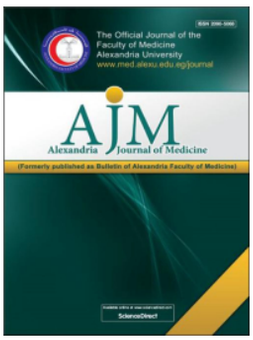

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Assessment of risk factors associated with HTLV-1/-2 infection among people living with HIV/AIDS in Bauchi State, Nigeria

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ABSTRACT

Introduction: Human T-cell lymphotropic virus (HTLV) is associated with shorter survival of HIV co-infected persons due to masked immunosuppression. Since both retroviruses share similar routes of transmission, there is a need to determine risk factors associated with these pathogens. This study aimed to assess the risk factors associated with HTLV-1/-2 and HIV co-infected among persons attending a secondary hospital in Ningi, Bauchi State, Nigeria.

Methods: Blood samples were collected from 182 HIV infected persons and analysed for anti-HTLV-1/2 IgM and IgG antibodies using commercial Enzyme-Linked Immunosorbent Assay (ELISA) kits. Interviewer-based questionnaire were used to collate sociodemographic and risk factor data of the subjects and clinical history were obtained from participants' medical records.

Results: The seroprevalence of anti-HTLV-1/-2 IgM and IgG were 9.9% and 19.8%, respectively. Out of the 80 ART-naïve, 25 (31.3%) were IgM seropositive. Out of 102 ART-experienced, 11 (10.8%) were anti-HTLV-1/-2 IgM positive. There was a significant association between ART status and seroprevalence of anti-HTLV-1/-2 IgM (p=0.009). However, there was no significance association between seroprevalence of HTLV IgM and gender of the subjects (p=0.06). There was a significant association between the seroprevalence of anti-HTLV-1/-2 IgG and education level of subjects (p=0.039). However, no association between anti-HTLV-1/-2 IgG and other sociodemographic variables studied (p> 0.05). History of injury from sharp objects (aOR: 5.3, p<0.0001) and consistent protective sexual practice (aOR: 2.27, p=0.033) were associated with seroprevalence of anti-HTLV-1/-2 IgM.

Discussion: High seroprevalence of HTLV-1/-2 and HIV co-infection was reported. ART status, protective sexual intercourse and injuries with sharp objects were identified risk factors of co-infection. It's recommended to consider HTLV screening for all HIV infected persons and vice versa.

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KEYWORDS
HIV coinfection; immunoassay; serosurvey; risk analysis

1. Introduction

Human T-cell lymphotropic virus (HTLV) is associated with shorter survival of HIV coinfected persons due to masked immunosuppression [1]. Coinfection of HTLV and HIV is common in areas endemic for HTLV because these viruses have similar transmission routes, such as unprotected sexual intercourse, breastfeeding, blood transfusion and organ/tissue transplantation, and injectable drug use [1]. Studies suggest that people living with HIV (PLWHIV) infected with HTLV-1 are more likely to develop myelopathies and neurological disease [2]. However, the effect of HTLV-2 in HIV-positive individuals is unclear [3]. In addition, coinfection may mask the diagnosis of acquired immunodeficiency syndrome (AIDS), since CD4 + T-cell counts significantly increase in affected persons [4,5].

In Africa, HTLV/HIV coinfection rates vary by countries, and studies showed a prevalence as high as 37% [6]. There is no report of HTLV/HIV coinfection rates in Northeastern Nigeria. However, there are a few seroprevalence reports from different study populations with peculiar risk factors of HTLV infection. For instance, a seroprevalence of HTLV of 3.2% was reported among pregnant women in Zaria, Nigeria [7]. Surprisingly, in 2015, none of the 300 blood donors studied had HTLV-1 antibody [8]. In Ilorin anti-HLTV-1/2 IgM seroprevalence of 25.7% was reported among HIV infected persons [6].

To prevent HTLV-1/-2 transmission during blood transfusion, screening of blood donation for HTLV-1/-2 infection has been implemented in several developed nations [9]. Mother-to-infant transmission, particularly through breastfeeding; sexual transmission, mainly heterosexually; and parenteral transmission through injection drug use and percutaneous injuries during tattooing seem to be the major routes of transmission for HTLV-1/-2 and it varies in different geographic locations [9]. Because most persons seropositive for HTLV-1/-2 are those <30 years old and in high endemic regions, it is

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believed that unprotected sexual intercourse serves an important route of transmission in these patients [10].

