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Sociodemographic and Clinical Factors Associated with Seroprevalence of HSV2 Infection among Antenatal Clinic Attendees in Benin

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Author's contribution

This whole work was carried out by the author EIK.

Original Research Article

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ABSTRACT

Background: Knowledge of the Sociodemoraphic factors associated with HSV-2 seroprevalence and identification of the associated patient-recognizable clinical features will enable informed preventive public health interventions. There's yet no documented data on the clinical and sociodemographic factors associated with HSV 2 Seroprevalence among pregnant women in Nigeria.
Objectives: To identify sociodemographic and clinical correlates of HSV-2 seroprevalence among pregnant women attending ante-natal clinics in Benin, Nigeria.
Study Location, Design and Duration: All the participants were prospectively recruited from the two major hospitals in Benin: University of Benin Teaching Hospital and Central Hospital, Benin. The cross-sectional study took place between November 2011 and June 2012.
Methodology: Participants were recruited on booking. Data on their sociodemographic profiles, clinical history and obstetric characteristics were obtained by the use of structured questionnaires and hospital case records. Their blood samples were also promptly collected on recruition. Each participant's serum was analyzed for HSV-2 IgG antibodies by gG-based type-specific ELISA. Counselling and testing for HIV were also carried out. Data analysis was done using SPSS version 16.
Results: The average age of the 674 enrolled participants was 30.6±5.2 years and most

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of them were married and had complete secondary education. Seroprevalence of HSV-2 was 46.3%. Factors that was significantly associated with HSV-2 seropositivity included age, level of education, parity, HIV seropositivity and positive history of sexually transmitted infections. The HSV-2-infected were also significantly more likely to recall episodes of genital rashes (occurrence of rashes of any type in the external genitalia), vaginal discharge and urethral discharge.

Conclusion: Risk factors for HSV-2 infection among pregnant women could include increasing age, higher parity, education below secondary level, HIV-positive status, and positive history of sexually transmitted infections. History of genital rashes, vaginal discharge and urethral discharge syndromes were associated with HSV-2 infection.

Keywords: Seroprevalence; human herpes virus 2; sociodemographic; syndromes; sexually transmitted infections (STI's); risk factors.

1. INTRODUCTION

Human Herpesvirus 2 (HSV-2) is the predominant cause of genital herpes in the sub-Saharan African environment [1,2]. The infection is estimated to affect 30-80% of women of reproductive age in this environment. Humans are the only natural hosts [3] and human-to-human transmission, via sexual contact is so efficient that the infection has been described as a silent pandemic [1,2]. This is because transmission through viral shedding still goes on, even by the predominantly asymptomatic cases [4,5].

High prevalence of HSV-2 infection is known to be potentially associated with impaired efficacy of HIV control and negative obstetric outcomes [6,7]. There is, therefore, need for effective public health control of this infection [4]. Based on local evidence, several countries have formulated HSV-2 infection control policies, especially with regard to pregnancy [8,9].

Since HSV-2 infection is life-long and has no known cure, primary prevention is the mainstay of its control [10,11]. Local epidemiological data is required for an effective primary prevention [4]. Despite the well known asymptomatic nature of HSV-2 infections [12], prevalence has been shown to be significantly associated with urethral and vaginal discharges [13]. It seems necessary, for epidemiological purposes, to verify the association of HSV-2 seropositivity with the known patient-recognizable sexually transmitted infection (STI) syndromes. The association with some sociodemographic factors also requires ascertaining.

There is dearth of data on the epidemiology of this infection among pregnant women in Nigeria, although there is some documentation on the infection among commercial sex workers and among sexually transmitted infection clinic attendees [14,15]. This study is aimed at determining the sociodemographic and clinical factors associated with seroprevalence of Human Herpesvirus 2 infection among pregnant women in Benin, Nigeria.

2. METHODOLOGY

2.1 Study Location, Design and Duration

The participants were ante-natal clinic attendees of the two major tertiary hospitals in Benin metropolis: University of Benin teaching Hospital (UBTH) and Central Hospital, Benin-City

(CHB). UBTH serves as a major referral centre for Edo State, and adjourning Ondo and Delta States, while CHB is transiting to a teaching hospital and sub serves secondary and tertiary health care delivery for Benin-Capital-City and other parts of Edo State. The cross-sectional study took place between November 2011 and June 2012.

