



SEROLOGICAL SURVEY OF IMMUNOGLOBULIN G ANTIBODY AMONG DIFFERENT POPULATIONS WITH ASSYMTOMATIC SHEDDING OF GENITAL HERPES IN KATSINA STATE

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ABSTRACT

Herpes Simplex Virus type 2 (HSV-2) is a significant public health problem being one of the most prevalent sexually transmitted infections worldwide and the leading cause of genital ulcerative disease that is common both in industrialized and developing countries. Therefore, a study on the serological survey of Immunoglobulins G antibody among different populations with asymptomatic shedding of genital herpes in Katsina State, north-western Nigeria was carried out. A total of 460 (86 HIV, 136 feverish patients, 125 pregnant women and 113 normal Individuals) blood samples were collected from six hospitals located across the three senatorial zones of the State. The serum was separated from the blood and used for the analysis. The participant's socio-demographic information and clinical presentations were also noted with the aid of a questionnaire. Viral antibodies were detected by HSV-2 IgG ELISA Kits. The HSV-2 IgG was detected in 72.8% of the serum tested. The prevalence among patients presenting with fever was 70.6%, and it was 74.4% in the pregnant women. The prevalence in HIV positive patients was 75.6% while it was 73.5% in the apparently healthy individuals. There was a significant association between HIV positivity, feverish condition and HSV-2 prevalence. Higher prevalence was recorded at General Hospital Dutsinma 89.6% and there was a statistically significant association between prevalence and hospital studied. Generally, older participants were more vulnerable to HSV-2 infection than younger ones. There was no statistical significant association between sex of the participants and HSV-2 infection. None of the sociodemographic factors was significantly associated with HSV-2 infection except marital status. There was no significant association between socio-economic status, sexual activity, use of protection, number of sexual partners, clinical manifestation, level of education, and occupation of the participants with HSV-2 infection. The present study indicates that prevalence of HSV-2 appears to be relatively high and older participants were more vulnerable to HSV-2 infection in Katsina State. There is need for educating populace on HSV-2 infection and its mode of transmission to reduce the level of its spread between individuals in the population.

Keywords: HSV-2; IgG; Genital; Serum; Antibody

INTRODUCTION

Herpes simplex virus type-2 is the most common cause of genital herpes (Looker *et al.*, 2008). The disease is manifested by macules and papules followed by vesicles, pustules, and ulcers (Hadeel *et al.*, 2015). In males, primary infection leads to a cluster of vesicular lesions on erythematous bases on the glans or shaft of the penis (Tobian *et al.*, 2009). In females, painful lesions occur bilaterally on the vulva and cervicitis occurs in 90 % of women (Martin *et al.*, 2009). Headache, fever, depression and inguinal lymphadenopathy are often systemic

signs and symptoms of genital herpes infection (Brook *et al.*, 2010). Genital lesions due to herpes are often very painful, and can lead to substantial psychological morbidity (Stanberry *et al.*, 2000). The virus can also be passed from mother to child during birth resulting to the neonatal infection that is very serious. Without treatment, 80% of infants with disseminated disease die, and those who do survive are often have damaged brain (Tyler, 2004). Majority of the infections are asymptomatic and this enhances HSV-2 transmission because

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asymptomatic individuals shed the virus and However, the large majority of persons with genital herpes do not know they have the disease and infection and reactivation are typically asymptomatic. This typical asymptomatic nature of genital herpes facilitates its spread in the population, genital herpes is associated with considerable morbidity and even mortality (Tobian *et al.*, 2009). The virus annually affects an estimate of 417 million persons in the reproductive age range worldwide (WHO, 2015).

MATERIAL AND METHODS

Study Area

The study was carried out in Katsina State located at the extreme northern margin of Nigeria. The State covers a total area of about 23,938sqkm (3,370sq) with a total population of 5,801,584 people, going by 2006 census (FGN, 2007). It lies between latitudes 11°08'N and 13°22'N and longitudes 6°52'E and 9°20'E. The State has thirty four (34) local government areas which are divided into three (3) senatorial zones according to their geographical locations namely; Funtua zone, Katsina zone and Daura zone (Dauda *et al.*, 2011).

