



Seroprevalence of Herpes Simplex Virus Type 2 and HIV Co-Infection Among Pregnant Women in Jigawa State

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Abstract: Herpes simplex virus type 2 (HSV-2) infections is one of the most common sexually transmitted infections Worldwide. It facilitates the acquisition of HIV and is the primary cause of genital herpes which when acquired by women during pregnancy account for half of the morbidity and mortality among neonates. Lifelong latent HSV-2 infection raises concern among women of reproductive age considering the risk of neonatal transmission. In Nigeria screening for HSV-2 and co-infection with HIV in antenatal clinics is not routinely done. A cross-sectional study, was carried out among pregnant women attending antenatal clinics in four hospitals in Jigawa state. A total of 300 consenting pregnant women were enrolled, the study involved collection of sociodemographic data and laboratory determination of HSV-2 immunoglobulin G (IgG) and HIV seroprevalence using WHO standard procedure of Enzyme Linked Immunosorbent Assay (ELISA) test kit (DIAPRO Diagnostic Bioprobes, Milano, Italy), UNI-GOLD Wicklow, Ireland and ALERE Determine, respectively. Statistical significance was determined at $p < 0.05$. Of the 300 samples tested, overall seroprevalence of 55 (18.3%) and 44 (14.7%) for HSV-2 and HIV were recorded. The HSV-2 and HIV Co-infection rate was 16 (5.3%) among respondent. About 87.5% of the co-infection occurred in respondents that were in their 2nd Trimester. Additionally, co-infection was found to be high among respondents between the age of 15-34yrs with 81.3%. In this study, education status, parity, stage of pregnancy, occupation, History of blood transfusion had no statistical significance with HSV-2 and HIV co-infection ($p > 0.05$). This study has demonstrated the existence and risk of neonatal herpes in the study area. It is recommended that HSV testing should be placed among the standard medical checkup tests in the area, again advocacy and public awareness on the potential public health burden of HSV-2 and HIV co-infection should be observed.

Keywords: HIV, HSV-2, Virus, Co-infection, ELISA, STIs, Neonatal

1. Introduction

Herpes Simplex virus type 2 (HSV-2) is one of the most common sexually transmitted infection worldwide, HSV-2 is the predominant cause of genital herpes, although it leads to periodic recurrences of painful genital ulcers in symptomatic individuals; it is asymptomatic in about 80%–90% of individuals in whom viral reactivation and shedding occur undetected [1]. Hence, HSV-2 transmissions can remain sustainable in the general public and the prevalence rates can reach very high levels if interventions to curb the infection

are not taken.

There is a direct relationship between HSV-2 and HIV prevalence, and both viruses have reciprocal biological interactions [2]. Due to ulcerative lesions caused by HSV-2 progression, it has been associated with the risk of HIV acquisition and HIV transmission. Furthermore, in HIV-positive patients, infection with HSV-2 accelerates replication and genital shedding of the virus; thus, such individuals are more likely to transmit HIV [3]. In fact, HSV-2 is the primary cause of genital ulcers, among potentials co-factor of HIV herpes viruses are commonly mentioned because they are ubiquitous and contagious. It has been

reported that, among HIV positive patient's co-infection with HSV-2 stands at 30%–70% in Europe and 50%–90% was recorded for Africa [4].

HSV-2 and HIV are two lifelong viral sexually transmitted infections (STIs) of global health importance. HSV-2 and HIV co-infection among pregnant women may increase the risk of perinatal transmission of HIV [3]. Genital lesions due to herpes are often very painful, and can lead to substantial psychological morbidity, the virus can also be passed from mother to child during birth which can be very serious, without treatment 80% of infants with disseminated disease die and those who do survive often have brain damage. Herpes simplex virus and HIV may also adversely affect the outcome of pregnancy, leading to spontaneous Abortion, premature delivery and low birth weight infants [5]. Co-infection with HSV-2 and HIV among pregnant women may increase the risk of maternal-to-fetal transmission of HIV by as much as 25% [6].

