# Original Article

# Sexual behavioral correlates with HSV-2 seroprevalence among pregnant women in Nigeria

Eziyi I Kalu<sup>1</sup>, Chiedozie K Ojide<sup>2</sup>, Adeola Fowotade<sup>3</sup>, Victor U Nwadike<sup>4</sup>

#### **Abstract**

Introduction: The burden of HSV-2 infection, the cause of most cases of genital herpes in Nigeria, varies from region to region; and so are the associated factors. This infection is known to be responsible for several negative pregnancy outcomes. There is currently no documented data on sexual behavioral factors associated with the occurrence of HSV-2 infection or seroprevalence among pregnant women in Nigeria. This study aimed at identifying the sexual behavioral correlates of HSV-2 seroprevalence among pregnant women in Benin City, Nigeria. Methodology: The cross-sectional study design was adopted and the study took place between November 2011 and June 2012. Four hundred and ten consenting ante-natal clinic patients in two major tertiary hospitals in Benin City were consecutively and prospectively included. Data sources were represented by questionnaires, the patient's case records and laboratory investigations. Each patient's serum was analyzed for HSV-2 antibody detection. Data analysis was performed using SPSS version 16.

Results: Four hundred and ten patients were enrolled with average age 30.6 years. Seroprevalence of HSV-2 antibody was 47.3%. Sexual behavioral factors that were significantly associated with HSV-2 seroprevalence included early exposure to sexual intercourse, number of sex partners, involvement in polygamous marriages, involvement of husband in extra-marital affairs and hormonal contraceptive use.

Conclusion: The prevalence of HSV-2 among pregnant women in Benin City is high. Public health campaigns aimed at: delaying onset of sexual activity; encouraging monogamous relationships; and emphasizing that hormonal contraceptives do not protect from STI's, are recommended.

**Key words:** Herpes simplex Virus 2; seroprevalence; sexually transmitted infections; STI's risk factors; pregnancy.

J Infect Dev Ctries 2014; 8(8):1006-1012. doi:10.3855/jidc.4336

(Received 17 October 2013 – Accepted 16 December 2013)

Copyright © 2014 Kalu *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## Introduction

Genital herpes, an infection commonly caused by human herpes simplex virus 2 (HSV-2) in Nigeria and in most regions of the world, has been described as a silent pandemic with different countries being at different stages of the epidemic [1,2]. Humans are the only natural host [3]. The fact that transmission through viral shedding continues, also in the frequent asymptomatic cases, has sustained the worsening of the pandemic [4]. The HSV-2 pandemic is further reinforced by the HIV pandemic and vice versa; and it is becoming clear that the efforts at controlling the spread of HIV may remain ineffective if control of HSV-2 infection, along with other sexually transmitted infections (STI) is not integrated [4,5]. Furthermore, HSV-2 infection has been reported to produce a wide range of deleterious obstetric effects, ranging from

neonatal herpes, neonatal death, neuronal deficits, mental handicap, congenital malformations, intrauterine fetal death, preterm labour, low birth weight babies, and spontaneous abortions [6,7].

Since the HSV-2 infection is life-long and has no known cure, primary prevention remains the mainstay of its control. Hence it is important to understand the factors that are associated with the occurrence of infection [8]. There is yet no documented behavioural correlate of this infection or seroprevalence in Nigeria. This study is aimed at determining the behavioral correlates of HSV-2 seroprevalence among pregnant women in Benin, Nigeria.

<sup>&</sup>lt;sup>1</sup> Department of Medical Microbiology, Federal Medical Centre, Umuahia, Abia State, Nigeria

<sup>&</sup>lt;sup>2</sup> Department of Medical Microbiology and Parasitology, University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State, Nigeria

<sup>&</sup>lt;sup>3</sup> Department of Medical Microbiology and Parasitology, University College Hospital, Ibadan, Nigeria

<sup>&</sup>lt;sup>4</sup> Department of Medical Microbiology, Federal Medical Centre, Abeokuta, Ogun State, Nigeria

# Methodology

Study location, design and duration

Participants were ante-natal clinic patients of the two major tertiary hospitals in Benin City, Nigeria: University of Benin Teaching Hospital and Central Hospital, Benin-City. The cross-sectional study took place between November 2011 and June 2012. Participants were consecutively and prospectively recruited.