2.2 Data Collection

The consenting participants were prospectively recruited. Structured questionnaire was used to collect data on specific participants' sociodemographic and clinical profiles. Obstetric data was obtained from hospital case records. Blood samples were obtained from the participants on enrollment and the serum was separated and used for glycoprotein G-based type-specific assay for HSV-2 IgG antibodies.

2.2.1 Laboratory procedures

Blood samples were collected in 5 ml plain vacutainer tubes and allowed to clot and sera separated by centrifugation at room temperature. Storage was in cryovials at -20ºC.

2.2.1.1 HSV-2 assay procedure

HSV-2 IgG assay utilized Enzyme Linked Immunosorbent Assay (ELISA) kit by Dia. Pro. Diagnostic Bioprobes, Milano, Italy. This is a glycoprotein G-based enzyme-linked immunosorbent assay (ELISA) technique. All specimens and kit reagents were brought to room temperature and gently mixed before the assay. Procedures were performed in accordance with instructions in the kit manual. Each batch of tests ran with both positive and negative controls and results were qualitative.

2.2.1.2 HIV immunoassay procedure

The HIV statuses of the respondents were previously determined using Determine ® HIV 1/2 by Inverness Medical Innovations South Africa; and HIV 1 and 2 STAT PAK Assay kit by CHEMBIO Diagnostic system, INC, New York, USA in accordance with Nigerian Federal Ministry of Health guidelines [16].

2.3 Data Analysis

Data collected was analyzed using the SPSS version 16 computer software. Fisher's exact and Chi^2 tests were used to test associations. Statistical significance was ascribed based on p-values <0.05.

3. RESULTS

The age range of the 674 participants was 18 to 44 years while their mean age was 30.6±5.2 years. Majority (96.6%) were in the 20-40 age range; were married (85.2%); were Christians (82.5%); had completed secondary education (93.5%) and were nulliparous (43.5%) Table 1.

HSV-2 antibodies were present in 312 (46.3%) of the participants. Generally, seroprevalence of HSV-2 infection significantly increased with age (p=0.001); unmarried status (p = 0.003); low level of education (p = 0.001); higher parity (p = 0.004); and HIV seropositivity (p=0.001).

There was no significant association between occurrence of the infection and religion (p = 0.16).

Table 1. Participants' characteristics and their association with HSV-2 seropositivity

Characteristics	HSV-2 antibodies present (%)	No. tested (%) Total =674(100%)	P-value
Age			
15-20	2(28.6)	7(1)	P = .001
21-25	38(38.8)	98(14.5)	
26-30	96(39.7)	242(35.9)	
31-35	109(48.4)	225(33.4)	
36-40	59(68.6)	86(12.8)	
41-45	8(50)	16(2.4)	
Marital Status			
Married	245(43.2)	574(85.2)	P = .003
Single	33 (71.4)	53(7.8)	
Divorced	17 (70.8)	22(3.3)	
Widowed	17 (68.8)	25(3.7)	
Level of education			
University graduate and above	93(44.3)	210(31.2)	P = .001
Post-secondary	129(44.2)	292(33.3)	
Secondary completed	60(46.9)	128(19.0)	
Secondary uncompleted	14(100)	14(2.1)	
Primary completed	16(59.3)	27(4.0)	
Primary uncompleted	0(0)	3(0.4)	
Religion			
Christianity	250(45.0)	556(82.5)	P = 0.16
Islam	62(52.5)	118(17.5)	
Parity			
Nullipara	72(40.4)	293(43.5)	P = .004
Primipara	57(49.1)	190(28.2)	
Para-2	37(50)	123(18.2)	
Para-3	18(66.7)	43(6.4)	
Para-4	10(83.3)	20(3.0)	
Para-5 or more	0(0)	5(0.7)	
HIV-Status			
Positive	36(69.2)	84(12.5)	P = .001
Negative	158(44.1)	590(87.5)	

Majority (73.4%) of the participants had a positive history of sexually transmitted infections and the prevalence of HSV-2 infection was significantly higher in this group (p = 0.001). Only a small proportion could recall episodes of urethral discharge. HSV-2 antibody was also significantly more prevalent among those who could recall episodes of urethral discharge and vaginal discharge (p = 0.012 and 0.001, respectively). Only 9% of the participants could recall having had painful ulcers at the external genitalia; and there was no significant association between prevalence of HSV-2 infection and positive history of genital ulcers and (p = 0.490). History of occurrence of rashes of any morphology in the external genitalia was prevalent among 56.8% of the participants; and the prevalence of HSV-2 infection was significantly more in this subgroup (p = 0.001) Table 2.