Herpes simplex type-2 virus infection in pregnancy often manifests clinically in a manner similar to that in a non-pregnant female and are commonly asymptomatic except in few cases of disseminated disease [7]. Genital herpes among pregnant women is associated with definite risk for neonatal meningoencephalitis [8]. And mortality from neonatal herpes is well above 50% even in developed countries [1]. Regardless of antiviral therapy, neonatal meningoencephalitis kills about 50% of affected babies and leaves the survivors with permanent neurological deficit, while disseminated neonatal disease kills nearly 90% of the infected infants [8]. Early detection and treatment of HSV-2 during pregnancy are invaluable in limiting the risk of vertical transmission of HSV-2 to the fetus/newborn as well as disseminated maternal disease. For women with primary HSV-2 presenting with genital ulceration at the time of labor, the risk of transmission can be reduced via cesarean section [1]. Furthermore, pregnant women infected with genital herpes can transmit the virus to the foetus, which can lead to serious neonatal complications, such as neurologic problems, brain damage and even death [9]. Study in the United States of America (USA) shows that four of nine infants born to women who acquired genital herpes shortly before labour developed neonatal infection of which one died [10]. While some studies report poor outcome in reduction of HIV acquisition and transmission via the use of antivirals for treatment of HSV-2, it has been suggested that high-dose antivirals may reduce HIV viral load in HSV-2/HIV co-infected patients [11]. However, it is clear that strategies to curb the HIV pandemic via the intervention measures for HSV infection control continue to be evaluated. HSV infection is said to be a significant factor because it increases the risk of the acquisition and transmission of HIV, in pregnant women it enhances the mother to child transmission (MTCT) of HIV. The reciprocal enhancement of HSV and HIV viral replication in the presence of concurrent infection has also been described by several researchers [12]. This study aims to determine the seroprevalence of HSV-2 and HIV co-infection among pregnant women in Jigawa state and identify

the risk factors involved in the progression of the infection. To the best of our knowledge this is the first report of HSV-2 seroprevalence and HIV co-infection in Jigawa State of Nigeria. It is hope that the study will serve as a highlight for policy makers to take informed decision on HSV-2 and HIV management strategies.

2. Materials and Methods

2.1. Study Area

The study was conducted in four Hospitals of the three senatorial districts of Jigawa State. Jigawa is located in North West geographical zone between Latitudes 11°E13°N and Longitudes 8°E13°E. The samples were collected from Rasheed Shekoni Teaching Hospital, Dutse General Hospital, Gumel General Hospital and Hadejia General Hospital, Jigawa, the four hospitals have high rate of client load and they are general government hospitals also a referral center.

2.2. Study Population

The study population comprises of 300 pregnant women selected at random from each hospital in the geopolitical zones. The participant used were enlisted after they granted their full consent to participate in the study.

2.3. Inclusion Criteria

Only pregnant women attending antenatal clinics in General Hospital Gumel, General Hospital Hadejia, Dutse General Hospital and Rasheed Shekoni Specialist Hospital Dutse, Jigawa State, Nigeria who agreed to participate in the study were included.

2.3.1. Exclusion Criteria

All pregnant women attending antenatal clinics in the three hospitals that declined to give consent for inclusion were excluded from the study.

2.3.2. Informed Consent

Informed written consent was obtained from all the experimental population before inclusion using approved protocol.

2.4. Ethical Clearance

Ethical clearance for the study was obtained from Ministry of Health Dutse, Jigawa state. Before conducting the study.

2.5. Sample Collection and Sample Size

Samples were collected from Rasheed Shekoni Teaching Hospital, Dutse General Hospital, Gumel General Hospital and Hadejia General Hospital, of Jigawa State. The four hospitals have high rate of client load and they are all public hospitals and each among them serve as referral center.

A random sampling technique was used to obtain the study sample size in which all pregnant women that suit the set inclusion criteria were recruited for the study. The sample

size was determined using Reed-Frost model $N = \frac{z^2 P q}{d^2}$ as reported previously by [13].