#### Ethical issues

Informed written consents were sought and consecutively consenting pregnant women were recruited into the study. The study obtained ethical approval (ADM/E22/A/VOL.VII/740) from the Ethical committee of the University of Benin Teaching Hospital.

## Inclusion and exclusion criteria

Consenting pregnant women attending antenatal clinic in both University of Benin Hospital and Central Hospital between November 2011 and June 2012 were included in the study. Exclusion criteria were absence of pregnancy and failure to sign the consent form. No clinical diagnostic criteria were used in the study.

## Data collection

Sources of data were represented by questionnaires, hospital records, and laboratory investigations. Blood samples were obtained from participants and the serum was separated and used for the HSV-2 IgG antibody assay. A structured questionnaire was used to collect data on specific participants' sociodemographic and behavioural profiles.

# Laboratory procedures

Blood samples were collected in 5 ml plain vacutainer tubes and allowed to clot and sera separated by centrifugation at room temperature. Samples were stored in cryovials at -20°C. The HSV-2 IgG assay procedure was utilized the enzyme-linked immunosorbent assay (ELISA) kit (Dia. Pro. Diagnostic Bioprobes srl, Milano, Italy). This is a glycoprotein G-based type-specific ELISA technique and test result was qualitative. All specimens and kit reagents were brought to room temperature and gently mixed. Procedures were performed in accordance with manufacturer's instructions. Quality control and test validation was included into the test protocols.

# Data analysis

Collected data was analyzed using the SPSS version 16.0 software. Chi Square was used to test associations. Statistical significance was ascribed based on p values < 0.05.

# Results

Patients general and obstetric characteristics

The mean age of the 410 pregnant women studied was  $30.6 \pm 5.2$  years (range, 18 - 44 years). The majority of them (96.6%) were in the 21-40 years age bracket. Most of the participants (85.1%) were married and belonged to the Christian faith (81.7%) as shown in Table 1. A total of 382 (93.4%) of the study population completed at least secondary education, while the remaining 16.4% either did not have secondary education at all or had an incomplete secondary education (Table 1).

Most of the respondents (43.4%) were nulliparous, 28.3% primiparous; while a total of 27.5% of them were multiparous. Only two (0.7%) of the participants were grand-multiparae (Table 2). Regarding the gestational age at which participants were recruited into the study, 45.3%, 39.8% and 14.6% of the women were at the third, second and first trimesters respectively as shown in Table 2.

Of the 410 pregnant women studied 194 tested positive for HSV-2 antibody giving a prevalence rate of 47.3% (Table 3). The socio-demographic characteristics of the seropositive women were essentially similar to those of the study population. Their ages ranged from 16-45 years with a mean of  $32.4 \pm 4.9$  years. The majority of seropositive patients (184/194; 94.8%) fell into the 21-40 years age bracket, were married (161/194; 83.0%) and of Christian faith (164/194; 84.5%). Also 94.8% (184/194) of seropositive women had completed at least secondary education. Their obstetric characteristics are also similar to that of the study population with the majority comprising of nulliparous women (95/194; 49.0%) and women in their third trimester (91/194; 46.9%).

# Seroprevalence and behavioral characteristics

The majority of participants, 371 (90.5%), had only one sexual partner during the previous 12 months. The prevalence of HSV-2 was lowest in this group (45.8%) when compared to those with two or three recent partners (59.4% and 71.4% respectively).

