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International Journal of Infectious Diseases

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Community-based intervention is necessary for the control of HIV in North-Central Nigeria

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ARTICLE INFO

Article history: Received 3 November 2011 Received in revised form 23 September 2012 Accepted 26 September 2012

Corresponding Editor: Mark Holodniy, California, USA

Keywords:
HIV
Prevalence
Cross-sectional
Logistic regression

North-Central Nigeria

SUMMARY

Objectives: To determine factors associated with the observed high prevalence of HIV in North-Central Nigeria.

Methods: In a cross-sectional multisite study conducted in 2007, behavioral, medical, and demographic data were obtained from pregnant women (N = 1011) who were tested for the presence of antibody against HIV-1 and HIV-2.

Results: The overall prevalence of HIV-1 in the 1011 women included in the study was 10.3% (95% confidence interval (CI) 8.4–12.2). In the multivariate analysis, HIV-1 seropositivity was significantly associated with women from the Makurdi (odds ratio (OR) 31.3, 95% CI 3.8–255.7) and Minna (OR 15.4, 95% CI 1.7–135.1) sites in comparison with Panyam site. The presence of tuberculosis (OR 10.7, 95% CI 2.4–48.3) was also significantly associated with HIV-1 seropositive status. Factors associated with HIV-1 also differed between sites. The presence of antibody against HIV-2 was not observed.

Conclusions: The high HIV-1 prevalence observed in this study corroborates previous observations in North-Central Nigeria. Disparity in the prevalence across communities was also seen. This is the only detailed socio-epidemiological and behavioral study that has explored potential factors associated with HIV-1 in North-Central Nigeria, and it revealed that differences in risk factors explain the disparity in prevalence across communities.

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1. Introduction

Nigeria is the most populous country in Africa, ¹ and as a result of its huge population, even with the relatively low HIV prevalence of 4.1%, it currently has the second largest number (3.1 million) of people living with HIV in the world. ² In terms of prevalence, the burden of HIV in Nigeria varies between the different regions, states, and communities, but no community is free from this disease. ^{1,3,4} Over time, North-Central Nigeria, which consists of six states and the Federal Capital Territory (FCT), has come to have the highest HIV prevalence among the six geopolitical zones of Nigeria. ^{2,5} Factors explaining the high prevalence in this geopolitical zone were not documented even at the time of the 2010 sentinel survey, but detailed socio-epidemiological and behavioral studies were recommended. ^{2,5} For effective control, the risk factors

associated with HIV in the population must be understood.⁶ Thus this study was carried out in response to the recommendations of the sentinel survey, to assess factors associated with HIV-1 and HIV-2 prevalence in the North-Central geopolitical zone in 2007.

2. Methods

2.1. Participants and study sites

A cross-sectional study was conducted on pregnant women utilizing antenatal clinics between August 2007 and November 2007. The study was conducted on people residing in the zone at the time of the study, regardless of their being indigenes of the zone or not. Of the seven states in North-Central Nigeria, four – Benue, FCT, Niger, and Plateau – were randomly selected. Benue State was randomly selected to provide an urban site (population of 20 000 people and above); alternating the states alphabetically, FCT and Plateau State were chosen to provide rural sites (population of less than 20 000 people), while Niger State was

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the second urban site. The population of pregnant women in the national sentinel survey was adopted. Due to limited resources, this is considered the most practical group to study. 1.2.5 In each state, the first rural or urban site on the list of sites used for the 2005 HIV/syphilis sentinel survey was also used for this study. The public health facilities/hospitals providing antenatal care for pregnant women at the sites used for the 2005 HIV/syphilis sentinel survey were also adopted. The site selection criteria for the 2005 HIV/syphilis sentinel survey were as follows: 5 (1) availability of functional antenatal clinic services with qualified staff; (2) provision of healthcare services to relatively large numbers of antenatal clinic attendees per week, so that an adequate sample size can be obtained; (3) catchment population comprising varied demographic groups; (4) performance of routine laboratory tests; and (5) experience of conducting similar surveys.

