

Seroprevalence of Herpes Simplex Virus Type 2 (HSV-2) among Pregnant Women Accessing Antenatal Care in a Tertiary Healthcare Facility in Central Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author GRP designed the study. Authors VBO and BAU helped in sample collection and managed the laboratory analysis. Authors BAU and CKE searched for literatures while author VBO performed the statistical analysis and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Herpes simplex virus type 2 (HSV-2) infections is one of the most common sexually transmitted infections worldwide. Due to lack of documented HSV-2 studies among pregnant women in the study area, a detailed cross-sectional study was therefore carried out to evaluate the prevalence of HSV-2 infection among pregnant women accessing antenatal care in Federal Medical Centre, Keffi, Nigeria. After ethical clearance, blood samples were aseptically collected from 220 pregnant women who gave informed consent and completed a self-administered questionnaire. Blood samples were screened for HSV-2 specific IgG antibody using an Enzyme Linked Immunosorbent Assay (ELISA) test kit (Cortez Diagnostic Inc, USA). The Chi-square test was performed to identify possible risk factors associated with the viral seropositivity. Overall, 78 (35.5%) had IgG antibodies

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against HSV-2. Participants aged < 20 years old recorded a highest prevalence of 38.1%, while the lowest prevalence (29.3%) was recorded in those aged 31-40 years old ($p > 0.05$). There was a statistically significant association between the seroprevalence of HSV-2 in pregnant women in relation to occupation. Pregnant women who are full housewives had the highest prevalence (68.9%) of the infection, followed by others (33.3%), farmers (31.0%) while the least prevalence (5.3%) was recorded among civil servants. However, in this study, educational status, parity, stage of pregnancy and history of blood transfusion had no statistically significant association with HSV-2 infection ($p > 0.05$) but there was arithmetic difference in most of the risk factors. A high prevalence of the viral infection was reported in this study. Therefore, type-specific serologic tests might be useful for identifying pregnant women at risk for HSV infection and guiding counseling regarding the risk for acquiring genital herpes during pregnancy are suggested.

Keywords: HSV-2; Pregnant women; ELISA; seroprevalence; Keffi.

1. INTRODUCTION

Herpes viruses derive their name from the Greek word *herpein*, which means to creep. They are dsDNA virus that belongs to the family Alpha herpesvirinae, subfamily Herpesviridae. There are eight herpes viruses which includes; Herpes simplex virus type 1 (HSV-1), HSV-2, Varicella-zoster virus, Epstein-Barr virus and Human cytomegalovirus. Herpes viruses cause persistent infections in human around the world [1]. HSV-1 and HSV-2 is ubiquitous, contagious and can be spread when an infected person is producing and shedding the viruses [2,3].

Infections with HSV are transmitted through contact with herpes lesions, mucosal surfaces, genital secretions, or oral secretions [4]. HSV-1 and HSV-2 can be shed from normal-appearing oral or skin [5,6]. Normally, a person can only get HSV-2 infection during genital contact with one who had a genital HSV-2 infection. Transmission commonly occurs from contact with an infected partner who does not have visible lesions and who may not know that he or she is infected [5]. In persons with asymptomatic HSV-2 infections, genital HSV shedding occurs on 10.2% of days, compared to 20.1% of days among those with symptomatic infections [5].

Genital herpes may be caused by either HSV-1 or HSV-2 but globally the large majority of cases are caused by HSV-2 [7]. Primary infection of HSV acquired by women during pregnancy accounts for half of the morbidity and mortality among neonates [8]; while the remaining half result from the reactivation of an old infection. Infections with both strains are widespread in all human populations and result in persistent and latent infections [9,10]. After initial infection, the virus can reside as life-long virus and remains latent until the opportunity for recurrence, thus genital herpes is generally a recurrent and

incurable viral disease [12]. The majority of both primary and recurrent infections are asymptomatic; however, in symptomatic cases, lesions might be accompanied with pain and obviously affect the quality of the life in patients. HSV can easily spread in populations because of the asymptomatic nature of the disease, and this could be a suitable marker to evaluate the sexual behaviours of such population [7]. It was reported that 70% of newborn with neonatal herpes infection were infected by their mothers with unrecognized symptoms [8,10].

Primary genital HSV-2 infection in pregnant women can result in abortion, premature labor, congenital and neonatal herpes [11]. Neonatal infection with HSV is divided into localised, central nervous system (CNS) disease and disseminated disease. Localised congenital HSV infection is limited to the skin, eye or mouth whereas CNS disease results in encephalitis, and disseminated disease leads to multiple organ damage. It has also been reported that 80% of infants with disseminated disease die without treatment and those who survive are often suffering damaged brain [11,12].