The fight against endemic diseases is a constant challenge in Nigeria, particularly in the Northeastern geopolitical zone, because primary and secondary health-care services are grossly inadequate and deficient in meeting the needs of the citizens. The social condition of the population of Northwestern Nigeria is characterized by underdevelopment, poverty, low education, and limited infrastructure, all due to over 10 years of ongoing security challenges characterized by war.

A seroprevalence of 4.9% HTLV-1 was reported in the study on ART-naïve HIV infected attending the University of Abuja Teaching Hospital [11]. However, the study did not differentiate the various categories of infection using IgG and IgM and did not determine risk factors associated with the HIV/HTLV coinfections. To be built on this, the present study aimed to determine the seroprevalence and risk factors of HTLV-1/-2 among HIV infected persons attending General Hospital Ningi, Bauchi State, Northeastern Nigeria.

2. Materials and methods

2.1. Study area and population

This hospital-based, cross-sectional study consisted of 182 (76 males and 106 females) HIV infected subjects (ART-Naïve and Experienced) of different age groups (mean±SD: 31.2 ± 12.9 years) attending the General Hospital Ningi, Bauchi State, North-Eastern Nigeria. The subjects were divided into two study groups viz; 80 (44.0%) ART-naïve and 102 (56.0%) ART-experienced. The sample size was determined from a previous cross-sectional study that reported 4.9% seroprevalence of HTLV among HIV infected person in Abuja, Nigeria [11], a minimum sample size of 73 was calculated. However, to improve the statistical credence of the study, the size was increased to 182 voluntary participants.

2.2. Ethical consideration

The study was conducted in accordance with the Declaration of the Helsinki and had its ethical aspects evaluated and approved (Reference Number MOH/GEN/S/1409/I) by the Human Ethical Research Committee of the Ministry of Health, Bauchi State, Nigeria. All subjects have signed a written informed consent.

2.3. Clinical history of the subjects

With the permission of the physicians, subjects' clinical information was obtained from their hospital record files. Only confirmed HIV seropositive subjects (ART-naïve and experienced), voluntarily willing to participate were randomly enrolled in the study.

2.4. Sample collection and preparation

Five milliliters (5 ml) of whole blood samples was collected aseptically and spun at 12,000/g for 10 min to harvest their serum samples for HTLV-1/2 serological tests. Samples were collected from May 7 to October 10, 2018. Blood samples were analyzed consecutively within 1 h of collection.

2.5. Laboratory analytical procedures

2.5.1. Enzyme-linked immunosorbent assay for anti-HTLV IgM and IgG antibodies

Indirect anti-HTLV-1/2 IgM (product code: SL2422Hu) and IgG (product code: SL2421Hu) ELISA were carried out according to the description and instructions by kits manufacturer (Sunlong Biotech ®, China).

2.5.2. Statistical analysis

All generated data were analyzed using SPSS software version 26.0 (IBM California, USA). The prevalence of HTLV-1 and −2 was expressed in simple proportions and percentages for the study groups. Chi-square contingency table was used to determine the associations between seroprevalence of HTLV-1/-2 infections and risk factors of infection. A confidence interval of 95%, p-values <0.05 were considered statistically significant.

3. Results

The seroprevalence of anti-HTLV-1/-2 IgM and IgG was 9.9% and 19.8%, respectively. Female subjects comprised 106 (58.2%), whereas 76 (41.8%) were males. After ELISA screening for anti-HTLV-1/-2 IgM, 20 (26.3%) males and 16 (15.1%) females were seropositive. Out of the 80 (44.0%) ART-naïve, 25 (31.3%) were IgM seropositive. Whereas, out of 102 (56.0%) ART-experienced, 11 (10.8%) were anti-HTLV-1/-2 IgM seropositive. There was a significant association between ART status and seroprevalence of anti-HTLV-1/-2 IgM (p = 0.009). However, there was no significant association between seroprevalence of HTLV IgM and the gender of the subjects (p = 0.06) (Table 1).