Table 2. Sexually transmitted infection (STI)yndromes and HSV-2 seroprevalence

	HSV-2 antibodies positive (%)	Total number tested (%)	P-value
History of STI			
Positive	277(56.0)	495(73.4)	P=.001
Negative	35 (19.6)	179 (26.6)	
Urethral discharge			
Positive	47(63.5)	74(11.2)	P = .012
Negative	265(44.2)	600(88.8)	
Abnormal vaginal discharge			
Positive	186(70.5)	264(40.0)	P = .001
Negative	126(30.7)	410(60.0)	
Painful genital ulcers			
Positive	24(38.7)	62(9.2)	P = .23
Negative	288(47.1)	612(90.8)	
Genital rashes of any type			
Positive	223(58.4)	382(56.8)	P = .001
Negative	89 (30.5)	292(43.2)	

4. DISCUSSION

The 46.3% HSV-2 seroprevalence found in the study population is high; and is higher than the 20.7%, 33.6% and 26% found among pregnant populations in two respective sub-Saharan African countries, Tanzania and Senegal [17-19]. This finding is also a lot higher than 7.5%, 11.5%, 14.5% and 22.0% found among pregnant populations in India, Australia, Mexico and USA [20-23].

Age was one of the socio-demographic variables found to be significantly associated with increased prevalence of HSV-2 infection in this population. This association is attributable to the fact that HSV-2 seroprevalence simply accumulates in a community with time (as long as transmission continues), since the infection is lifelong [10,11]. Similar observations have been made in several previous studies among persons of reproductive age [21,24] and suggests that the infection is acquired in early reproductive years and that primary control measures should commence early. Increased prevalence of HSV-2 infection was also significantly associated with education below secondary school level and unmarried statuses in this study. These findings corroborate previous reports from Brazil and Croatia [25,26]. The finding on the effect of education could be attributable to the well-known effect of ignorance in determining the distribution of disease; while the finding on effect of marital status could be due to the indiscreet sexual behaviours that often characterize unmarried statuses. In this study, multiparity was also found to be significantly associated with increased HSV-2 seroprevalence, as has also been reported in India and USA [20,27]. It, therefore, follows that age-above-30, education below secondary level, unmarried status, and multiparity ought to be taken into consideration while designing primary prevention strategies.

Furthermore, in individual case management, the presence of these factors could help in raising the index of suspicion of HSV-2 infection; since they are potentially useful screening criteria, if validated. Such screening protocol could also incorporate positive HIV status, positive history of sexually transmitted infections, positive history of abnormal vaginal

discharge and positive history of genital rashes, all of which were found to be significantly associated with HSV-2 infection in this present study.

The non-specific or asymptomatic nature of genital herpes and the prohibitive cost of serological screening informed the need to verify the predictive effect of certain patient-recognizable STI syndromes on HSV-2 seropositivity. These verified associations could be useful in formulating case definitions for epidemiological surveys and guide public enlightenment campaigns [1,4].

Contrary to expectations, positive history of genital ulcers was not highly prevalent in this population and there was no significant association of genital ulcers with HSV-2 seroprevalence. This result agrees with a study report from India in which only one of the HSV-2 infected participants had a history of genital ulcer disease [28]. Moreover, LGV and not genital herpes, was the major cause of genital ulcer disease (GUD) in a group of Nigerian females [29].

Close to half of the participants recalled having had rashes of any morphology in the genital region (genital rashes) and this feature was found to be significantly associated with HSV-2 seropositivity. The predictive effect of 'genital rashes' was assessed because positive history of painful genital ulcers (a secondary genital herpes skin lesion) had been previously reported as infrequent among the HSV-2-infected [28,29]. Moreover, 'genital rashes', though not a classical STI syndrome, is a clinical feature that could be easily understood by the participants. Case detection and recognition by the patients could improve if occurrence of genital rashes is promoted as an indication for sexual health-seeking activity. The typical sexually transmitted infection syndromes that were more significantly associated with HSV-2 seropositivity were urethral discharge and vaginal discharge. In a previous study among pregnant women in India, vaginal discharge was the most frequent feature among the HSV-2-infected [28]. Moreso, previous history of urethritis of Chlamydia spp. and Trichomonas spp. origin, was significantly associated with HSV-2 infection as reported in Australia and India [13,21]. Moreover, bacterial vaginosis has been shown to significantly increase the risk of acquisition of HSV-2 in previous reports [13,28-30].