Study Design and Population

The study was a descriptive cross-sectional and study population comprised of males and females among HIV patients, pregnant women, feverish patients and apparently healthy individuals. The hospitals selected for the study were; General Hospital Funtua, Children's and Maternity Hospital Malumfashi, General Hospital Dutsinma, General Hospital Katsina, General Hospital Daura, General Hospital Baure.

Ethical Approval and Consent

Ethical approval was obtained from the Ethical Committee of General Hospital Services Management Board, Katsina State. Consent form was obtained from patients prior to enrolment in the study.

transmit the disease (Phipp *et al.*, 2015).

Blood Sample Collection

A total of 460 blood samples were collected aseptically using 5ml syringe from patients who gave consent by the laboratory technologist in the selected hospitals of Katsina State. The whole blood was allowed to clot for 30 minutes and centrifuged at 1000rpm for 10 minutes. The serum was carefully removed with a transfer pipette and transferred aseptically to a sterile labeled serum storage screw-capped container and stored at -20°C in a freezer until analyzed.

Serological Assay for HSV-2 IgM Antibody

The serum samples were analyzed using HSV-2 IgM specific ELISA kits manufactured by Diagnostic Automation / Cortez Diagnostics Inc, USA. The manufacturer's instructions were strictly followed.

RESULTS

A total of 460 participants over 10 year of age from four different populations were recruited for the study with different characteristics (Table 1). This include 86 (18.7%) HIV patients, 136 (29.6%) feverish patients, 113 (24.6%) apparently healthy individuals and 125 (27.2%) pregnant women. Among the participants, 258 (56.1%) were females and 202 (43.9%) were males.

Of the 460 sera analysed, 72.8% were positive for IgG. The higher prevalence rates was seen HIV 75.6% participants while least was observed among patients presenting with fever were 70.6%. while IgG prevalence rates among HIV positives patients were 75.6%. There was an association between feverish condition and HIV positivity with HSV-2 infection (Table 2). Analysis of the results by hospital showed that higher prevalence rate of 89.6% was recorded in General Hospital Dutsinma while the least was recorded in General Hospital Baure (53.1%: 34/64). There was a significant association between prevalence and the hospitals ($\chi^2=25.415$, $df=5$, $p=0.003$) (Table 3).

Table 1: General characteristics of the participants in Katsina State, Nigeria

Parameter	Frequency	Percent (%)
Age Group (Years)		
10 – 20	75	16.3
21 – 30	163	35.4
31 – 40	142	30.9
41 – 50	58	12.6
51 and above	22	4.8
Socioeconomic Status		
Low	280	32.5
High	180	67.5
Marital Status		
Married	279	60.7
Single	158	34.3
Divorced	18	3.9
Widowed	5	1.1
Level of Education		
Tertiary	121	26.3
Secondary	138	30.0
Primary	107	23.3
None	94	20.4
Occupation		
Civil servant	137	29.8
Farmer	65	14.1
Self-employed	118	25.7
Unemployed	140	30.4
Gender		
Female	257	55.9
Male	203	44.1

Table 1: Prevalence of genital herpes according to participant's category among different populations in Katsina State, Nigeria

Category	Total	Immunoglobulin G		
		Positive (%)	Negative (%)	P-value
HIV Patients	86	65 (75.6)	21 (24.4)	0.030
Fever Patients	136	96 (70.6)	40 (29.4)	0.002
Pregnant Women	125	93 (74.4)	32 (25.6)	0.432
Healthy Persons	113	81 (73.5)	32 (28.3)	0.213
Total	460	335 (72.8)		

Table 2: Prevalence rate of genital herpes among different populations by hospital in Katsina State, Nigeria

