondary education status" also present a higher risk than other levels of education. This could be explained by the fact that health enlightenment tools in our environment seemed skewed towards the educated, the uneducated are not properly enlightened and could be falling prey to avoidable behaviours (high risk) and higher exposure to sexually transmitted infections. These findings were fairly in agreement with previous studies (Sadik et al., 2012). Haddow et al. 2006 reported younger age as a risk factor among other things.

There is no significant association between HSV 2 and spontaneous miscarriages, foetal death, congenital malformation, preterm delivery and IUGR. This could be due to limited sample size. There was a strong significant association between Herpes simplex type 2 in this study with exposure to cats. This could be explained by the fact that in our environment, most people that rear cat are mere farmers with low socio economic status and low educational status who may not be benefiting maximally from health enlightenment tools.

CONCLUSION

Although seroprevalence of CMV and HSV-1 and 2 was low it was associated with significant adverse pregnancy outcomes in this study. Risk factors associated with these infections were also demonstrated and if these are properly exploited may serve as a guide for screening, early diagnosis and treatment.

Limitations of the Study

1. This is a hospital based study, community based study will be more accurate.
2. The assay is a qualitative screening test, for positive cases, more complex quantitative testing method may be required as confirmatory.
3. False negative result may result if the patient is tested during the window period.

RECOMMENDATIONS

It is therefore recommended that all pregnant women should be routinely ask for risk factor for CMV and HSV infection at the first antenatal visit especially pregnant women with BOH and thus offer screening accordingly.

Awareness amongst clinicians and patients about CMV and HSV infections and their consequences should be developed. It may also be necessary to consider the development of vaccines for HSV and CMV to prevent their infection and resultant morbidity and mortality as a pragmatic move in an attempt to curb this health problem. I think that this effort will eliminate these infections in our environment.

REFERENCES

- Adler SP, Nigro G, Pereira L (2007). Recent advances in the prevention and treatment of congenital cytomegalovirus infections. *Semin Perinatol.* 31:10–18.
- Arif A, Montur R, Nizamuddin A (2003). Seroprevalence of *Toxoplasma gondii* amongst pregnant women of Bangladesh, Bangladesh Armed Forces Medical Journal. 31: 75-79.
- Boppana SB, Rivera LB, Fowler KB, Mach M, Britt WJ (2001). Intrauterine transmission of cytomegalovirus to infants of women with preconceptional immunity. *N Engl J Med.* 344:1366–1371.
- Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L (2003). Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *JAMA* 289:203–9.
- Cannon, DS Schmid, TB Hyde (2010). Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol.* 20(4):202-13; Doi:10.1002/rmv.655.
- Chayavichitsilp P, Buckwalter JV, Krakowski AC, Friedlander SF (2009). Herpes simplex. *Pediatrics in Review.* 30(4), 119-129.
- Council for International organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Biomedical Research Involving Human subjects, Geneva; 1993.
- Cowan FM, French RS, Mayaud P, Gopal R, Robinson NJ, de Oliveira SA (2004). Seroepidemiological study of herpes simplex virus types 1 and 2 in Brazil, Estonia, India, Morocco, and Sri Lanka. *Sexually Transmitted Infections.* 79(4):286–90.
- Fowler KB, Stagno S, Pass RF (2004). Interval between births and risk of congenital cytomegalovirus infection. *Clinical Infectious Disease.* 38(7):1035–7. [MEDLINE:15034839].
- Gomwalk NE, Ahmad AA (1989). Prevalence of rubella antibodies on the African continent. *Rev Infect Dis.* 11(1):116-21.
- Gumber S, Arora U, Devi P (2008). Occurrence of cytomegalovirus and herpes simplex virus infections in pregnancy. *Indian J Med Microbiol.* 26:204-5.
- Gupta R, Warren T, Wald A (2007). Genital herpes. *Lancet.* 370(9605), 2127-2137.
- Gutiérrez J, Fernández F, Vergara MJ, Suárez S, Soto MJ, Maroto MC (2000). Comparison of several ELISA tests for detecting the presence