Thus the antenatal clinics at the following facilities were involved: Federal Medical Centre, Makurdi, Benue State; Bwari General Hospital, Bwari, FCT; General Hospital, Minna, Niger State; and the Church of Christ in Nigeria Community Development Program Hospital, Panyam, Plateau State. It is important to note that facilities at rural sites provide services to people residing nearby regardless of whether they reside in rural or urban settlements, and so do the facilities at urban sites. Therefore there is a representation of both types of settlement at both rural and urban sites. The states of origin of the participants were diverse and thus the study subjects were further grouped into geopolitical zones of origin for better statistical analysis. It should be noted that a participant residing in a rural settlement might attend a clinic in an urban site, usually because the clinic is nearer or due to individual preferences, and vice versa.

2.2. Procedures and measures

A self-administered, structured questionnaire was completed by each woman to collect data on their behavioral, medical, and demographic characteristics. In the case where the woman was illiterate, a research assistant interviewed the woman in English or in the Hausa language to complete the questionnaire appropriately. This difference in data collection between the literate and illiterate women could be a limitation to the study, because the illiterate women may have given false responses due to privacy reasons.

The behavioral characteristics recorded were the total number of sexual partners ever had and the number of sexual partners in the past 12 months. The medical characteristics recorded were the number of previous pregnancies, abortions/miscarriages, number of living children, history of blood transfusion, presence or absence of frequent diarrhea in the past 6 months, history of tuberculosis (TB), and presence or absence of symptoms of sexually transmitted diseases (STD; presence of foul smelling or colored or abnormal vaginal discharge).

The demographic characteristics recorded were marital status, family type (monogamous or polygamous), age, age at first marriage, number of wives in the family, occupation, spouse's occupation, educational status, residence, type of accommodation (shared house, flat/bungalow, or duplex), ownership of accommodation (self/spouse, rented, or official), income, and state of origin. Skilled occupation was defined as an occupation that requires at least a secondary school education or 2 years of professional training.

Venous blood was tested for HIV using two rapid tests, in accordance with the national guidelines on the prevention of mother-to-child transmission of HIV in Nigeria. Determine HIV-1/2 (ABBOTT Laboratories) was used as a screening test, and positive samples were confirmed using Shantest HIV Triline (WB) Rapid Test (Shanta Biotechnics Ltd, Hyderabad, India). There was no intermediate result.

2.3. Data analysis

All statistical tests were two-sided and a *p*-value of less than 0.05 was considered statistically significant. The Chi-square test of association was used for the analysis of categorical data and the *t*-test was used for continuous data. Confidence intervals of proportions were determined using the modified Wald method.⁹ Univariate and multivariate logistic regression was used to assess factors associated with HIV-1. The analysis was also stratified by site (i.e., Makurdi site and non-Makurdi sites) because there was a wide variation in HIV prevalence between the Makurdi and non-Makurdi sites. Data from the non-Makurdi sites could not be analyzed individually due to the low prevalence and relatively small sample size. Variables that were statistically significant in the univariate model were included in the multivariate model, however this was not applied to the analysis done by site.

The statistical analysis was carried out using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Characteristics of the participants

A total of 1011 women attending antenatal clinics were approached, consented to participation (none refused), and were recruited: 234 from Bwari, 420 from Makurdi, 254 from Minna, and 103 from Panyam. Table 1 gives comprehensive details of the clinical and socio-demographic characteristics of these women. The women involved in the study had a mean (standard deviation (SD)) age of 26.5 (\pm 5.3) years and a mean (SD) age at first marriage of 21.2 (\pm 4.4) years. Most (62.8%) women were living in urban settlements and most had at least a secondary school education (71.5%); 67.5% had an unskilled occupation. The mean (SD) numbers of pregnancies, abortion/miscarriages, and children the women had were 2.4 (\pm 2.1), 0.5 (\pm 0.8) and 1.7 (\pm 1.7), respectively.

3.2. HIV-1 prevalence among the participants

The overall prevalence of HIV-1 in the 1011 women included in the study was 10.3% (n = 104) (95% confidence interval (CI) 8.4–12.2). The HIV-1 prevalence by site varied widely (Figure 1), from as low as 1.0% (95% CI <0.01–5.8) in Panyam to as high as 17.9% (95% CI 14.45–21.8) in Makurdi. Bwari and Minna had similar prevalences of 5.6% (95% CI 2.6–8.5%) and 5.9% (95% CI 3.0–8.8%), respectively.

