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Original Research Article

Sexual behavioural correlates of herpes simplex virus type 2 infections among pregnant women in South-western Nigeria

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ABSTRACT

Background: Herpes simplex virus type 2 (HSV-2) is the most common cause of genital ulcer disease. It leads to lifelong latent infection and this raises concerns among women of reproductive age, considering the risk of neonatal transmission. This study was undertaken to identify the sexual behavioural correlates of HSV-2 infection as well as negative pregnancy outcomes.
Methods: The cross-sectional study was conducted between March and August 2013, in the antenatal clinic of the University College Hospital Ibadan. A total of 270 pregnant women aged 20 to 44 years were enrolled and their serum samples were tested for HSV-2 IgG using type specific third generation ELISA (DIAPRO Milano Italy). Pretested validated questionnaire were used to obtain bio-data, sexual behaviour and obstetrics history of the participants. Data analyses was done using SPSS version 20.
Results: The seroprevalence of HSV-2 type specific IgG was 33.3% (90/270). Logistic regression analysis showed that multiple lifetime sexual partners, early age at sexual debut, previous history of sexually transmitted infections (STIs) and having spouses whose work keep them away from home, were independent risk factors for HSV-2 infection. Obstetrics complications such as intrauterine foetal death, congenital malformations and spontaneous abortion were also strongly associated.
Conclusions: The predictors of HSV-2 infection in this study may be important in selecting candidates for screening tests and developing strategies towards effective health promotion campaign.

Keywords: HSV-2**,** Pregnant women, Sexual risk behaviour, Vertical transmission

INTRODUCTION

Herpes simplex virus type 2 (HSV 2) is the primary cause of genital herpes, the most common sexually transmitted disease in the world and the commonest cause of genital ulcer disease.[1-3] The occurrence of genital herpes among pregnant women is associated with several complications particularly the transmission of the virus to their newborn.[4-7] Compared with recurrent HSV-2 infection, the risk of transmission from mother to newborn can increase 10-fold in maternal primary infection in pregnancy, particularly the third trimester.[2,5]

The maternal disease is associated with definite risks for neonatal meningoencephalitis or disseminated herpes.[1,2] Studies have shown that about one fourth of HSV-infected neonates develop disseminated disease and one third have meningoencephalitis.[5,8-10] Even with antiviral therapy, neonatal meningoencephalitis kills about 50% of affected babies and leaves the survivors with permanent

neurological deficit, while disseminated neonatal disease kills close to 90% of the infected infants.[1,2,5]

Genital herpes in pregnancy is also associated with obstetric complications like intrauterine growth retardation, intrauterine death, prematurity and spontaneous abortion.[11] It can also lead to a fatal disseminated herpes in the mother and congenital anomalies in the newborn.[11,12]

For effective interventions to prevent vertical transmission of HSV-2 infection, there is need to identify women at risk for the infection, prevent the sero-negative pregnant women from getting infected, reduce viral shedding and complications among the infected pregnant women.[13] HSV-2 type-specific screening of all pregnant women has been adopted by several countries with resultant reduction in prevalence rates.[14-16] However, in resource poor countries where routine screening of all pregnant women cannot be achieved, targeted screening of those at risk for infection has been advocated.[17-19] Thus understanding the factors associated with genital herpes particularly the sexual risk behaviours and negative pregnancy outcomes is warranted. This study was undertaken to identify the sexual behavioural correlates as well as negative pregnancy outcomes associated with HSV 2 infection.

METHODS

Study design

This was cross-sectional; hospital based and was conducted in the antenatal clinic at the University College Hospital over a 9 months period from March to August 2013. Blood samples of consenting pregnant women were collected and tested for HSV-2 IgG antibodies. Pretested structured questionnaires were filled by trained personnel during interview with consenting women. The questionnaire included information on the socio-demographic features, sexual practices and behavior, history of STIs and other potential risk factors for HSV-2 infections.

