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Co-infection and associated risk factors of herpes simplex virus type-1 and human immunodeficiency virus among patients attending Faith Alive Foundation Hospital Jos, North Central Nigeria

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ABSTRACT

Background: Studies have reported that Genital herpes is of high public health implications in immuno-compromised individuals. **Aim:** The study seeks to determine how common herpes simplex virus -1 (HSV-1) infections are among human immunodeficiency virus (HIV) carriers and identify associated risk factors. **Methods:** Eighty-seven (87) apparently healthy subjects were tested for HSV-1 and HIV-1 using an Enzyme-Linked Immunosorbent Assay (ELISA) test Kit (Clinotech, Canada, USA), containing HSV-1 type-specific glycoprotein; Determine Kit (Inverness Medicom, Japan) and UniGold Kit (Trinity Biotech, Bray, Ireland), containing recombinant antigens. **Results:** Of 87 sera, 76(87.4%), and 30(34.5%) were seropositive for HSV-1 and HIV respectively while the co-infection seroprevalence rate of both viruses was 26(29.9%). The co-infection seroprevalence rate of HSV-1 and HIV-1 was highest in the age group ≥ 45 years (47.4%) while the age group 15-24 years had the lowest co-infection seroprevalence rate of 14.3% ($p > 0.05$). Women had a higher co-infection seroprevalence rate of 34.0% than men (24.3%). Of all the socio-demographics assessed, only the level of education was significantly associated with the prevalence of HIV and HSV-1/HIV co-infection respectively ($p = 0.003$; 0.001). **Conclusions:** The present study showed that HSV-1 infections are common among HIV carriers and HSV-1 is endemic in the study population as all age groups were affected. This finding underscores the need for further research to understand the interactions between HSV-1 and HIV to provide effective methods of reducing the infection burden.

Introduction

Herpes simplex viruses are ubiquitous, host-adapted pathogens, belonging to the family,

Herpesviridae and cause a wide variety of disease states. They are two types, Herpes simplex virus

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type 1 (HSV-1) and type 2 (HSV-2) [1]. Both are closely related but differ in epidemiology. Herpes simplex virus-1 is traditionally associated with orofacial disease (cold sores) on the lips, mouth, and face), while HSV-2 is traditionally associated with the genital disease; however, lesion location is not necessarily indicative of viral type [1,2]. Up to 80% of HSV infections are asymptomatic but HSV-1 may become latent in the sensory neural ganglia (the trigeminal ganglion) [3] and recurs periodically as outbreaks near the site of the original infection within a year [3,4]. Symptomatic infections can be characterized by significant morbidity and recurrence. It has been estimated that 20% to 40% of Americans suffer recurrent Herpes simplex infections which are often triggered by excess sunlight, fever, stress, acute illness, and medications or conditions that weaken the immune system such as cancer, HIV/AIDS, or the use of corticosteroids [5]. The prevalence of HSV infection worldwide has increased over the last several decades, making it a major public health concern. Prompt recognition of herpes simplex virus infection and early initiation of therapy is of utmost importance in the management of the disease. In immune-compromised hosts such as HIV/AIDS patients, infections can cause life-threatening complications. HSV-1 is contracted through direct contact (sexual and non-sexual) with an active lesion or body fluid of an infected person [6]. Most people become exposed to this virus early in life and in adulthood, up to 90% have antibodies to HSV-1 [7, 8]. In 1994, HSV-1 had been isolated in Nigeria [9] and in 1996 [10], a prevalence rate of 4.3% was reported. Risk factors for increased HSV-1 childhood infections include poor hygiene, overcrowding, lower socioeconomic status, and birth [10]. Although there is no cure yet, the available treatments help in reducing viral reproduction and shedding and alleviating the severity of symptomatic episodes [11,12]. Although, genital herpes is traditionally associated with HSV-2, several reports in different countries have implicated HSV-1 with genital herpes which could aid the spread of HIV [1]. Overall, HSV-2 has garnered appropriate attention in epidemiological studies because of the well-documented virologic, clinical and epidemiological synergisms between the virus and other infections such as HIV. However, a proper assessment of the public health impact of genital herpes in different populations requires more information on the interactions between HSV-1 and HIV. The role of human herpes