2.5.1. Data and Blood Sample Collection

A structured closed ended questionnaire designed for the study was used to obtain data on demographic and social status of the participants. Venous blood (5ml) was drawn aseptically by venipuncture into vacutainer tubes. Separation of the serum was performed by centrifugation of the blood samples at 1,600 revolutions per minutes (rpm) for 5 minutes using bench top centrifuge. Serum samples were collected into freshly labelled Cyro tubes and stored at 4°C in a cool box with ices blocks and transported to the Microbiology Laboratory, FUD for ELISA analysis.

2.5.2. Sample Analysis

All samples were screened using qualitative sandwich third- generation Diapro HSV-2 specific enzyme-linked immunosorbent assay (ELISA) kit that is type specific IgG against the glycoprotein G of HSV-2 (DIAPRO Diagnostic Bio probes, Milano, Italy). The samples were screened for HIV antibody according WHO standard procedure of using rapid immunoassay kit (Alere Determine® HIV1&2 Chiba, Japan); thereafter, all positive samples were retested with another immunoassay kit (Trinity Biotech Uni-Gold™ HIV,

Wicklow, Ireland) and Stat pack kits according to manufacturer's guideline.

2.6. Statistical Analysis

Statistical analyses were observed using SPSS version 20 (IBM, USA). Pearson's Chi square test was performed at 95% confidence interval, and all statistical significance were established at $p < 0.05$.

3. Result

A total of 300 pregnant women were recruited in this study. Tables 1 and 2 showed the prevalence of HSV-2 co-infections and non-co-infections with HIV among respondent. The analysis indicated that a total number of 16 (5.3%) were under co-infections of HIV and HSV-2 while the remaining 284 (94.7%) of the respondents were under non-co-infections of HIV and HSV-2. Risk factors associated with HSV-2 infection were also studied, and the result is given in Table 3. Table 4: showed significantly ($P < 0.05$) higher percentage of HSV-2 infection among pregnant women reactive for HIV infection. (36.4%) of HIV positive pregnant women are also reactive for HSV-2 infection but with just (15.2%) of HIV non-reactive pregnant women being HSV-2 cases.

Table 1. Seroprevalence of HSV-2 and HIV Co-Infection disaggregated by demographic characteristics.

Variable	Frequency (%)	Frequency (%)	χ^2	(p Value)
Co-Infection (n=16)		Non-Co-Infection (n=284)		
Age Group			1.181	(0.404)
15 – 24	5 (31.3%)	117 (41.2%)		
25 – 34	8 (50.0%)	141 (49.6%)		
35 – 44	3 (18.7%)	26 (9.2%)		
Educational Status			4.586	(0.204)
Non formal	10 (62.5%)	119 (41.9%)		
Primary	3 (18.8%)	111 (39.1%)		
Secondary	3 (18.8%)	36 (12.7%)		
Tertiary	0 (0.0%)	18 (6.3%)		
Trimester			1.043	(0.593)
First	0 (0.0%)	11 (3.9%)		
Second	14 (87.5%)	222 (78.1%)		
Third	2 (12.5%)	51 (18.0%)		
Parity			0.773	(0.942)
None	1 (6.3%)	7 (2.5%)		
One	2 (12.5%)	47 (16.5%)		
Two	7 (43.7%)	147 (51.8%)		
Three	3 (18.8%)	39 (13.7%)		
Four	2 (12.5%)	34 (11.9%)		
Five	1 (6.3%)	10 (3.5%)		
Occupation			1.608	(0.657)
Civil servant	0 (0.0%)	17 (6.0%)		
House wives	11 (68.7%)	167 (58.8%)		
Trader	4 (25.0%)	67 (25.6%)		
Others	1 (6.3%)	33 (11.6%)		
Type of Marriage			0.267	(0.605)
Monogamy	11 (68.7%)	177 (62.3%)		
Polygamy	5 (31.3%)	107 (37.7%)		

Table 2. Seroprevalence of HIV among pregnant women in some selected hospital Jigawa State, with respect to some demographic variables.