3.3. Factors associated with HIV-1: overall

In the multivariate analysis, HIV-1 seropositivity was significantly associated with women from the Makurdi (OR 31.3, 95% CI 3.8–255.7) and Minna (OR 15.4, 95% CI 1.7–135.1) sites in comparison with Panyam site. The presence of tuberculosis (OR 10.7, 95% CI 2.4–48.3) was also significantly associated with HIV-1 seropositive status (Table 2).

3.4. Factors associated with HIV-1: Makurdi site

At the Makurdi site, HIV-1 seropositivity was significantly associated with having had an abortion or miscarriage (OR 4.6, 95% CI 1.1–19.9). Other factors were not statistically significant. (For full details see the **Supplementary Material**, Table S1.)

3.5. Factors associated with HIV-1: non-Makurdi sites

Combination of the data from all the sites excluding Makurdi showed that HIV-1 seropositive status was significantly associated

 Table 1

 Socio-demographic and clinical characteristics of the participants (N=1011)

Characteristic	Makurdi (n = 420)	Bwari (n = 234)	Minna (n = 254)	Panyam (<i>n</i> = 103)	All (N=1011)
HIV-1 prevalence	75 (17.9)	13 (5.6)	15 (5.9)	1 (1.0)	104
Socio-demographics	, ,	, ,	, ,	, ,	
Age group, years (N=944)					
15–19	17 (4.5)	12 (5.3)	24 (9.8)	5 (5.1)	58
20–24	101 (27.0)	64 (28.2)	79 (32.4)	32 (32.3)	276
25–29	138 (36.9)	79 (34.8)	84 (34.4)	32 (32.3)	333
30–34	83 (22.2)	54 (23.8)	43 (17.6)	15 (15.2)	195
≥35	35 (9.4)	18 (7.9)	14 (5.7)	15 (15.2)	82
Age at first marriage, years, mean (SD) (N=971) Zone (N=984)	22.1 (4.5)	22.4 (4.2)	18.8 (4.0)	20.7 (2.8)	21.2 (4.4
North-Central	321 (78.5)	85 (37.4)	187 (75.7)	100 (99.0)	693
North-East	9 (2.2)	12 (5.3)	1 (0.4)	0	22
North-West	9 (2.2)	38 (16.7)	30 (12.1)	0	77
South-East	49 (12.0)	39 (17.2)	9 (3.6)	1 (1.0)	98
South-South	16 (3.9)	40 (17.6)	6 (2.4)	0	62
South-West	5 (1.2)	13 (5.7)	14 (5.7)	0	32
Marital status (N=1001)					
Married	404 (98.3)	233 (99.6)	252 (99.6)	102 (99.0)	991
Separated	1 (0.2)	0	1 (0.4)	0	2
Single	4 (1.0)	1 (0.4)	0	0	5
Widowed	2 (0.5)	0	0	1 (1.0)	3
Number of wives husband has (N=973)					
1	354 (90.3)	215 (92.3)	171 (69.2)	88 (87.1)	828
2	34 (8.7)	16 (6.9)	59 (23.9)	12 (11.9)	121
3	2 (0.5)	1 (0.4)	13 (5.3)	1 (1.0)	17
>3	2 (0.5)	1 (0.4)	4 (1.6)	0	7
Level of education (N=908)					
No education	9 (2.3)	6 (2.7)	1 (0.5)	1 (1.0)	17
Quranic	1 (0.3)	0	21 (10.9)	0	22
Primary	87 (22.1)	45 (20.4)	52 (27.1)	36 (35.6)	220
Secondary	154 (39.1)	109 (49.3)	86 (44.8)	58 (57.4)	407
Post-secondary	143 (36.3)	61 (27.6)	32 (16.7)	6 (5.9)	242
Residence (N=967)					
Rural	46 (12.0)	207 (88.5)	9 (3.7)	98 (95.1)	360
Urban	338 (88.0)	27 (11.5)	237 (96.3)	5 (4.9)	607
Occupation (N=952)	100 (00 0)			0.4.(00.0)	
Housewife	120 (30.0)	82 (35.7)	113 (51.4)	34 (33.3)	349
Unskilled worker	118 (29.5)	67 (29.1)	57 (25.9)	52 (51.0)	294