viruses in facilitating the transmission of HIV has been reported. Herpes simplex virus type 1 leads to increased morbidity and mortality during HIV/AIDS [13]. On the other hand, the occurrence and reoccurrence of symptomatic and asymptomatic HSV-1 infection has been linked to compromised immunity due to HIV [14]. However, there is a paucity of information on the true epidemiologic synergy between these two viruses in Nigeria and Africa in general. Routinely, sexually transmitted diseases commonly diagnosed in Nigeria include gonorrhoea, syphilis and hepatitis infections at the complete neglect of HSV-1 and HSV-2. Therefore, reports that genital HSV-1 may facilitate HIV-1 infection informed the design of this study aimed to determine the prevalence of HSV-1 infections among HIV-positive patients and to identify possible risk factors for these infections.

Materials and Methods

Study population

The present study is a descriptive and a cross-sectional study among randomly subjects who visited Faith Alive Foundation Hospital for voluntary counselling and screening for HIV. Thirty seven (37) males and 50 females were enlisted for the study. Although, gender restriction was observed in sample collection, the sexually active age group (15-50 years) was considered.

Study area

Faith Alive Foundation Hospital (FAFH) is located in Jos, Plateau State, Nigeria. The State is named after the picturesque Jos Plateau, a mountainous area in the north of the state with captivating rock formations. It has a population of around 3.5 million people and over forty ethnolinguistic groups. These ethnic groups are predominantly farmers and have similar cultural and traditional ways of life as people from other parts of the country. The climate on the Plateau is a semi-temperate climate with temperatures ranging from 18 °C (64.4 °F) to 25 °C (77.0 °F).

Ethical consideration

Ethical approval for the study was obtained from the ethical committee of Faith Alive Foundation Hospital, Jos, Plateau State.

Data collection

Structured close-ended questionnaires were used to collect socio-demographic data while about 5 ml of blood was collected by venipuncture from each patient after obtaining ethical approval from the

hospital and informed consent from the patients. The blood was allowed to clot, centrifuged at 1000 rpm for 5 minutes and serum was aspirated into a sterile eppendorf tube and stored at -20°C till tested.

Screening of the samples by ELISA

Each serum sample was initially screened for HIV with Determine™ (Inverness Medicom, Japan) which is a rapid test kit, and samples with non-reactive results were reported as negative while reactive samples in the initial testing were further tested using UniGold Kit (Trinity Biotech, Bray, Ireland), containing recombinant antigens. Discordant samples were confirmed using Gennie Fast (Bio-Rad Laboratories, Marnes La Coquette France and Steenvoorde, France). Samples that were reactive in the first test but negative in the second were recorded as negative. The HIV testing algorithm in this study was only employed for research purpose however there is a more current HIV testing algorithm especially for routine diagnostic purposes. These rapid testing kits comprise single-use immunoassays for the detection of anti-HIV-1 antibodies to human immunodeficiency virus type 1 (one-step procedure for serum/plasma or two-step procedures for whole blood). The test incorporates a combination of immuno-chromatography and immuno concentration. The rapid kits are quick and easy to use, delivering clear, dependable results in just 15 minutes. All samples were screened for antibodies to HSV-1 using an HSV-1-specific ELISA test kit (Clinotech, Canada, USA). The ELISA Kit relies on the specific recognition between an antibody and an antigen. The HSV-1 ELISA kit used in this study contains Purified HSV antigen coated on the surface of microwells. Diluted patient serum is added to wells. HSV-1 IgA-specific antibody, if present, binds to the antigen. The results are read by a microwell reader and compared in a parallel manner with the calibrator and controls. The screening of samples was done according to the kit manufacturer's instructions.

Statistical analysis

Data was analyzed using Chi-Square Calculator (<https://www.socscistatistics.com/tests/chisquare2/default2.aspx>). Pearson's chi-square test was performed at a 95% confidence interval and the significance level was accepted at $p < 0.05$.