Hospital	Total	Immunoglobulin G		
		Positives (%)	Negatives (%)	P-value
GH Dutsinma	67	60 (89.6)	07 (10.4)	0.003
GH Katsina	88	65 (73.9)	23 (26.1)	
GH Baure	64	34 (53.1)	30 (46.9)	
GH Daura	86	63 (73.3)	23 (26.7)	
GH Funtua	74	59 (79.7)	15 (20.3)	
MCH Malumfashi	81	54 (66.7)	27 (33.3)	
Total	460	335 (72.8)	125 (27.2)	

Key: GH= General Hospital; MCH= Maternal and Children Hospital

Analysis of the results according to Senatorial District showed higher prevalence rate of 81.3% in Katsina Central while Katsina North had the least 64.7%. There was a statistical significant association between prevalence and Senatorial Districts ($\chi^2=9.835$, d.f= 2, p= 0.007). Analysis

of the results according to age groups is shown in Table 5. Higher prevalence was recorded among participants in age group 41-50 years 84.5% while participants in age group 16-20 years had the lowest 64.0%.

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There was no significant association between age of the participants and prevalence ($\chi^2=10.386$, $df=4$, $p=0.239$). The results were analysed by sex as shown in Table 6. Although there was no significant association between sex of the participants and HSV-2 prevalence ($\chi^2=0.150$, $df=1$, $p=0.314$), however, females had higher prevalence 73.5 % compared to males 71.9% and however, male participants were two times more likely to be infected than females (OR=2.017, 95% C.I=0.397-5.730).

The data and results were analysed according to socio-demographic factors as shown in Table 7. Higher prevalence of 77.7% was detected among those with high socio-economic status while those with low socio-economic status had lower prevalence rates of 69.8%. There was no statistically significant association between socio-economic status and HSV-2 prevalence ($\chi^2=3.341$, $df=1$, $p=0.063$). However those with high socio-economic status were two times more likely to be infected with the virus

compared to those with low socio-economic status (OR=2.007, 95% C.I=0.321-5.210).

The higher prevalence rates of 76.3% were recorded among uneducated participants while those with secondary school level had the lowest of 70.1%. Similarly, there was no statistically significant association between educational level and HSV-2 prevalence ($\chi^2=1.847$, $df=3$, $p=0.605$). Analysis of the results by occupation showed that civil servants had higher prevalence rate of 78.4% while lower rate of 60.0% was obtained among farmers. There was no statistically significant association between occupation and HSV-2 prevalence ($\chi^2=6.791$, $df=3$, $p=0.079$).

The data and results when analysed according to marital status of the participants showed that the divorced had higher prevalence rate of 80.0% while lowest of 66.7% was obtained among widows. There was no statistically significant association between HSV-2 prevalence and marital status ($\chi^2=2.601$, $df=3$, $p=0.046$).

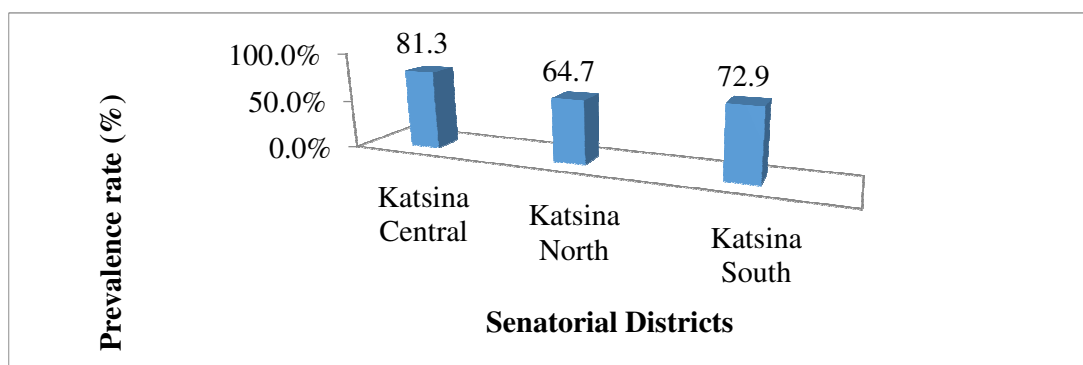


Figure 1: Prevalence rate of genital herpes in relation to senatorial district of Katsina State, Nigeria