Table 1. General characteristics of respondents

Characteristics	Frequency	Percentage %
Age group (years)		
15-20	4	1.0
21-25	62	15.1
26-30	146	35.6
31-35	135	32.9
36-40	53	12.9
41-45	10	2.4
Religion		
Christianity	335	81.7
Islam	75	18.3
Marital status		
Married	349	85.1
Single	32	7.8
Divorced	13	3.2
Widowed	16	3.9
Level of Education		
Graduate & Above	129	31.5
Post secondary	175	42.7
Secondary completed	78	19.2
Secondary uncompleted	9	2.2
Primary completed	17	4.1
Primary uncompleted	2	0.5

Table 2. Obstetric characteristics of respondents

Obstetric characteristics	Frequency	0/0
Trimester		
1 <sup>st</sup> Trimester	60	14.6
2 <sup>nd</sup> Trimester	163	39.8
3 <sup>rd</sup> Trimester	187	45.3
Parity		
Nullipara	178	43.4
Primipara	116	28.3
Para-2	74	18.0
Para-3	27	6.6
Para-4	12	2.9
Para-5 or more	3	0.7

Table 3. Seroprevalence of HSV<sub>2</sub>-antibody among participants

Participants	Frequency (%)
HSV <sub>2</sub> -Ab Positive	194 (47.3)
HSV <sub>2</sub> -Ab Negative	216 (52.7)
Total	410 (100.0)

The observed association between number of sex partners in the previous 12 months and the prevalence of HSV-2 was statistically significant (p = 0.023) (Table 4). Table 4 also shows an increase in prevalence of HSV-2 correlated to the number of lifetime sex partners from 33.2% in participants with only one lifetime sex partner to 90.1% in those with five. This observed trend was also statistically significant (p = 0.031).

Prevalence of HSV-2 decreased as the age of first sexual exposure increased. This association was also found to be statistically significant (p = 0.043) (Table 4). No particular trend in prevalence was followed regarding the total number of years of sexual exposure.

Only a small proportion of the participants reported involvement in polygamous marriages and the involvement of their husbands in extramarital affairs: 25/410 (6.1%) and 64/410 (15.6%)

respectively. Nevertheless, there were statistically significant increases in prevalence of HSV-2 among these categories of participants (Table 4). Although there was an increased HSV-2 prevalence (55%) among participants that practiced sex under the influence of alcohol compared to their counterpart who did not (46.5%), there was no statistical significance (p = 0.072). On the contrary, use of hormonal contraceptives for at least more than one year in the past is associated with statistically significant increase in HSV-2 prevalence (p = 0.021) (Table 4).

## **Discussion**

We detected 47.3% HSV-2 seroprevalence rate but since there is no data in our country we could not compare this rate with other studies. This figure however seems close to the values found among high risk groups: 59% among commercial sex workers in

Table 4. Behavioural factors and HSV-2 infection

Behavioural Factor	Number tested	HSV-2 Ab Positive (%)	$\chi^2$	P-value
Number of sexual partners in the	past one year			
1	371	170 (45.8)		
2	32	19 (59.4)	5.69	0.023
3	7	5 (71.4)		
Number of life time sex partners				
1	199	66 (33.2)		
2	113	37 (37.6)		
3	60	45 (75.0)	4.57	0.031
4	27	23 (85.2)		
5	11	10 (90.1)		
Age at first sexual exposure (year	rs)			
≤ 15	86	59 (68.6)		
16-20	163	98 (60.1)	2.96	0.043
21-25	151	35 (23.2)		
26-30	10	2 (20.0)		
Total number of years of sexual of	exposure (years)			
≤ 5	183	81 (44.3)		
6-10	106	49 (46.2)		
11-15	65	36 (55.4)	0.01	0.529
16-20	48	25 (52.1)		
>20	8	3 (37.5)		
Involvement in polygamous mari	riage			
Yes	25	20 (80.0)	11.8	0.001
No	385	174 (45.2)		
Husband's involvement in extran	narital affairs.			
Yes	64	39 (60.9)	10.3	0.001
No	346	155 (44.8)		
Sex under influence of alcohol				
Yes	40	22 (55.0)	3.64	0.072
No	370	172 (46.5)		
Use of hormonal contraceptives i	n the past (> 1 year)			
Yes	270	143 (53.0)	9.45	0.021
No	130	51 (39.2)		

Nigeria [9]; and 56.3% among hotel/bar workers in Tanzania [10]. Although this seroprevalence result falls within the range of 30%-80% found among women of reproductive age in sub-Saharan Africa [11], it is higher than HSV-2 seroprevalences found in several studies among populations of pregnant women in the sub-Saharan Africa region: 20.7% and 33.6% from different locations in Tanzania [12,13]; and 26% in Senegal [14].