Skilled worker	162 (40.5)	81 (35.2)	50 (22.7)	16 (15.7)	309
Spouse occupation (N=921)					
Unskilled worker	130 (37.2)	74 (32.2)	131 (54.6)	79 (77.5)	414
Skilled worker	219 (62.8)	156 (67.8)	109 (45.4)	23 (22.5)	507
Accommodation (N=965)	10 (10)	2 (4 2)	5 (2.0)	4 (4.0)	25
Duplex	16 (4.2)	3 (1.3)	5 (2.0)	1 (1.0)	25
Flat	141 (36.8)	74 (31.9)	50 (20.2)	14 (13.6)	279
Compound	226 (59.0)	155 (66.8)	192 (77.7)	88 (85.4)	661
Accommodation ownership (N=973)	24 (27)	40 (5.0)	40 (7.0)	2 (2.0)	68
Official	34 (8.7)	13 (5.6)	18 (7.3)	2 (2.0)	67
Personal	104 (26.7)	45 (19.3)	108 (43.5)	68 (66.7)	325
Rented	244 (62.6)	172 (73.8)	119 (48.0)	14 (13.7)	549
Squatting	8 (2.1)	3 (1.3)	3 (1.2)	18 (17.6)	32
Sexual and clinical characteristics					
Previous pregnancies (N=939)	90 (20.2)	AC (20.1)	20 (12 2)	0 (10.2)	165
No Yes	80 (20.2)	46 (20.1)	30 (13.3)	9 (10.2)	165
	317 (79.8)	183 (79.9)	195 (86.7)	79 (89.8)	774
Ever aborted or had a miscarriage (N=907)	220 (C0.0)	150 (70.7)	104 (02 C)	40 (57.1)	C21
No Voc	230 (60.8)	159 (70.7)	184 (83.6)	48 (57.1)	621
Yes	148 (39.2)	66 (29.3)	36 (16.4)	36 (42.9)	286
Have any living children (N=935) No	142 (36.0)	83 (36.6)	44 (19.6)	24 (27.0)	293
Yes	252 (64.0)	, ,	, ,	, ,	642
History of blood transfusion (N=989)	232 (04.0)	144 (63.4)	181 (80.4)	65 (73.0)	042
Yes	40 (10.1)	11 (4.7)	11 (42)	3 (2.9)	65
	, ,	` ,	11 (4.3)	, ,	
No Frequent diarrhea in the past 6 months (N=959)	358 (89.9)	223 (95.3)	243 (95.7)	100 (97.1)	924
Yes	8 (2.2)	0	1 (0.4)	0	9
	, ,		, ,		
No Lictory of TP (N=075)	360 (97.8)	234 (100.0)	253 (99.6)	103 (100.0)	950
History of TB (N=975)	7 (1 0)	1 (0 4)	1 (0.4)	1 (1 0)	10
Yes	7 (1.8)	1 (0.4)	1 (0.4)	1 (1.0)	10
No Deck above	377 (98.2)	232 (99.1)	253 (99.6)	101 (98.1)	963
Probably	0	1 (0.4)	0	1 (1.0)	2
Symptoms of STD (N=975)	125 (22.0)	CO (20.1)	E4 (04.0)	20 (27.2)	202
Symptoms No symptoms	135 (33.8)	68 (29.1)	51 (21.3)	28 (27.2)	282
1901 5 (111111/1111)	264 (66.2)	166 (70.9)	188 (78.7)	75 (72.8)	693

Table 1 (Continued)

Characteristic	Makurdi (n=420)	Bwari (n=234)	Minna (n=254)	Panyam (<i>n</i> = 103)	All (N=1011)
1	234 (63.9)	131 (56.5)	212 (89.8)	69 (68.3)	646
2	71 (19.4)	57 (24.6)	17 (7.2)	20 (19.8)	165
3	27 (7.4)	28 (12.1)	6 (2.5)	6 (5.9)	67
>3	34 (9.3)	16 (6.9)	1 (0.4)	6 (5.9)	57
Sex partners in past year $(N=948)$	• •	, ,	, ,	, ,	
1	359 (95.7)	229 (98.3)	237 (99.2)	99 (98.0)	924
>1	16 (4.3)	4 (1.7)	2 (0.8)	2 (2.0)	24

SD. standard deviation: STD. sexually transmitted disease: TB. tuberculosis.

with previous pregnancy (OR 25.3, 95% CI 1.5–423.5) and living in an official house compared to a rented house (OR 17.7, 95% CI 1.2–272.3). (Full details of the analysis of non-Makurdi sites are available as **Supplementary Material**, Table S2.)