- of IgG and IgM against herpes simplex viruses. *Microbios*.103(405):127-32
- Gurgose MK, Yilmaz E, Godekmerdan A (2006). Seroprevalence of Mumps, Varicella and Rubella Antibodies in Children 1-16 years of age in eastern Turkey. *Turk J Pediatr*.48:185-8.
- Haddow LJ,Sullivan EA,Taylor J (2006). Herpes simplex virus type 2 infection in women attending an antenatal clinic in the south Pacific island nation of Vanuatu.On line J Am sex Transm Dis Assoc September 13.
- Hamdan HZ, Abdelbagi IE, Nasser NM, Adam I (2011). Seroprevalence of cytomegalovirus and rubella among pregnant women in Western Sudan. *Virol J*. 8: 217.
- Jerome KR, Morrow RA (2007). Herpes simplex viruses and Herpes B virus. In P. R. Murray.editor, *Manual of clinical microbiology*.9th ed.Washington, D.C.: ASM. pp. 1523-1536.
- Jiang L, YUZH, DU ND, Tong Z.M, Jiang T, Zhang Cx, Lu ZH (2008). Biosensors and Bioelectronics.24(3):376-382.
- John E (2003). Sample size Estimation: John Eng. Sample size Estimation: How many individuals should be studied? *Radiology*. 227:309-313.
- Karabulut A, Polat Y, Turk M, Balci YI (2011). Evaluation of Rubella, T. gondii, Cytomegalovirus seroprevalences among pregnant women in Denizli province. *Turk J Med Sci* . 41:159-164.
- Kim CS (2008). Congenital perinatal cytomegalovirus infection. *Korean Journal of Pediatrics*. 53(1),14-20.
- Kimberlin DW (2005). Herpes simplex virus infections in neonates and early childhood. *Seminars in Pediatric Infectious Diseases*. 16(4), 271-281.
- Kimberlin DW, Lin CY, Jacobs RF, Powell DA, Corey L, Gruber WC (2001). Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. *Pediatrics*. 108:230-8.
- Kimberlin DW, Whitley RJ (2005). Neonatal herpes: what have we learned. *Semin Pediatr Infect Dis*. 16:7-16.
- Kramer A, Schwebke I, Kampf G (2006). How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infect Dis*. 6:130. Doi:10.1186/1471-2334-6-130 28.
- Ludwig A, Hengel I (2009). Epidemiological Impact and Disease Burden of Congenital Cytomegalovirus Infection in Europe. *J. of Euro. Surveillance*.14 (9):19140.
- Matos SB, Meyer Lima,WFM (2011). Seroprevalence of Cytomegalovirus infection among healthy blood donors in Bahia State, Brazil. *Revista Brasileira de Hematologia eHemoterapia* 3(1):1516-8484
- McIver CJ, Jacques CF, Chow SS, Munro SC, Scott GM, Roberts JA (2005). Development of multiplex PCRs for detection of common viral pathogens and agents of congenital infections. *Journal of Clinical Microbiology*. 43(10):5102-10. [MEDLINE: 16207970].
- Mendelson E, Aboudy Y, Smetana Z, Tepperberg M,Grossman Z (2006). Laboratory assessment and diagnosis of congenital viral infections: Rubella, cytomegalovirus,vericella zoster virus, herpes simplex virus, parvo B19 and human immunodeficiency virus. *Reprod Toxicol*. 21:350-382.
- Miller GG, Dummer JS (2007). Herpes simplex and varicella zoster viruses: forgotten but not gone. *American Journal of Transplantation*. 7(4), 741-747.
- Molhotra V, Bhardwaj Y (1991). Comparison of enzyme linked immunosorbant assay and haemagglutination test in serological diagnosis of toxoplasmosis. *J Communicable Dis*. 23:154-156.
- Nabi SN, Wasey A, Haider KMTS, Khan AA, Hoque MM et al 2012 Seroprevalen of TORCH antibody in pregnant women. *J Armed Forces Med Coll*.8:35-9.
- Nahmias AJ, Lee FK, Keyserling HL (1996). The epidemiology of genital herpes. In: Stanberry LR, ed. *Genital and Neonatal Herpes*. Chichester, England: John Wiley. 93-108.