This figure is still remarkably higher than findings from studies on pregnant populations outside Africa: 7.5% in India [15], 11.5% in Australia [16], 14.5% in Mexico [17], and 22% in USA [18]. The implication of this finding is that HSV-2 transmission in Benin, Nigeria is efficient; and it indicates that there could be underlying peculiar factors in the environment that enable the sustenance of such a high level of transmission efficiency.

Several sexual behavioral factors were observed, in this study, to be significantly contributory to the high HSV-2 prevalence, in keeping with the assertion that the presence of HSV-2 antibodies is a marker of indiscrete sexual behavior [28, 29]. It is therefore instructive that the following considerations should be included in individual case management and primary prevention strategies: more than one sex partner in the past 12 months; more than one lifetime sex partner; early sexual exposure; involvement in polygamous marriages; and use of hormonal contraceptives.

Early exposure to sexual intercourse has therefore been linked to increased risk of sexually transmitted infections (STIs) during adolescence [30, 31]. The increased STI risk is due, in part, to a biologic predisposition of the immature cervix to infection if exposed [32] and to the increased likelihood of engaging in riskier sexual behaviors among persons who initiate sexual intercourse at younger ages [31, 34]. Although, early sexual exposure as found in this study was significantly associated with HSV-2 seroprevalence, the total number of years of exposure was not significantly associated. This posits that the effect of early sexual exposure derives from the associated loose morals and inefficient parental control during adolescence. Primary preventive strategies, such as encouraging the use of condom, should address this gap in parenting.

In a previous report from Kenya [27], hormonal contraceptive use was found to reduce the risk of HSV-2 and HIV infection; this is contrary to our finding in this study where use of hormonal contraceptives was found to be significantly associated with higher prevalence of HSV-2. Our finding is

however in agreement with another study report from Kenya [35]. Misguided confidence in the protective role of hormonal contraceptives may explain the significantly increased prevalence of HSV-2 among hormonal contraceptive users in this study. There ought to be serious public enlightenment campaign about the limitations of contraceptive use.

Assessment of these sexual behavioral factors in individual case management could help in raising the index of suspicion of HSV-2 seroprevalence and are potentially useful screening criteria, if validated. These factors also ought to be taken into consideration while designing primary prevention strategies for STIs.

# Conclusion

The prevalence of HSV-2 among pregnant women in Benin City, Nigeria, is high. Number of sexual partners in the last 12 months, number of lifetime partners, early sexual exposure sexual involvement in polygamy are associated sexual behavioral factors. Primary prevention remains the most effective strategy to control HSV-2 infection and associated complications. Public health campaigns aimed at delaying onset of sexual activity and monogamous relationships encouraging recommended. Also there ought to be serious public enlightenment on the limitations of hormonal contraceptives use for protection against STIs.

# **Acknowledgements**

We wish to appreciate all the Staff of the Antenatal Clinics of both University of Benin Teaching Hospital and Central Hospital Benin City for their co-operation and support during the study.

## References

- Looker KJ, Garnett GP, Schmid GP (2008) An estimate of the global prevalence and incidence of herpes simplex virus type 2 infection. Bull World Health Organ; 86 (10): 737-816. Available from: Available: http://www.who.int/bulletin/volumes/86/10/07-046128/en/. Accessed December 2011.
- Oni AA, Adu FD, Ekweozor CC, Bakare RA (1996) Genital herpes simplex virus infection in females in Ibadan Nigeria. West Afr J Med 15: 107-110.
- Dordevic H (2006) Serological response to herpes simplex virus type 1 and 2 infection among women of reproductive age. Med Pregl 59: 591-597.
- 4. Corey L, Handsfield HH (2000) Genital Herpes and public health: addressing a global problem. JAMA 283: 791-794.
- Kolawole O M, Adu. FD, Agbede OO, Oni AA, Bakare RA (2008) Epidemiological Patterns of Human Immunodeficiency Virus and Herpes Simplex Virus Co-Infection in Ibadan, Nigeria. Afr J Biomed Res 11: 23-26.