4. Discussion

As expected, ^{1–3,5} this cross-sectional survey showed a relatively high HIV-1 seroprevalence of 10.3% and individual prevalence varied from one community to another. Of note, the observed prevalence was higher than that determined in the 2005 sentinel survey (6.1%)⁵ held before this study and higher than that found in the recent 2010 sentinel survey (7.5%).2 This difference in prevalence between our study and those of the sentinel surveys could be due to the fact that we explored a lesser number of sites and therefore a lesser population, since we adopted the same sampling approach, sites, and personnel for sampling. The discrepancy in prevalence from one site to another has previously been observed in Nigeria and among other African countries, and this could be due to the diversity in exposure to risk factors. 4,10,11 The very high prevalence witnessed in Makurdi is not surprising, as Benue State has always had an extremely high prevalence in this geopolitical zone. 1-3,5,8 Panyam on the other hand is a remote rural settlement, and a previous survey has shown that remote rural settlements in the country tend to have a low prevalence.⁵ These remote settlements may have a low prevalence because of the limited exposure to/interaction with neighboring communities, thereby limiting the inward spread of the epidemic. Furthermore practices such as prostitution, which can spread the epidemic

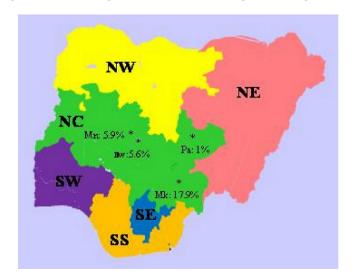


Figure 1. Map of Nigeria showing the geopolitical zones and sampling sites. The sampling sites are indicated with asterisks and the anti-HIV-1 antibody prevalence at each site is given as the percentage to one decimal place. (Sites: Bw, Bwari; Mk, Makurdi; Mn, Minna; Pa, Panyam. Geopolitical zones: NC, North-Central; NE, North-East; NW, North-West; SE, South-East; SS, South-South; SW, South-West.).

faster, are usually not practiced in such remote places, where virtually all the members of the community are known to each other. The absence of anti-HIV-2 antibody in this study corroborates the results of previous studies, 4.12 which have also reported the absence/low prevalence of HIV-2 in their cohorts.

Two characteristics – ever having TB and being from the Makurdi site – were found to be associated with anti-HIV-1 antibodies in North-Central Nigeria; this finding is also in agreement with previous observations. The observation on TB is logical since HIV predisposes to the acquisition of TB and has continually been associated with HIV in developing countries. The observation on the Makurdi site is in agreement with the sentinel studies showing that Benue State (the state in which Makurdi site is located) remains the state with the highest prevalence of HIV-1 in Nigeria. The observation of HIV-1 in Nigeria.

Although factors like having ever had an abortion, having symptoms of an STD, and having multiple partners, which are all indications of high-risk sexual activities, were not significantly associated with HIV-1 in our study after adjustments, previous studies both within and outside Nigeria have linked sexual activity to HIV transmission. 6,15-20 These associations necessitate education on safe sexual practices in order to curb the epidemic in affected communities, because high-risk sexual activities are a major route of HIV transmission.

An important factor that was also not significantly associated with HIV-1 serostatus in the adjusted model was a history of blood transfusion. Studies have observed anti-HIV-1 antibody prevalence of 3% to as high as 70% among healthy blood donors in different communities in Nigeria. ^{18,21,22} A study conducted in Nigeria has observed the presence of HIV antigen and cDNA among HIV-seronegative blood donors. ²³ Thus there is a high risk of HIV transmission through blood transfusion from non-seroconverted donors in the window period. This calls for critical scrutiny of the safety of blood transfusion in Nigeria. Proper screening of blood donors with the use of highly sensitive HIV nucleic acid-based assays and also a more efficient blood banking system to avoid last minute transfusions of potentially unsafe blood, are required.