Genital herpes infection in pregnant women is of particular importance because of the risk to the fetus and the newborn [13]. Its role in enhancing human immunodeficiency virus (HIV) acquisition and transmission makes it an important public health problem [2]. The severest form of neonatal disease occurs when infection of the mother occurs during the last stage of pregnancy, at a time when the maternal protective antibodies develop much more slowly for passive transfer to the fetus [14]. This last trimester of pregnancy is also the period when urinary tract infection of the mother is at its peak [8]. The need, therefore, to screen pregnant women for asymptomatic HSV infection as part of antenatal care cannot be overemphasized. The information on HSV and its

seroprevalence in pregnant women is very limited in Central, Nigeria. The aim of the present study was to evaluate the seroprevalence of HSV-2 infection among pregnant women accessing antenatal care in a tertiary healthcare facility in Central, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area and Population

The area of study for this research was Keffi approximately 68 Km from Abuja, the Federal Capital Territory and 128Km from Lafia, the capital of Nasarawa State. Keffi is located between latitude 8 5'N of the equator and longitude 7 8'E and situated on an altitude of 850 M above sea level [15].

The study population was 220 recruited pregnant women accessing antenatal care in the Federal Medical Centre, Keffi. The socio-demographic information of the participants was obtained by a structured questionnaire prior to sample collection.

2.2 Sample Collection

After obtaining a written informed consent from each participant, 5 ml blood samples was collected by vein puncture into a sterile plain tube, allowed to clot for 30 minutes and centrifuged at 3000 rpm for 5 minutes. Each resultant serum was transferred into a new labeled cryovials and stored at -20°C until ready for the ELISA analysis.

2.3 Laboratory Investigation

The HSV-2 specific IgG ELISA test kit (Cortez Diagnostic Inc, USA) was used to detect the HSV-2 IgG antibodies in the sera. This was performed according to the manufacturer's instructions.

2.3.1 Enzyme Linked Immunosorbent Assay (ELISA) procedure

The desired number of coated strips was placed into the holder and 1:40 dilution each was prepared by adding 5 µl of each of the sample, negative control, positive control and calibrator to 200 µl of the sample diluents and mixed well. 100 µl of diluted sera, calibrator and control was each dispensed into the appropriate well. For the reagent blank, 100 µl of the sample diluents was

dispensed in 1A well position. The holder was tapped gently to remove air bubbles from the liquid content in the wells. The sample was incubated for 30 min at room temperature. After the incubation period, the liquid content was removed from all the wells and washed properly using 100 µl of the washing buffer. The mixture was slightly agitated and dapped onto a tissue paper pad. This step is repeated three times. 100 µl of enzyme conjugate was dispensed into each well after the washing step and the test further incubated for 30 min at room temperature. The enzyme conjugate was discarded after the incubation and the washing up step was repeated using the washing buffer. After this step, 100 µl of tetramethyl benzidine (TMB) chromogenic substrate was dispensed into each well and incubated for 30 minutes at room temperature after which 100 µl of 2N HCl was then added to stop the reaction. The absorbance of content of the microplate was read at 450 nm with a microwell reader (BIO-RAD PR2100).

2.4 Ethical Approval

Ethical Approval for this study was obtained from the Ethical Review Committee on Human Research, Federal Medical Centre, Keffi, Nigeria.

2.5 Statistical Analysis

The data obtained were subjected to descriptive statistical analysis using SPSS version 17.0. Chi-square statistical test was used to determine association and value obtained were considered statistically significant at $p \leq 0.05$.

3. RESULTS

A total of 220 pregnant women were recruited in this study. There was an overall HSV-2 prevalence of 35.5%. Age, educational status, parity, stage of pregnancy and history of blood transfusion were not significantly associated with the viral prevalence ($p > 0.05$) but occupation was significantly associated with the infection ($p < 0.05$) as shown on Table 1.