- Torok E, Moran E, Cooke F (2009). Congenital infections. In: Oxford Handbook of Infectious Diseases and Microbiology. 1<sup>st</sup> edition. New York: Oxford University Press. 824 – 826.
- Centers for disease Control and Prevention (2013) National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of STD Prevention. Sexually transmitted diseases: Genital Herpes- CDC fact sheet. Available: http://www.cdc.gov/std/Herpes/STDFact-Herpes.htm. Accessed June 2013.
- 9. Dada AJ, Ajayi AO, Diamondstone L (1998) A sero-survey of *Haemophilis ducreyi*, Syphilis, and Herpes simplex virus type-2 and their association with HIV among sex workers in Lagos, Nigeria. Sex Transm Dis. 25: 237–242.
- Tassiopoulos KK, Seage G, Sam N, Kiwelu I, Shao J, Ao TTH, Essex M, Coplan P, Rosenberg Z, Hughes M, Kapiga S (2007) Predictors of Herpes Simplex Virus Type 2 Prevalence and Incidence among Bar and Hotel Workers in Moshi, Tanzania. J Infect Dis 195: 493-501.
- 11. Weiss H (2004) Epidemiology of herpes simplex virus 2 infection in the developing world. Herpes. 11: 24-34.
- 12. Yahya-Malima KI, Evien-Olsen B, Matee MI, Fylkenes K and Haans L (2008) HIV-1, HSV-2and syphilis among pregnant women in a rural area of Tanzania: prevalence and risk factors. BMC infect Dis 8: 75.
- 13. Msuya SE, Uriyo J, Hussain A, Mbizvo EM, Jeansson S, Sam NE, Stray-Pedersen B (2009) Prevalence of sexually transmitted infections among pregnant women with known HIV status in northern Tanzania. Reproductive Health 6: 4.
- Diawara S, Kane CT, Legoff J, Gaye AG, Mboup S (2008) Low seroprevalence of Herpes simplex virus type 2 among pregnant women in Senegal. International J of STD and AIDS 19: 159-160.
- Rathore S, Jamwal A, Gupta V (2010). Herpes simplex virus type 2: Seroprevalence in antenatal women. Indian J Sex Transm Dis 31: 11–15.
- Tideman RL, Taylor J, Marks C, Seifert C, Berry G, Trudinger B, Cunningham A, Mindel A (2001) Sexual and demographic risk factors for herpes simplex type 1 and 2 in women attending an antenatal clinic. Sex Transm Infect. 77: 413-415.
- Herrera-Ortiz A, Conde-Glez CJ, Vergara-Ortega DN, García-Cisneros S, Olamendi-Portugal L, and Sánchez-Alemán MA (2013) Avidity of Antibodies against HSV-2 and Risk to Neonatal Transmission among Mexican Pregnant Women. Infect Dis Obstet Gynecol. 2013: 1-6.
- Xu F, Markowitz LE, Gottlieb SL, Berman SM (2007) Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States. Am J Obstet Gynecol 196: 1-6.
- Smith JS, Robinson NJ (2002) Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. J Infect Dis 186: 23-28.
- Smith JS, Herrero R, Muñoz N, Eluf-Neto J, Ngelangel C, Bosch FX, Ashley RL (2001) Prevalence and risk factors for herpes simplex virus type 2 infection among middle-age