Table 3: Prevalence of genital herpes in relation to age of participant in Katsina State, Nigeria

Age group	Total	Immunoglobulin G		
		Positives (%)	Negative (%)	P-value
10-20	75	48 (64.0)	27 (36.0)	0.239
21-30	163	113 (69.3)	50 (30.7)	
31-40	142	107 (75.4)	35 (24.6)	
41-50	58	49 (84.5)	09 (15.5)	
51 and above	22	18 (81.8)	04 (18.2)	
Total	460	335 (72.8)	125 (27.2)	

Table 4: Prevalence of genital herpes in relation to gender among different populations in Katsina State, Nigeria

Gender	Total	Immunoglobulin G			
		Positives (%)	Negatives (%)	P-value	Odd Ratio
Male	203	146 (71.9)	57 (28.1)	0.314	0.065
Female	257	189 (73.5)	68 (26.5)		
Total	460	335 (72.8)	125 (27.2)		

Table 5: Prevalence of genital herpes in relation to socio-demographic factors

Factors	Total	Immunoglobulin G		
		Positives (%)	Negative (%)	P-value
Socio-economic				
High	180	139 (77.7)	41 (22.3)	0.063
Low	280	196 (69.8)	84 (30.2)	
Education				
None	93	71 (76.3)	30 (21.6)	0.605
Primary	108	76 (70.4)	35 (37.8)	
Secondary	137	96 (70.1)	44 (27.1)	
Tertiary	122	92 (75.4)	22 (40.0)	
Occupation				
Civil servant	139	109 (78.4)	30 (21.6)	0.779
Self employed	126	91 (72.2)	35 (37.8)	
Unemployed	146	102 (72.9)	44 (27.1)	
Farmer	55	33 (60.0)	22 (40.0)	
Marital status				
Single	157	109 (69.4)	48 (30.6)	0.046
Married	280	210 (75.0)	70 (25.0)	
Widow	18	12 (66.7)	06 (33.3)	
Divorced	05	4 (80.0)	01 (20.0)	

Analysis of data and results according to possible risk factors that might predispose to the infection is shown in Table 8. Majority 73.4% of the participants that claimed not to be involved in any sexual activity had higher prevalence compared to those that claimed to be involved 72.5%. There was no statistically significant association between sexual activity and HSV-2 prevalence ($\chi^2= 0.033$, $df= 1$, $p= 0.856$). However, those who claimed to be involved in sexual activity were 1.1 times more likely to be infected than those that claimed not to be involved (OR=1.067, 95% C.I=1.004-2.730). The participants who claimed to have single sexual partner had a lower prevalence rate 70.9% compared to those who claimed to have more than one sexual partner 74.1%. There was

no significant association between sexual partner and HSV-2 prevalence ($\chi^2= 0.433$, $df= 1$, $p= 0.511$). However, those with more than one sexual partner were almost two times more likely to be infected than those with single sexual partner (OR=1.789, 95% C.I=1.970-3.412). The participants who claimed to use protection had higher prevalence rate (74.0%) compared to those who did not claim to use any protection (72.3%). There was no statistically significant association between the use of protection and HSV-2 prevalence ($\chi^2= 1.116$, $df= 1$, $p= 0.734$). However, those who claimed to use protection were almost 1.0 times more likely to be infected than those did not claimed (OR=1.004, 95% C.I=0.121-3.000).

Table 6: Prevalence rate of genital herpes in relation to risk factors among different population in Katsina State, Nigeria

Variables	Total	IgM			
		Positive (%)	Negative (%)	P-value	Odd ratio
Sexual active					
Yes	124	91 (73.4)	33 (26.6)	0.856	0.872
No	335	243 (72.5)	92 (27.5)		
Partners					
Yes	165	117 (70.9)	48 (29.1)	0.511	1.012
No	170	126 (74.1)	44 (25.9)		
Protection					
Yes	123	91 (74.0)	32 (26.0)	0.734	0.933
No	231	167 (72.3)	64 (27.7)		

DISCUSSION

Infection with HSV-2 has been shown to occur mostly among sexually-active individuals (Kahsay *et al.*, 2015) and majority of the participants recruited in this study were sexually active. In addition, HSV-2 is known to establish lifelong infection that recurs more often and detecting antibodies to the virus is often used to identify carriers of HSV-2 (Rathore *et al.*, 2010; Soumyabrata *et al.*, 2015). Hence, these infected patients are carriers of HSV-2 and might continue to be source of the virus in the community.