Study area and population

The participants were pregnant women attending antenatal clinic in the University College Hospital, a tertiary health institution located in Southwestern Nigeria. The sample size was calculated based on HSV 2 seroprevalence of 22% found among pregnant women in Senegal, in Sub-Saharan Africa, to give a 95% confidence level and margin of error of ±5%.[20] We assessed 308 pregnant women for eligibility and excluded those already diagnosed with HSV-2 infection. Of the 280 found eligible, 270 consenting pregnant women with ages ranging between 22 and 44 years were recruited. The main reason for non-participation was lack of time (no=10). A written informed consent was obtained following explanation of the concept of the study to each pregnant woman before their inclusion in the study.

Laboratory investigations

All samples were screened, using qualitative sandwich third generation enzyme linked immunosorbent assay (ELISA) that is type-specific IgG against the Glycoprotein-G of HSV-2(DIAPRO Diagnostic Bioprobes Milano Italy).

Data analysis

Standard descriptive and inferential statistical analysis was carried out using SPSS version 20. (SPSS Inc. Illinios, USA). The Mean, standard deviation and test of comparison using student's t-test was derived for continuous variables, while categorical variables were summarized as proportions, and further analyzed using Chi square and Fisher's exact test to assess association between the variables. Multivariable logistic regression models were developed. All factors for which association reached statistical significance at $p<0.05$ were included in the multivariate model. The final multivariate logistic regression model was reached by excluding factors 1 at a time until all remaining factors were significant at the $p<0.05$ level.

RESULTS

The sample comprised 270 pregnant women with a mean age of 32.3 (SD4.8) years. Majority of the women, 254 (94.1%) were in a monogamous relationship, 198 (73.3%) had tertiary-level education while 12 (4.4%) had only primary-level education. Multiparous respondents constituted the majority with 178 (65.9%) of the participants and 23 (8.5%) were grandmultiparous (parity greater than 5times). More than half of these women 164 (60.7%) were in their second trimester and 57 (21.1%) presented to the antenatal clinic in their third trimester (Table 1).

Prevalence of HSV-2 infection

We found the prevalence of HSV-2 infection to be 90/270 (33.3%). The distribution according to pregnancy trimester was 18.9%, 62.2% and 18.9% in the 1st, 2nd and 3rd trimesters respectively. The mean age of pregnant women found positive for anti HSV-2 antibody was 32.8 (SD5.1) years as compared with 32.0 (SD4.6) years among the sero-negative respondents in the study, student t test showed no statistically significant difference between the mean age ($p=0.174$).

Risk factors for HSV-2 infection among the participants

Among the respondents, HSV-2 infection was significantly associated with early age at first sexual intercourse, multiple sexual partners and lifetime sexual partners, polygamy, past history of other sexually

transmitted infections (STIs) and having spouses whose work keep them away from home (Table 2).

Based on logistic regression analysis, predictors of HSV-2 infection include multiple lifetime sexual partners, early age at sexual debut, previous history of STIs and having spouses whose work keep them away from home. Obstetric complications such as spontaneous abortion, intrauterine fetal death and congenital malformations were also strongly associated (Table 3).

Table 1: Socio-demographic characteristic of the pregnant women.

Variable	Frequency	Percentage (%)
Age group (years)		
22-28	56	20.7
29-35	151	55.9
≥ 35	63	23.3
Type of family		
Monogamous	254	94.1
Polygamous	16	5.9
Level of education		
Primary	12	4.4
Secondary	60	22.2
Tertiary	198	73.3
Marital status		
Married	255	94.4
Single	15	5.6
Employment status		
Employed (government/private)	104	38.5
Self employed	109	40.4
Unemployed	57	21.1
Religion		
Christian	209	77.4
Islam	61	22.6
Gestational age		
1st trimester	49	18.1
2nd trimester	164	60.7
3rd trimester	57	21.1
Parity		
Primiparous	69	25.6
Multiparous	178	65.9
Grandmultiparous	23	8.5

Table 2: Sexual risk factors associated with HSV-2 infection among pregnant women.