Variable	Frequency (%)	Frequency (%)	X ²	(P Value)
No. Examined		No. Positive		
History of blood transfusion		13 (29.5%)	2.633	(0.105)
Yes	57 (19.0%)	31 (70.5%)		
No	243 (81.0%)			
Syphilis			5.762	(0.016) *
Reactive	101 (33.7%)	23 (52.3%)		
Non-Reactive	199 (66.3%)	21 (47.7%)		
Knowledge on HSV-2				
Yes	2 (0.7%)	6 (13.6%)	8.416	(0.000) *
No	298 (99.3%)	38 (86.4%)		

KEY: * indicate level of significant of $p < 0.05$.**Table 3.** Risk Factors for Herpes Simplex Type 2 Virus and Human Immunodeficiency Virus Co-Infection in Respondents.

Risk Factors	Co-Infection (N=16)	Non-Infection (N=284)	χ^2 (p Value)
	Frequency (%)	Frequency (%)	
History of STIs			7.868 (0.005) *
YES	11 (68.8%)	97 (34.2%)	
NO	5 (31.2%)	187 (65.8%)	
Syphilis			12.930 (0.000) *
REACTIVE	12 (75.0%)	89 (31.3%)	
NON-REACTIVE	4 (25.0%)	195 (68.7%)	
Infected Partner			9.419 (0.009) *
YES	2 (12.5%)	8 (2.8%)	
NO	0 (0%)	79 (27.8%)	
DON'T KNOW	14 (87.5%)	197 (69%)	

KEY: * indicate level of significant of $p < 0.05$.**Table 4.** Frequency of infections with HSV-2 in pregnant women positive with HIV.

HIV		HSV-2		Total	p Value
		Reactive	Non-Reactive		
Reactive	Count	16	28	44	0.001
	% within HIV	36.4%	63.6%	100.0%	
Non-Reactive	Count	39	217	256	100.0%
	% within HIV	15.2%	84.8%	100.0%	
Total	Count	55	245	300	

C. I.=1.58-6.42, O. R.=3.18, $\chi^2=11.196$.Key: - C. I.=Confidence interval, O. R.=Odds Ratio, $P < 0.05$ is taken for significant disease co-infection.

3. Discussion

Genital herpes is one of the most common sexually transmitted infections among women of reproductive age; it can be contracted and transmitted to the fetus during pregnancy and the new born. Herpes simplex virus infection is a global public health problem; it can cause significant distress and have devastating impact on the social and psychological wellness of an individual [14]. Pregnant women with genital herpes caused by HSV-2 can transmit the virus to their neonate at birth, the greatest risk of transmission to the fetus and newborn occurs in cases of initial maternal infection contracted in the second half of pregnancy, which is a potential cause of neonatal mortality and morbidity [15].

The overall seroprevalence of 18.3% HSV-2 infection was

recorded in this study which is lower than the 35.5% reported in a similar study among pregnant women attending F. M. C., Keffi, Nigeria by [16] and 33.3% among pregnant women in Ibadan in Nigeria [17]. But agrees with 7.5% and 21% reported among pregnant women in India and USA, respectively [18].

HIV Seroprevalence rate of 14.7% was recorded in this study, this is relatively high when compare to 2.4% rate found among pregnant women in Lokoja, North central reported by [19].

The percentage of respondents who were co-infected with HSV-2 and HIV was found to be 5.3% which is related to the co-infection rate of 2.8% and 2.4% reported by [12, 19] respectively; but lower than that of [16, 20]. The co-infection rate of 5.3% obtained from this study is quite low when compared with 38.8% found among pregnant women in Ibadan, Nigeria [17] and 44.6% reported by [21] among

patent attending sexually transmitted infections clinics in Ibadan. The relatively low prevalence of HSV-2 and HIV co-infection in this study can be attributed to the differences in the study population between previous studies and this present one, while their study population was among commercial sex workers and STI clinic attendees. Co-infection occurs most in those between 15-34yrs with (81.3%), while those in 35-45yrs (18.7%). Similar observations were reported by earlier works those young middle-aged subjects are more sexually active which makes them more vulnerable [8]. Co-infection is high among women without any formal education (62.5%) and least among women with primary and secondary education (18.8%), which could result from lack of enlightenment and awareness of the disease. It was observed that there is no association between parity and co-infection among respondents with ($p=0.918$ and $\chi^2=1.453$).