- Obeid E (2007). Prevalence of Herpes Simplex Virus type 1 and 2 and associated sociodemographic variables in pregnant women attending King FAHD Hospital of the University. *J.Family. Community med*. Jan -April;14(1):3-7.
- Olusanya O, Okpere EE, Ezimokhai M (1985). The importance of social class in voluntary fertility control in a developing country. *West Africa J. Med*. 4: 4.
- Paschale MD, Monaco MT, Paganini A (2012). Rubella antibody screening during pregnancy in an urban area of Northern Italy. *Infect Dis Rep*.4:59-62.
- Peckham CS, Johnson C, Ades A, Pearl K, Chin KS (1987). Early acquisition of cytomegalovirus infection. *Arch Dis Child*.62(8):780-785. Doi:10.1136/adc.62.8.780.
- Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS (2003). Rubella and congenital rubella syndrome: global update. *Rev Panam Salud Publica*.14:306-315.
- Sadik MS, Fatima H, Jamil K, Patil C (2012). Study of TORCH profile in patients with bad obstetric history. *Biol Med*.4:95-101.
- Schoub BD, Johnson S, Mc Anerney JM (1993). Is antenatal screening for Rubella and cytomegalovirus justified? *S Afr Med J* .83(2):108-110.
- Sheffield JS, Hill J, Laibl V, Hollier LM, Sanchez P, Wendel GD (2005). Valacyclovir suppression to prevent recurrent herpes at delivery: a randomized controlled trial [abstract]. *Obstetrics & Gynaecology*. 105(4 Suppl).
- Stone KM, Reiff-Eldridge R, White AD, Cordero JF, Brown Z, Alexander ER (2004). Pregnancy outcomes following systemic prenatal acyclovir exposure: Conclusions from the international acyclovir in pregnancy registry, 1984-1999. *Birth Defects Research. Part A, Clinical and MolecularTeratology*. 70(4):201-7.
- Surpam RB, Kamlakar UP, Khadse RK, Qazi MS, Jalgaonkar SV (2006). Serological study for TORCH infections in women with bad obstetric history. *J Gynec Obstet India*.56:41-3
- Tabatabaee M, Tayyebi D (2009). Seroepidemiologic study of human cytomegalovirus inpregnant women in Valiasr Hospital of Kazeroon, Fars, Iran. *J Matern Fetal Neonatal Med*. 22(6):517-2. Doi: 10.1080/14767050902801678.
- Turbadkar D, Mathur M, Rele M (2006). Seroprevalence of Torch Infection in bad obstetric history. *Indian J Med Microbiol*. 21(2): 108-110.
- Uyar Y, Balci A, Akcali A, Cabar C (2008). Prevalence of rubella and cytomegalovirus antibodies among pregnant women in northern Turkey. *New Microbiol*.31:451-5.
- Vilibik-Cavlek T, Ljubin-Sternak S, Ban M, Kolaric B, Sviben M, Mlinaric-Galinovic G (2011). Seroprevalence of TORCH infections in women of childbearing age in Croatia. *J Matern Fetal Neonatal Med*. 24:280-3.
- Whitley RJ (2006). Herpes simplex encephalitis: adolescents and adults. *Antiviral Research*. 71(2-3), 141-148.
- Xu F, Sternberg MR, Kottiri BJ, McQuillan GM, Lee FK, Nahmias AJ, Berman SM, Markowitz LE (2006). Trends in Herpes Simplex Virus type 1 and type 2 seroprevalence in the United States. *JAMA*. 296:964-73.
- Zakayo M, Anthony KN (2014). Seroprevalence of Cytomegalovirus (CMV) among pregnant in Thika, Kenya. *BMC research Notes*. 7:794 doi:10.1186/1756-0500-77-794.

How to cite this article: Umelo CC, Eifediyi RA, Jombo SE, Oriafio N, Eigbefoh JO (2017). Seroprevalence and Risk Factors for Cytomegalovirus and Herpes Simplex Virus Infections among Pregnant Women in Irrua, Nigeria. *Int. Inv. J. Med. Med. Sci*. Vol. 4(5): 71-80