The mean age of the subjects was 31.2 ± 12.9 years with a range between 12 and 80 years. Anti-HTLV-1/-2 IgG was highest among subjects within 15–24 years (20.0%) and least among those within 24–35 years (4.2%). Those without formal education had the highest seroprevalence of anti-HTLV-1/-2 IgG (18.2%). Subjects who were married had the highest anti-HTLV-1/-2 IgG (11.8%). Persons with the high-income category (>150 USD per month) had the highest seroprevalence of ant-HTLV-1/-2 IgG (33.3%). There was a significant association between the seroprevalence of anti-HTLV-1/-2 IgG

Table 1. Prevalence of HTLV-1 and -2 among HIV patients tested.

Characteristics	No. screened	No. (%) negative For HTLV IgM	No (%) positive For HTLV IgM	p-value
Sex				
Male	76	56 (73.7)	20 (26.3)	
Female	106	90 (84.1)	16 (15.1)	
Total	182	146 (80.2)	36 (19.8)	0.0636
ART Status				
ART-naïve	80	55 (68.7)	25 (31.3)	
ART-experienced	102	91 (89.2)	11 (10.8)	
Total	182 (100)	146 (80.2)	26 (19.8)	0.0009

Table 2. Distribution of anti-HTLV IgG by sociodemographic characteristics of study participants.

Variables	Observation	No. tested	No. anti-HTLV IgG positive (%)	p-value
Age range (years)	<15	10	2 (20.0)	
	15–24	54	6 (11.1)	
	25–34	48	2 (4.2)	
	35–44	42	4 (9.5)	
	>44	28	4 (14.3)	
	Total	182	18 (9.9)	0.461
Educational level	No formal education	76	12 (18.2)	
	Primary	24	0 (0.0)	
	Secondary	43	2 (4.7)	
	College	30	4 (13.3)	
	Total	182	18 (9.9)	0.039*
Marital status	Single	25	2 (8.0)	
	Married	119	14 (11.8)	
	Divorced	24	2 (8.3)	
	Widow/widower	14	0 (0.0)	
	Total	182	18 (9.9)	0.537
Income per month (USD)	<50	142	14 (9.9)	
	50–150	34	2 (5.9)	
	>150	6	2 (33.3)	
	Total	182	18 (9.9)	0.116

* indicates significant association between the variables.

and the education level of subjects (p = 0.039). However, no association existed between HTLV-1/-2 and other sociodemographic variables studied (p> 0.05) (Table 2). History of injury from sharp objects (p < 0.0001) and consistent protective sexual practice (p = 0.033) was the only risk factor associated with seroprevalence of acute HTLV-1/-2 (p < 0.0001) (Table 3).

4. Discussion

In the last decade, HTLV infection is becoming a pathogen of significant public health concern, especially in areas of high endemicity where seroprevalence of more than 2% exists [12]. In this study seroprevalence of anti-HTLV-1/-2 IgM and IgG recorded were 9.9% and 19.8%, respectively. Even though none of the HTLV/HIV coinfected persons had clinical leukemia at the time of this study, HTLV/HIV coinfection, T-cell leukemia, and neurological diseases are more likely to be diagnosed in future. Probably due to the absence of or non-adherence (defaulters) to ART regimen that improves patients' immunity and perhaps anti-retroviral resistance [13]. Hence, persons with HIV and HTLV coinfections should be closely monitored for likely complications associated with HTLV infection.

The prevalence rate of 19.8% for recent HTLV-1/-2 infection in HIV/AIDS patient reported in this study was lower than 25.7% HTLV −1/-2 IgM seroprevalence reported by Adeoye et al. [6]. However, IgM seroprevalence was significantly higher than 4.9% seroprevalence of HIV–1/HTLV co–infection in Abuja [11], and 1.8% HTLV/HIV–1 coinfection in KwaZulu–Natal by Rego et al. [14] and 5.2% HTLV/HIV coinfection prevalence in Guinea–Bissau [15]. The difference is most likely due to the difference in the laboratory protocol in detecting HTLV. Nucleic acid amplification tests were used to diagnose HTLV in these studies, whereas antibody detection was solely

Table 3. Risk factors of anti-HTLV-1/-2 IgM among study participants.