Variable	HSV-2 IgG		X^2	P value
	Positive N (%)	Negative N (%)		
Type of family				
Monogamous	80 (88.9)	174 (96.7)	6.511	0.011*
Polygamous	10 (11.1)	6 (3.3)		
Husband's work keeps him away from home				
Yes	72 (80)	123 (68.3)	4.071	0.029*
No	18 (20)	57 (31.7)		
Contact with persons with genital ulcer				
Yes	3 (3.3)	8 (4.4)	0.190	0.471
No	87 (96.7)	172 (95.6)		
Current sex partners				
One	70 (77.8)	167 (92.8)	12.583	<0.001*
More than one	20 (33.3)	13 (7.2)		
Lifetime sex partners				
One	38 (42.2)	128 (71.1)	21.145	<0.001*
More than one	52 (57.8)	52 (28.9)		

Continued.

Variable	HSV-2 IgG		X^2	P value
	Positive N (%)	Negative N (%)		
Age at first sexual exposure				
<15 years	5 (5.6)	1 (0.5)	19.316	<0.001*
16-20 years	28 (31.1)	33 (18.3)		
21-25 years	37 (41.1)	80 (44.4)		
26-30 years	11 (12.2)	53 (29.4)		
>30 years	9 (10.0)	13 (7.2)		
Condom use				
Yes	38 (42.2)	86 (47.8)	0.746	0.232
No	52 (57.8)	94 (52.2)		
Past STI[1]				
Yes	31 (34.4)	22 (12.2)	18.781	<0.001*
No	59 (65.6)	158 (87.8)		

*Significant at 5% level of significance.[1]Sexually Transmitted infection.

Table 3: Logistic regression analysis of sexual risk behaviours and obstetrics complications associated with HSV-2 infection.

Variable	P-value	Odd's ratio	95% CI
Type of family			
Monogamous (Ref)		1.000	
Polygamous	0.041*	4.277	1.060-17.253
Past STI[1]			
Yes	0.008*	2.503	1.268-4.940
No (Ref)		1.000	
Life time sexual partners			
One (Ref)		1.000	1.350-4.259
More than one	0.003*	2.398	
Husband's work keeps him away from home			
Yes	0.035*	2.113	1.055-4.232
No (Ref)		1.000	
Age at sexual debut (years)			
<15		1.000	
16-20	0.180	5.247	0.465-59.155
21-25	0.857	0.909	0.320-2.579
26-30	0.048*	0.563	0.212-0.934
>30	0.027*	0.285	0.094-0.865
History of IUFD[2]			
Yes	0.013*	2.663	1.231-5.758
No(Ref)		1.000	
History of congenital malformation			
Yes	0.035*	10.281	1.184-89.243
No		1.000	
History of spontaneous abortion			
Yes	0.003*	2.570	1.378-4.791
No (Ref)		1.000	

*Significant at 5% level of significance. Ref – Reference Group; STI[1]- Sexually Transmitted Infection; IUFD[2]- Intra Uterine Foetal Death

DISCUSSION

In this cross sectional study, the sero-prevalence of HSV-2 infection was 33.3%. When compared with the prevalence rates ranging from 30% to 80% among women in Sub-Saharan African countries, the sero-prevalence rate of 33.3% in this pregnant population places it on the lower part of the scale.[21] However, this suggests that a higher percentage of our pregnant population is currently sero-negative and susceptible to primary HSV-2 infection which if acquired during pregnancy may lead to severe neonatal complications.