Results

Out of the 87 samples tested for the presence of antibodies to HSV-1 and HIV, 76 (87.4%), and 30 (34.5%) were seropositive for HSV-1 and HIV respectively, while HSV-1/HIV co-infection rate was 26(29.9%). The prevalence of HSV, HIV and HSV-1/HIV co-infections in relation to age and sex are shown in **table (1)**. The study subjects were divided into 4 age groups as follows: Group I aged from 15 to < 25 years, group II aged from 25 to < 35 years, group III aged from 35 to < 45 years and group IV aged ≥ 45 years. The prevalence of HSV-1 was highest in group III (94.7%), and lowest in group I (80.9%) ($X^2(3, N = 86) = 1.86, p = 0.601$). Age groups I and III had the highest prevalence (47.4%) of HIV ($X^2(3, N = 86) = 4.96, p = 0.174$). The co-infection seroprevalence rate of HSV-1/HIV was highest in the age group ≥ 45 years (47.4%) while the age group 15-24 years had the lowest co-infection seroprevalence rate of 14.3% ($X^2(3, N = 86) = 7.52, p = 0.057$). Of the 37 males and the 50 females tested, 34(91.7%) and 42(84.0%) were seropositive for HSV-1 respectively. Also, of the 37 males and the 50 females tested, 11(29.7%) and 19(38.0%) were seropositive for HIV respectively. The coinfection rate of HSV-1/HIV among male and female subjects was 9(24.3%) and 17(34.0%) respectively. There is no significant association between the prevalence of HSV/HIV co-infection ($p > 0.05$) among the sexes ($X^2(3, N = 86) = 1.19, p = 0.273$). While the marital status ($p > 0.05$) (**Figure 1**) of the study participants was not statistically significant ($X^2(3, N = 86) = 2.47, p = 0.289$), the level of education ($p < 0.05$) ($X^2(3, N = 86) = 16.9, p = 0.001$) among the study participants was statistically significant (**Figure 2**).

Table 1. HSV-1/HIV co-infections in clients visiting Faith Alive Foundation Hospital, Jos, Nigeria in relation to age and sex.

		HSV-1	HIV	HSV-1/HIV
Variable	No. tested	No. (%) positive	No. (%) positive	No. (%) positive
Age group (years)				
15-24	21	17(80.9)	5(23.8)	3(14.3)
25-34	28	24(85.7)	7(25.0)	6(21.4)
35-44	19	18(94.7)	9(47.4)	8(42.1)
≥45	19	17(89.5)	9(47.4)	9(47.4)
Total	87	76(87.4)	30(34.5)	26(29.9)
Sex				
Male				
15-24	5	4(80)	2(40.0)	1(20)
25-34	7	6(85.7)	2(28.6)	2(28.6)
35-44	13	13(100)	4(30.8)	3(23.1)
≥45	12	11(91.7)	3(25.0)	3(25.0)
Total Male	37	34(91.7)	11(29.7)	9(24.3)
Female				
15-24	16	13(81.3)	3(18.8)	2(12.5)
25-34	21	18(85.7)	5(23.8)	4(19.0)
35-44	6	5(83.3)	5(83.3)	5(83.3)
≥45	7	6(85.7)	6(85.7)	6(85.7)
Total Female	50	42(84.0)	19(38.0)	17(34.0)