The previously reported links between HIV infection and HSV-2 infection was further highlighted by this study [31]. Efforts to detect and control HSV-2 should be intensified as it translates to more effective HIV control [32].

5. CONCLUSIONS

The prevalence of HSV-2 infection among pregnant women in Benin is high. Prevention remains the potent means of controlling HSV-2 infection and the associated complications. Therefore, socioeconomic developmental challenges require addressing. Public health campaigns aimed at encouraging good health–seeking behavior on noticing genital rashes, urethral discharges, and vaginal discharges are recommended.

CONSENT

Written informed consent was obtained from the participants for carrying out and publishing this research work.

ETHICAL APPROVAL

Approval was obtained from the ethical committee of University of Benin Teaching Hospital, Benin for carrying out this study.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Looker KJ, Garnett GP, Schmid GP. An estimate of the global prevalence and incidence of herpes simplex virus type 2 infection. Bull World Health Organ. 2008;86(10):737-816.
2. Oni AA, Adu FD, Ekweozor CC, Bakare RA. Genital herpes simplex virus infection in females in Ibadan Nigeria. West Afr J Med. 1996;15(2):107-110.
3. Dordevic H. Serological response to herpes simplex virus type 1 and 2 infection among women of reproductive age. Med Pregl. 2006;59(11-12):591-7.
4. Corey L, Handsfield HH. Genital Herpes and public health: addressing a global problem. JAMA. 2000;283:791-4.
5. Kolawole OM, Adu FD, Agbede OO, Oni AA, Bakare RA. Epidemiological Patterns of Human Immunodeficiency Virus and Herpes Simplex Virus Co-Infection in Ibadan, Nigeria. Afr J Biomed Res. 2008;11:23-6.
6. Torok E, Moran E, Cooke F. Congenital infections. In: Oxford Handbook of Infectious Diseases and Microbiology. New York: Oxford University Press. 2009;824–6.
7. Centers for disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention. Division of STD Prevention. Sexually transmitted diseases: Genital Herpes-CDC fact sheet; 2013.
   Available: URL:http://www.cdc.gov/std/Herpes/STDFact-Herpes.htm
8. Board of the Australian Herpes Management Forum. Herpes simplex in pregnancy. 2nd. AHMF Australian Herpes Management Forum; 2009.
   Available: http://www.ahmf.com.au/guidelines/genital-herpes/herpes-and-pregnancy
9. New Zealand Herpes Foundation. Guidelines for the Management of Genital Herpes in New Zealand. 9th edition. Viral Sexually Transmitted Infection Education Foundation; 2009. Available from:
   URL:http://www.herpes.org.nz/pdfs/NZHF%20Guidelines%202009_FA_updated.pdf
10. Sandhaus S. Genital herpes in pregnant and non-pregnant women. Nurse Pract. 2001;26(4):25-7.
11. Jerome KR, Morrow RA. Herpes simplex viruses and Herpes B virus. In: Murray PR, editor. Manual of Clinical microbiology, volumeII. 9th ed. Washington: American Society for Microbiology Press. 2007;1523-1536.
12. Duran N, Yarkin F, Evruke C, Koksal F. Asymptomatic herpes simplex virus type 2 (HSV-2) infection among pregnant women in Turkey. Indian J Med Res. 2004;120(2):106-110.
13. Cherpes TL, Meyn LA, Krohn MA, Hillier SL. Risk factors for infection with Herpes Simplex Virus Type-2: Role of smoking, douching, uncircumcised males, and vaginal flora. Sexually Transmitted Diseases. 2003;10(5):405-410.
14. Dada AJ, Ajayi AO, Diamondstone L. 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.1998;25:237–42.