With reference to occupation house wives recorded highest prevalence of (68.8%), follow by Traders (25%), others (6.2%) and no record of it was found among civil servants, it could be due to lack of awareness of the disease. This however does not indicate a statistically significant with $P>0.05$. There was no significant association between stage of pregnancy and co-infection ($p=0.593$ and $\chi^2=1.042$), the prevalence was high among pregnant women in their second trimester (87.5%) and least among pregnant women in third trimester (12.5%), no record of co-infection was found among respondent in their first trimester, this report is in consonance with 47% and 65.2% findings of [16, 20] respectively.

History of blood transfusion among respondent was not found to be associated with the co-infection ($p=0.529$ and $\chi^2=0.395$), the viral co-infection was high among those who had no history of blood transfusion (75%) than those with history of blood transfusion (25%). Knowledge of HSV-2 has statistically significant with ($p=0.005$ and $\chi^2=7.956$), the co-infection was high among women who had no knowledge of the viral infection with (93.7%) than those with the knowledge (6.3%), which is similar to report by [22]. This may result from lack of awareness of the diseases.

With reference to history of STIs, women with history of STIs recorded high prevalence (68.8%) than those without history (31.2%). However, there is statistical significance of ($p=0.005$ and $\chi^2=7.868$), which agrees with previous studies of [16, 23]. Co-infection rate with Syphilis was found to be high with (75%) as compared to those that are non-reactive (25%). The relation between Syphilis and co-infection rate was significant with ($p=0.000$ and $\chi^2=12.930$). This agrees with findings of [24] that Genital ulcers from HSV-2 and Syphilis are associated with HIV acquisition.

In this study, it was observed that most of the respondent with HIV infection also had HSV-2, 36.4% of HIV positive pregnant women are also positive for HSV-2 infection while just 15.2% of HIV negative respondents are positive for HSV-2, it was statistically significant with $p=0.001$. The odds ratio of being at risk of contracting HSV-2 infection was 3.2 times higher for HIV positive pregnant women than

those that are HIV negative. This is similar with the findings of [19, 25]. that the presence of HSV-2 infection plays a critical role in the acquisition of the HIV infection. The mutual re-enforcement of transmission efficiency exhibited by HIV and HSV-2 infection could be contributory to high prevalence level of HSV-2 in some part of Nigeria, the increase shedding of HIV through genital herpes lesions and the fact that individual with HSV-2 remain potentially infection make important contribution to HIV transmission in African. [1].

This study adds to the scarce information available concerning HSV-2 and HIV Co-infection rates among the pregnant population. However, it is limited to a sample of pregnant women attending the four selected hospitals in the three Senatorial districts in Jigawa State which is not representative of all pregnant women in Nigeria.

4. Conclusion

In this research, association between HSV-2 and HIV co-infection was studied among pregnant women. The rate of HSV-2 and HIV co-infection among the pregnant women in Jigawa State was found to be 16 (5.3%), the factors that were found to be significantly associated with the occurrence were history of STIs, knowledge on HSV-2 infection and HIV status. Respondent with HSV-2 were 55 (18.3%) and HIV were 44 (14.7%). Hence it is necessary to routinely screen pregnant women for the possibility of HSV-2 infection to decrease neonatal herpes also control measures for HSV-2 and HIV infection is a logical approach as the synergistic effect of both viruses implies that the control of HSV-2 can be effective method of HIV prevention, thus bringing down the HIV pandemic to a low-level endemicity. These findings therefore indicate that health education, personal hygiene and screening interventions are highly required in an effort to prevent transmission to offspring which will help in reducing the risk of the infection among pregnant women in the area.

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