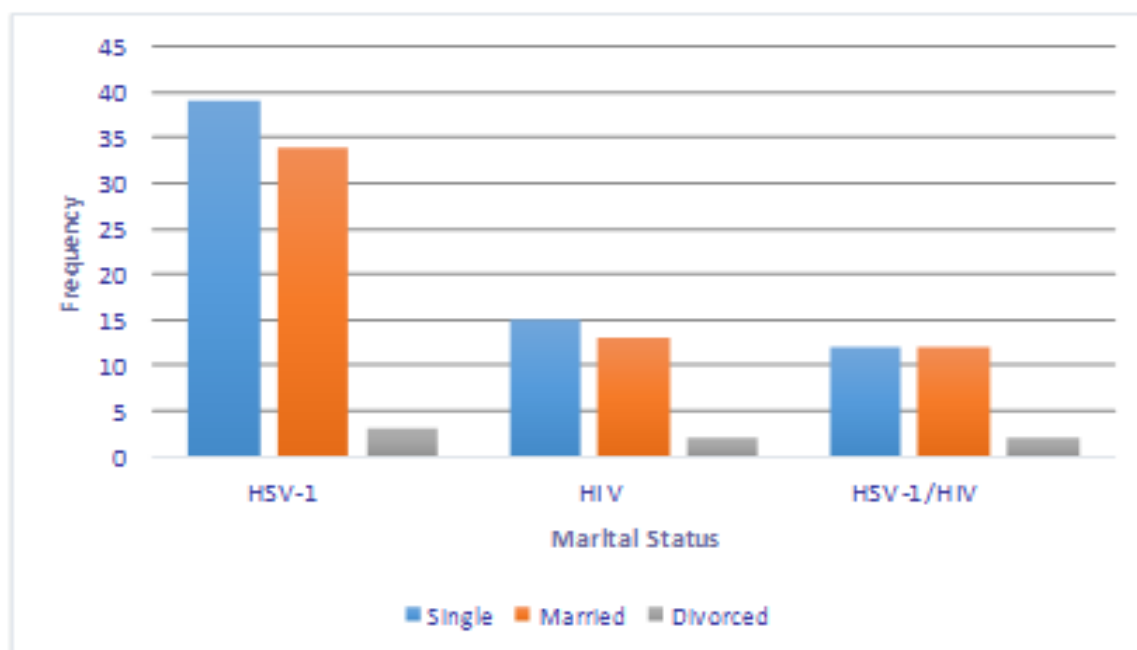
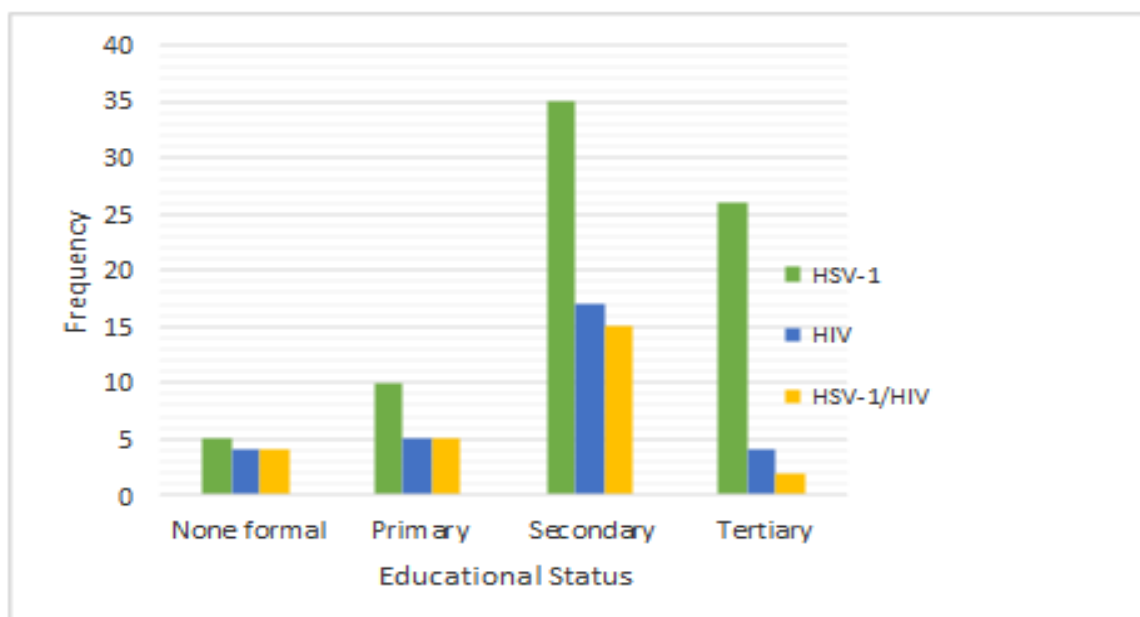
Figure 1. HSV-1, HIV and HSV-1/HIV Co-infections in clients visiting Faith Alive Foundation Hospital, Jos, Nigeria in relation to Marital Status.

Figure 2. HSV-1, HIV and HSV-1/HIV Co-infections in clients visiting Faith Alive Foundation Hospital, Jos, Nigeria in relation to educational status.



Discussion

The prevalence of HSV infection worldwide has increased over the last several decades, making it a major public health concern. Both HSV-1 and HSV-2 are known to cause a wide range of infections from isolated mucocutaneous lesions to disseminated infections (for example, blindness, and encephalitis) in all age groups [15]. In immune-compromised hosts such as HIV/AIDS, infections can cause life-threatening complications. Management of infections caused by HSV-1 requires prompt recognition as well as early initiation of therapy to avoid possible complications [5]. Therefore, assessment of HSV-1 antibody status is key to developing population-based treatment and disease prevention strategies [2, 16-17].