15. Agabi YA, Banwat EB, Mawak JD, Lar PM, Dashe N, Dashen MM, et al. Seroprevalence of herpes simplex virus type-2 among patients attending the Sexually Transmitted Infections Clinic in Jos, Nigeria. J Infect Dev Ctries. 2010;4(9):572-575.
16. Federal Ministry of Health (FMOH). National Guidelines for HIV and AIDS Treatment and Care in Adolescents and adults. Federal Ministry Of Health Abuja – Nigeria; 2010.
17. Yahya-Malima KI, Evien-Olsen B, Matee MI, Fylkenes K and Haans L. HIV-1, HSV-2 and syphilis among pregnant women in a rural area of Tanzania: prevalence and risk factors. BMC infect Dis. 2008;8:75. Doi: 10.1186/1471-2334-8-75.
18. Msuya SE, Uriyo J, Hussain A, Mbizvo EM, Jeansson S, Sam NE, et al. Prevalence of sexually transmitted infections among pregnant women with known HIV status in northern Tanzania. Reproductive Health. 2009;6:4. Doi: 10.1186/1742-4755-6-4.
19. Diawara S, Kane CT, Legoff J, Gaye AG, Mboup S. Low seroprevalence of Herpes simplex virus type 2 among pregnant women in Senegal. International J of STD and AIDS. 2008;19(3):159-160.
20. Rathore S, Jamwal A, and Gupta V. Herpes simplex virus type 2: Seroprevalence in antenatal women. Indian J Sex Transm Dis. 2010;31(1):11–15. doi:10.4103/0253-7184.68994.
21. Tideman RL, Taylor J, Marks C, Seifert C, Berry G, Trudinger B, et al. Sexual and demographic risk factors for herpes simplex type 1 and 2 in women attending an antenatal clinic. Sex Transm Infect. 2001;77(6):413-415.
22. Herrera-Ortiz A, Conde-Glez CJ, Vergara-Ortega DN, García-Cisneros S, Olamendi-Portugal L, Sánchez-Alemán MA, et al. Avidity of Antibodies against HSV-2 and Risk to Neonatal Transmission among Mexican Pregnant Women. Infectious Diseases in Obstetrics and Gynecology. 2013;2013:1-6.
23. Xu F, Markowitz LE, Gottlieb SL, Berman SM. Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States. Am J Obstet Gynecol. 2007;196(1):43.1-6.
24. Smith JS, Robinson NJ. Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. J Infect Dis. 2002;186:3-28. doi: 10.1086/343739.
25. Smith JS, Herrero R, Muñoz N, Eluf-Neto J, Ngelangel C, Bosch FX, Ashley RL. Prevalence and risk factors for herpes simplex virus type 2 infection among middle-age women in Brazil and the Philippines. Sex Transm Dis. 2001;28(4):187-194.
26. Miskulin M, Miskulin I, Milas J, Antolović-Pozgain A, Rudan S, Vuksić M. Prevalence and risk factors for herpes simplex virus type 2 infections in East Croatia. Coll Antropol. 2011;35(1):9-14.
27. Buchacz K, McFarland W, Hernandez M, Klausner JD, Page-Shafer K, Padian N, et al. 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 Transm Dis. 2000;27(7):393-400.
28. Madhivanan P, Krupp K, Chandrasekaran V, Karat C, Arun A, Klausner JD, et al. The Epidemiology of Herpes Simplex Virus Type-2 infection among married women in Mysore, India. Sexually Transmitted Diseases, November. 2007;34(11):000–000. Doi: 10.1097/OLQ.0b013e3180ca965a.
29. Fawole OI, Okesola AO, Fawole AO. Genital ulcers disease among sexually transmitted disease clinic attendees in Ibadan, Nigeria. Afr J Med Med Sci. 2000;29(1):17-22.
30. Biswas D, Borkakoty B, Mahanta J, Walia K, Saikia L, Akoijam BS. Seroprevalence and risk factors of Herpes Simplex virus type-2 infection among pregnant women in North-East India. BMC Infectious Diseases. 2011;11:325. Doi: 10.1186/1471-2334-11-32.

31. Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2- seropositive persons: a meta-analysis. J Infect Dis. 2002;185:45-52.
32. Watson-Jones D, Weiss HA, Rusizoka M, Changalucha J, Baisley K, Mugeye K, et al. Effect of Herpes Simplex Suppression on Incidence of HIV among Women in Tanzania. N Engl J Med. 2008;358:560-1571. Doi: 10.1056/NEJMoa0800260.

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