In this study, the higher prevalence of 72.8% found is lower than the 97.2% reported in Portacourt, Nigeria (Okonko *et al.*, 2015) and the 96.5% in Coitdevoire (Boni *et al.*, 2015) but similar to the 73.8% reported in Enugu, Nigeria (Ojinmah *et al.*, 2012), 73.0% in South Africa (Abbai *et al.*, 2015).

The high prevalence observed in this study may probably be due to population at risk of acquiring HSV-2 infection involved in this study. The populations included feverish pateints, HIV-positive patients and pregnant women. Fever has been shown to be a sign of HSV-2 infection (Aminu *et al.*, 2014) and pregnancy can serve as a factor that reactivates HSV-2 from its latent state (Edith *et al.*, 2014). In addition, HIV and HSV-2 act synergetically and HIV cases are found to be high in sub-saharan Africa and infection with HSV-2 has been shown to facilitate HIV transmission (Mawak *et al.*, 2009) and increase the risk of HIV acquisition (Schiffer *et al.*, 2014). These HSV-2 infected patients might therefore be at greater risk of HIV infection.

In this study, higher prevalence rate obtained among HIV-positive participants indicate the higher possibility of coinfection of HSV-2 infection among HIV-positive participants as postulated by Schiffer *et al.* (2014). The prevalence obtained among participants presenting with fever is higher than reported in Zaria, Nigeria (Aminu *et al.*, 2014). Genital herpes is a life-long incurable infection that causes medical, psychological and social concerns, therefore, these patients might be undergoing some of these concerns.

In this study, the prevalence found among pregnant women is lower than the reported in

Port-Harcourt, Nigeria (Okonko *et al.*, 2015). The higher IgG prevalence in this study could be probably due to active sexual life and also pregnancy has been reported as a factor that reactivates HSV-2 from its latent state. This also emphasizes the possible risk of neonatal infection. This could be due to the fact that pregnancy may activate the latent HSV-2 infection and possibly lead to neonatal infection. To our knowledge, no study had estimated the prevalence of HSV-2 among apparently healthy individuals in Nigeria. This shows that many in Nigeria are infected with the virus asymptomatically and it may be because of lack of awareness on its mode of transmission.

The higher prevalence among old age can be explained by the fact that HSV-2 infections persist for life, the prevalence increases with age through the sexually-active years. In line with the present study, studies in Nigeria (Mawak *et al.*, 2012; Kalu *et al.*, 2014) and other countries (Prathiba *et al.*, 2012; Herrera-Ortiz *et al.*, 2013; Amudha *et al.*, 2014) have shown a statistically significant association between HSV-2 infection and age of the participants.

Although in this study there was no statistically significant association observed between gender and HSV-2 prevalence, prevalence was higher in females than males. This disparity between genders could be probably due to of the difference in sample size between males and females or may also reflect anatomical differences in susceptibility to infection and greater efficiency of transmission from men to women as been observed by Bradley *et al.* (2014).

CONCLUSION

An overall 72.8% prevalence rate of antibodies to HSV-2 was obtained in this study. HIV positivity and feverish condition were significantly associated with HSV-2 infection. Of all the sociodemographic factors studied, only marital status was significantly associated with HSV-2 prevalence rate. Similarly, none of the risk factors studied were associated with HSV-2 in the study. However, females (2.02), low socioeconomic (2.01), no sexual activity (1.1), multiple sex partner (1.9), use of protection (1.0), STI (2.3) were more likely to be infected with HSV-2.

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