In this study, HSV-1 had a high seroprevalence rate confirming the endemicity of this viral infection in Nigeria and an increase in the prevalence rate from 4.3% in 1994 [9] to 87.3% is of great concern. The HSV-1 seroprevalence rate in this study is higher than that reported in other parts of the world. For instance, 78.6%, 51%, 60.4% and 52% of HSV-1 seroprevalence have been reported among attendees at sexually transmitted disease (STD) clinics in the USA [18], Norway [19], the United Kingdom [20] and the Netherlands [21] respectively. However, 46.1% and 55.4% HSV-1 seroprevalence rate has been reported among blood donors in the United Kingdom [20] and a

population-based cohort in Japan respectively [22]. In general, the seroprevalence of HSV-1 in Africa, Europe and Asia has been shown to remain high [23-25]. A high prevalence of HSV-1 antibodies among attendees at STD clinics is common because they constitute the risk group but in a population-based cohort in this study, may be of public health importance. This is because type-specific seroprevalence studies aid in determining the public health impact of genital herpes [4]. In addition, people who lack HSV-1 antibodies are three times more prone to a symptomatic HSV-2 infection [7, 22,26,27] which is capable of accelerating the progression and infectiousness of HIV [11]. Several reports have revealed a strong association between HSV-1 and genital herpes [2, 21, 27-30]. In support of these reports, other studies have demonstrated that genital herpes is the most potent sexually transmitted infection co-factor in the spread of HIV [31, 32].

The co-infection rate of HIV and HSV-1 in the present study compares favourably with a previous report by Hill et al. [33]. HSV-1 was the most common co-infected virus (88%) with HIV-1 and 2 amongst homosexual men attending a sexual health clinic in England and Wales [19]. In this study, HSV-1 and HIV co-infection ($p > 0.05$) among males and females was in consonance with Cowan et al. [20] and Hill et al. [33]. However, in the same environment as this study, a low co-infection rate (2.8%) between HSV-2 and HIV was

obtained by **Mawak et al.** [34]. In that report, both HIV-1 and HSV-2 seroprevalence was slightly higher among females than males. The difference in the co-infection rate in both studies could be attributed partly to the mode of transmission of both viruses (HSV-1 is by both sexual and non-sexual contact while HSV-2 is exclusively by sexual route) and the sample size of 180 samples in that report compared to 87 in this study. Nevertheless, both viruses are distinct but belong to the same family, Herpesviridae, partially cross-protect individuals infected by either of the viruses and both cause genital herpes. In the current study, the co-infection rate ($p > 0.05$) of HSV-1 and HIV among the married was not significantly different from the singles in disagreement with **Lowhagen et al.** [27].

HSV-1/HIV seroprevalence significantly decreased with an increase in the level of education in the current study. Education remains a major determinant of living standards and the key to combating sexually transmitted diseases [35]. However, reports have shown that the proportion of genital herpes due to HSV-1 rather than HSV-2 is increasing particularly in young people indicating that the degree of sexual activity may play a greater role in the transmission of sexually transmitted diseases [23-2].

Although assessment for genital herpes and the exact period when both infections were acquired was beyond the scope of this study, most HSV-1 infections are asymptomatic and could undergo latency and reactivate when the host-parasite equilibrium is distorted. At the time of sample collection, the study population were apparently healthy and voluntarily visited the Screening Centre for counselling and HIV testing. It was difficult to ascertain whether HSV-1 predisposed these subjects to HIV infection. There is a need for an in-depth study to ascertain the role of HSV-1 in the epidemiology of genital herpes and its association with HIV infection in Nigeria.

Conclusion

Co-infection rate of both viruses was significantly higher in ≥ 35 years old females compared to younger age groups. HSV-1 and HIV seroprevalence was higher in singles compared with the married. The prevalence rate of both infections decreased with an increase in the level of education of the people. Therefore, the present study recommends screening and treating HSV-1 infections to reduce the severity of HIV infection in HIV positive individuals.

Conflict of interest

All authors declared no conflict of interest

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