People with HSV-2 infection are often asymptomatic and periodically shed the virus.[5] They are the main sources of

spread of the infection, since they engage in sexual activities unaware of their HSV statuses.[2] Among the women positive for HSV-2 infection, about 89% were in a monogamous marriage, however, 80% had spouses whose occupation kept them away from home for several nights and they were twice more likely to have HSV-2 infection than women whose partners returned home every day. This suggests that their spouses are engaged in risky sexual behaviour such as unprotected sexual intercourse with multiple partners. Similar findings were reported in Tanzania by Yahaya et al, but differed from reports in some other countries.[3,11,22]

The inconsistent use of condom with their sexual partners prevailed (57.8%) among the HSV-2 sero-positive women and this was observed in similar studies on pregnant women.[7,21-24] This is of great concern as HSV-2 transmission can occur in long-standing monogamous relationships, and the virus may be transmitted to a susceptible partner after a long time of unprotected sexual contact with an asymptomatic but infected partner.[7] There is need for consistent use of condom as nearly everyone, with genital HSV-2 infection sheds virus intermittently without symptoms.[7] Sexually transmitted infections were also strongly associated with acquisition of HSV-2 infection and similar findings have been reported by some authors.[23,25-27]

The results of the index study re-emphasize the primary role of multiple sexual partners in the acquisition of HSV-2 infection. This is in agreement with other studies, which show that HSV-2 sero-positivity is associated with a greater number of lifetime sexual partners and multiple sexual partners within six months to the time of the study.[3,7,12,22-29] In the present study, women with more than one lifetime sexual partners were 2.4 times more likely to have HSV-2 infection than those with one lifetime sexual partner. This is similar to some other studies which observed that women with more than one lifetime sexual partners were twice as likely to have HSV-2 antibodies, than those with one partner.[23,30]

We observed that women who had their sexual debut before age 15 years of age were found more likely to acquire HSV-2 infection and this may be due to increased cumulative years of sexual activity.[31] Similar findings were reported in Sydney by Tiderman et al, in Turkey and Isreal by Duran et al and Dan et al respectively, in Tanzania by Watson-Jones et al, and in United Kingdom by Narouz et al.[23,25,26,32,33] A study done in India failed to demonstrate an increased risk of seropositivity with early age of first intercourse as observed by Rathore et al.[7] HSV-2 is an incurable disease that runs a chronic course, therefore, duration of sexual activities more accurately represent one's risk of exposure. These findings highlight the importance of measuring the duration of sexual risk behaviours and not solely their occurrence.

A higher percentage of the HSV-2 positive pregnant women (62.2%) were in their second trimester and were multiparous women (63.3%), this calls for concern. The circulating maternal HSV-2 IgG are able to cross the placenta to the foetus, preventing infection in the newborn.[4,5] However in the infected mother, the antibody response is not protective and reactivation takes place even in the presence of adequate antibody. The use of antivirals in pregnancy decreases reactivation of Herpes simplex virus infection, prevents neonatal herpes, and reduces the need for caesarean delivery.[4,5,8,31,34] Most guidelines propose caesarean section for women with primary HSV-2 infection within the last 4–6weeks of gestation, this is because they cannot complete their seroconversion prior to the time of delivery, and therefore they could infect their newborn.[4,5]

Analysis of some previous maternal obstetric complications in the respondents revealed that HSV-2 seropositivity was highly associated with history of previous spontaneous abortion, a finding in agreement to that reported in other studies.[11,25] Also strongly associated with HSV-2 infection were history of intrauterine foetal death and congenital malformation. Primary infection in the first trimester of pregnancy has been linked to an increase in spontaneous abortions, intrauterine foetal growth retardation and in rare cases, congenital malformations and intrauterine foetal death.[4,5] Women presenting with any of these bad obstetrics histories are candidates for HSV-2 screening.[11]

The factors found to be associated with a higher risk of HSV-2 infection in this study may be important in selecting candidates for screening tests. Two identified sexual risk behaviour for HSV-2 infection that could be important in mounting an effective health promotion campaign are the age of sexual debut, and the number of lifetime sexual partners.

CONCLUSION

The presence of risk factors for the acquisition of HSV-2 accounts for the regional prevalence heterogeneity and the observed high prevalence among certain populations. Until universal screening of all pregnant women is adopted, the factors found to be predictors of HSV-2 infection in this study may be important in selecting candidates for screening tests in prenatal clinics.

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