- women in Brazil and the Philippines. Sex Transm Dis 28:187-194
- Miskulin M, Miskulin I, Milas J, Antolović-Pozgain A, Rudan S, Vuksić M (2011) Prevalence and risk factors for herpes simplex virus type 2 infections in East Croatia. Coll Antropol 35: 9-14.
- 22. Buchacz K, McFarland W, Hernandez M, Klausner JD, Page-Shafer K, Padian N, Molitor F, Ruiz JD, Bolan G, Morrow S, Katz MH (2000) Prevalence and correlates of herpes simplex virus type 2 infection in a population-based survey of young women in low-income neighborhoods of Northern California. The Young Women's Survey Team. Sex Trans Dis 27: 393-400.
- Madhivananm P, Krupp K, Chandrasekaran V, Karat C, Arun A, Klausner JD, Reingold AL (2007) The Epidemiology of Herpes Simplex Virus Type-2 Infection among Married Women in Mysore, India. Sex Transm Dis 34: 313-318.
- Fawole OI, Okesola AO, Fawole AO (2000) Genital ulcers disease among sexually transmitted disease clinic attendees in Ibadan, Nigeria. Afr J Med Med Sci 29: 17-22.
- Biswas D, Borkakoty B, Mahanta J, Walia K, Saikia L, Akoijam BS (2011) Seroprevalence and risk factors of Herpes Simplex virus type-2 infection among pregnant women in North-East India. BMC Infect Dis 11: 325.
- 26. Cherpes TL, Meyn LA, Krohn MA, Hillier SL (2003) Risk Factors for Infection With Herpes Simplex Virus Type 2: Role of Smoking, Douching, Uncircumcised Males, and Vaginal Flora. Sex Transm Dis 30: 405-410.
- Chohan V, Baeten JM, Benki S, Graham SM, Lavreys L, Mandaliya K, Ndinya-Achola JO, Jaoko W, Overbaugh J, McClelland RS (2009) A Prospective Study of Risk Factors for Herpes Simplex Virus Type 2 Acquisition among High-Risk HIV-1 Seronegative Kenyan Women. Sex Transm Infect. 85: 489.
- 28. van de Laar MJW, Termorshuizen F, Slomka MJ, van Doornum GJJ, ssewaarde JM, Brown DWG, Coutinho RA, van den Hoek JA (1998) Prevalence and correlates of herpes simplex virus type 2 infection: evaluation of behavioural risk factors. Int. J. Epidemiol 27: 127-134.
- Cowan FM (2000) Testing for type-specific antibody to herpes simplex virus- implications for clinical practice. J Antimicrob Chemother. 45: 9-13.
- Watson-Jones D, Weiss HA, Rusizoka M, Changalucha J, Baisley K, Mugeye K, Tanton C, Ross D, Everett D, Clayton T, Balira R, Knight L, Hambleton I, Le Goff J, Belec L, Hayes R (2008) Effect of Herpes Simplex Suppression on Incidence of HIV among Women in Tanzania. N Engl J Med 358: 1560-1571.
- 31. Coker AL, Richter DL, Valois RF, McKeown RE, Garrison CZ, Vincent ML (1994) Correlates and consequences of early initiation of sexual intercourse. J Sch Health 64: 372–377.
- 32. Andersson-Ellstrom A, Forssman L, Milsom I (1996) Age of sexual debut related to life-style and reproductive health factors in a group of Swedish teenage girls. Acta Obstet Gynecol Scand 75: 484–489.
- 33. Kahn JA, Rosenthal SL, Succop PA, Ho GY, Burk RD (2002) Mediators of the association between age of first sexual intercourse and subsequent human papillomavirus infection. Pediatrics 109: E5.
- 34. Durbin M, DiClemente RJ, Siegel D, Krasnovsky F, Lazarus N, Camacho T (1993) Factors associated with multiple sex partners among junior high school students. J Adolesc Health 14: 202–207.

 Baeten JM, Benki S, Chohan V, Lavreys L, McClelland RS, Mandaliya K, Ndinya-Achola JO, Jaoko W, Overbaugh J (2007) Hormonal contraceptive use, herpes simplex virus infection, and risk of HIV-1 acquisition among Kenyan women. AIDS 21: 1771-1777.

# **Corresponding author**

Dr Ojide, Chiedozie Kingsley, Department of Medical Microbiology and Parasitology, University of Uyo Teaching

Hospital, Uyo, Akwa-Ibom State, Nigeria

Phone: +2348052534844

Email: edomann2001@yahoo.com

**Conflict of interests:** No conflict of interests is declared.