4. DISCUSSION

Genital herpes is a global public health problem, and for the person infected, it is a very painful condition. It can cause significant distress, and can have a devastating impact on the social and psychological wellness of an individual. In

Table 1. Seroprevalence of HSV-2 infection among pregnant women accessing antenatal care at Federal Medical Centre, Keffi, Nigeria with respect to some socio-demographic variables

Risk factors	No. examined	No. positive (%)	p value
Age (Years)			
< 20	21	8 (38.1)	0.9349
21-30	142	52 (36.6)	
31-40	41	12 (29.3)	
41-50	16	6 (37.5)	
Occupation			
Civil servants	95	5 (5.3)	0.0000
Housewives	90	62 (68.9)	
Farmers	29	9 (31.0)	
Others	6	2 (33.3)	
Educational status			
None	16	10 (62.5)	0.0889
Primary	90	40 (44.4)	
Secondary	61	15 (25.0)	
Tertiary	53	13 (24.5)	
Parity			
1	80	30 (37.5)	0.5888
2	58	22 (38.0)	
3-4	52	20 (38.5)	
>4	30	6 (20.0)	
Stage of pregnancy			
1 st trimester	50	18 (36.0)	0.0975
2 nd trimester	87	21 (24.1)	
3 rd trimester	83	39 (47.0)	
History of blood transfusion			
Yes	170	59 (34.7)	0.7691
No	50	19 (38.0)	

addition, pregnant women with genital herpes caused by infection by HSV-2 can transmit the virus to their neonate at birth, causing neonatal herpes, which is a potentially preventable cause of neonatal mortality and morbidity [10,16].

The overall seroprevalence of 35.5% HSV-2 infection recorded in this study is relatively high especially when compared to similar studies carried out in other countries. There have been reports of 4.2% in Turkey [8], < 33% in Cuba [9] and 10% of HSV-2 IgG seropositivity was found in antenatal women of reproductive age who experienced spontaneous abortions in Nepal [17]. Higher rates compared to findings in the present study have also been reported in Nigeria and other countries like 84% from pregnant women in Benin City, Nigeria [12], 49.1% in Zimbabwe [18], 3.95% in Kisumu, Kenya [19], 63.3% and 91.1% in Sudan [10,3] and 64.9% in India [7].

There was no statistically significant difference between the viral infection seroprevalence and

age of the subjects ($p > 0.05$). The highest infected group was 38.1% in those pregnant women with aged group less than 20 years and least in older age groups. This report is in consonance with the work of Egbagba and Mordi [12] in which age did not correlate with the prevalence of the viral infection and Amar *et al.* [7] which recorded highest prevalence in older age groups and least in younger age groups. A possible explanation for this outcome is that most of the women acquired HSV-2 infection early in childhood such that in later life, marriage and education acquisition had no apparently effect on the prevalence.

With reference to occupation, housewives recorded the highest prevalence (68.9%), followed by others (33.3%), farmers (31.0%) and the least seroprevalence was recorded among civil servants (5.3%). There was a statistically significant association between viral infection and occupation ($p \leq 0.05$). So it followed that the educated women were likely the civil servants

which made them have the least prevalence of the viral infection.

Educational status was not found to be associated with the seropositivity of the viral infection among pregnant women ($p > 0.05$) in this study. It was highest among women without any form of formal education (62.5%) and least among women with tertiary education (24.5%). Education has been acknowledged to be of advantage in various facets of life. It helps in making informed decision and also sourcing for useful information regarding health status on possible ways of avoiding sexually transmitted infections [20]. Paz-Bailey et al. [21] also reported same outcome in his study. No association was demonstrated between parity and the viral infection among the respondents ($p > 0.05$). The infection was highest among those pregnant women with 3-4 children (38.5%) and least among women with more than 4 children (20.0%). This finding is supported by other studies and can directly increase the duration and an indirect relationship with multiple sexual partners, both of which are independent risk factors [12,22].

There was no statistically significant association between stage of pregnancy and HSV-2 infection ($p > 0.05$). The prevalence was highest among those pregnant women in their third trimester (47.0%) and least among women in their second trimester (24.1%). This report is in consonance with the outcome of Amar et al. [7] in India but disagreed with the work of Idress and Elhag [10] in Sudan. The history of blood transfusion among the participants was not found to be associated with HSV-2 infection ($p > 0.05$). The viral seroprevalence was higher among those that had no history of blood transfusion (38.0%) than those who had a history of blood transfusion (34.7%).

5. CONCLUSION

A HSV-2 prevalence of 35.5% was reported in the present study. This finding is actually lower than that found elsewhere in Africa except for Kisumu, Kenya and comparable to black Americans, for whom the CDC does not recommend screening of asymptomatic pregnant women. Therefore, it is necessary to routinely screen pregnant women for the possibility of HSV-2 infection so that it could be minimized by proper treatment. The study supports the need for health education and personal hygiene which

will help in reducing the risks of the infection among pregnant women in the area.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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