Variables	Observation	No. tested	IgM positive (%)	aOR	p-value
History of blood transfusion	Yes	42	8 (19.0)		
	No	140	28 (20.0)		
	Total	182	36 (19.8)	0.9412	0.8919
Injection drug use	Yes	59	12 (20.3)		
	No	134	24 (17.9)		
	Total	182	36 (19.8)	1.1702	0.6901
Number of sex partners	None	56	8 (14.3)		
	Single	86	20 (23.2)		
	Double	25	4 (16.0)		
	>2	15	4 (26.7)		
	Total	182	36 (19.8)	NA	0.494
Consistent protective sexual practice	Yes	54	16 (29.6)		
	No	128	20 (15.6)		
	Total	182	36 (19.8)	2.2737	0.0328*
Scarification Mark	Yes	76	12 (15.7)		
	No	106	24 (22.6)		
	Total	182	36 (19.8)	0.6406	0.2546
History of injury from sharp objects	Yes	64	24 (37.5)		
	No	118	12 (10.2)		
	Total	182	36 (19.8)	5.3000	<0.001*

Key: NA = Not available, aOR = Adjusted Odd ratio.
* indicates significant association between the variables.

used in ours, due to its readily available in low- and middle-income countries such as Nigeria. The relatively high IgM seroprevalence reported in this study can be attributed to high regional endemicity, high-risk behaviors, and varied routes of HTLV exposure.

In our study, the highest prevalence of anti-HTLV-1/-2 IgG was highest among subjects within 15–24 years (20.0%) and least among those within 24–35 years (4.2%). This agreed with findings of Nasir et al. [11] who reported the highest prevalence of HTLV–1 among the age group 21–30 years. This could be because this population age range represents the leading sexually active age group in Nigeria. Besides, there is an assumption that the accumulation of sexual exposures with age in men with multiple sexual partners might have contributed to the findings obtained in this study [5].

There was a significant association between educational level and seroprevalence of anti-HTLV-1/-2 IgG. Indeed, level of education has long been considered an indicator of socioeconomic status, with advance educational exposure being one of the main factors that improve people's knowledge and perception of the health implications of preventive measures of infectious diseases including those of HIV/AIDS [1]. Although subjects without formal education had the highest seroprevalence of anti-HTLV-1/-2 IgG (18.2%), those with a college education had high HTLV-1/-2 IgG seroprevalence. This finding demonstrates that the population profile reflects cultural, sociodemographic, and behavioral differences, thereby influencing an individual's exposure to risk factors.

ART-naïve HIV infected person had a significantly higher seroprevalence of anti-HTLV-1/-2 IgM. This difference could be because patients who were on ART could have been experiencing subtle immunosuppression which might have increased their risk of contracting detectable HTLV, which reflected with the higher anti-HTLV IgM seropositivity in this category of subject. This justifies the new guidelines for Adults Living with HIV/AIDS that recommend the initiation of ART regardless of CD4 + T-cell count and the patient's symptoms [16] According to this protocol, the time between diagnosis of HIV infection and the initiation of ART tends to be lower, as observed in the present study, where 44.0% were ART naïve.

Even though no significant association between HTLV-1/-2 IgM seroprevalence and Injectable drug use. Injectable drug users had a higher prevalence of HTLV-1/-2 IgM. However, unprotected sexual practice was significantly associated with seroprevalence of HTLV-1/-2. Intravenous drug use is an important risk factor for infection with HIV [17]. Studies indicate that PLWHIV are at a high risk for HIV transmission through unsafe practices such as sharing non-sterile injecting equipment and unprotected sex. HIV infected persons often engage in more high-risk sexual behavior with multiple partners. This can transfer HTLV within the population and extend or prolong the generalized epidemic [18].

Globally, the highest prevalence of HTLV/HIV coinfection documented was 52% from an Iranian study [19]. This could possibly be due to the high rates of drug addiction and injection drug use, in addition to other risky behaviors such as needle sharing, tattooing, and multiple sexual partners. However, the lowest prevalence recorded was 0.0% was from Scotland [20]. Perhaps, this could be due to free needles and syringes policies which were made available to people who live with HIV/AIDS, thereby reduce needle sharing among people [21].

5. Conclusion

High seroprevalence of HTLV-1/-2 and HIV coinfection was reported. ART status, protective sexual intercourse, and injuries with sharp objects were identified risk factors of coinfection. Infected patients require monitoring for possible clinical manifestations, especially leukemia, and neurological diseases. It is recommended to consider HTLV screening for all HIV infected persons and vice versa.

Disclosure statement

No potential conflict of interest was reported by the authors.

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