Having frequent diarrhea and residing in an urban area have previously been associated with HIV serostatus. ^{17,24} However, these factors were not significantly associated with HIV serostatus in our study. Having frequent diarrhea is logical as the affected individuals may be immunocompromised as a result of the HIV infection, and living in an urban settlement in Nigeria might have an increased risk due to behavioral, lifestyle, and cultural differences when compared to the neighboring rural settlements.

Considering the Makurdi site scenario alone, a history of abortion was the only factor that was associated with HIV serostatus when adjusted for other factors. Other factors like ever having had a blood transfusion, history of TB, and having had symptoms of STD, which were found to be associated with HIV serostatus in an adjusted model, are similar to the findings observed in the main analysis in which all sites were combined. These results seem to infer that the study population at the Makurdi site might be similar to the whole study population with

Table 2Univariate and multivariate logistic regression of factors associated with HIV-1

Risk factor	Number of HIV-1-positive women/total number of women	HIV-1 prevalence	Univariate OR (95% CI)	Multivariate OR (95% CI)
Site				
Makurdi	75/420	17.9	22.2 (3.1–161.4) ^a	31.3 (3.8-255.7) ^a
Bwari	13/234	5.6	6.0 (0.8-46.5)	4.5 (0.6-35.5)
Minna	15/254	5.9	6.4 (0.8-49.1)	15.4 (1.7-135.1) ^a
Panyam	1/103	1.0	1.0 (ref.)	1.0 (ref.)
Residence				
Rural	27/360	7.5	1.0 (ref.)	
Urban	73/607	12.0	1.7 (1.06-2.7) ^a	0.4 (0.2-0.9)
Missing	4/44	9.1	=	
Abortion/miscarriage				
No	57/621	9.2	1.0 (ref.)	
Yes	40/286	14.0	1.6 (1.1-2.5) ^a	1.6 (0.9-2.6)
Missing	7/104	6.7	= '	
Blood transfusion				
Yes	18/65	27.7	$3.9(2.2-7.1)^a$	1.9 (0.9-4.3)
No	82/924	8.9	1.0 (ref.)	
Missing	4/22	18.2	- ` ´	
Diarrhea				
Yes	3/9	33.3	4.6 (1.1-18.5) ^a	2.2 (0.5-9.8)
No	94/950	9.9	1.0 (ref.)	
Missing	7/52	13.5	-	
Tuberculosis				
Yes	5/10	50.0	9.5 (2.7-33.3) ^a	$10.7 (2.4-48.3)^{a}$
No	92/963	9.6	1.0 (ref.)	,
Probably	0/2	0	= ' '	
Missing	7/36	19.4	-	
Symptoms of STD				
Symptoms	44/282	15.6	2.1 (1.4-3.1) ^a	1.6 (0.98-2.7)
No symptoms	57/693	8.2	1.0 (ref.)	, ,
Missing	3/36	8.3	- ` ´	
Number of sex partner	s in past year			
1	90/924	9.7	1.0 (ref.)	
>1	6/24	25.0	3.1 (1.2-8.0) ^a	1.4 (0.4-4.7)
Missing	8/63	12.7	- ` '	` ,

OR, odds ratio; CI, confidence interval; STD, sexually transmitted disease.

regards to exposure to HIV-1. However, other factors such as having an unskilled spouse, living in a shared house as opposed to living in a flat, and having a personal house as opposed to living in a rented apartment that were not observed as being significant in the main analysis, show that there are some peculiarities regarding the Makurdi site that distinguish it from the rest of the study population. These peculiarities which need to be further studied may also be responsible for the very high prevalence of 17.9% observed in Makurdi in comparison to the other sites. This difference for Makurdi is also supported by the fact that residing in urban settlements was found to be associated with HIV-1 serostatus in the whole study population and is in agreement with findings of a previous study.²⁴

Considering all the other sites together except Makurdi, two entirely different factors – having had a previous pregnancy and living in official quarters – were associated with HIV-1 serostatus. The disparities in factors associated with HIV-1 show the differences in the Makurdi and the non-Makurdi populations. Understanding these differences and addressing them will go a long way to decrease and stabilize the spread of HIV-1 in the country. Addressing these factors may be more influential in the control of HIV than promulgating various national health care policies that are not able to put individual community differences into consideration. ¹⁰

In conclusion, we found a high HIV-1 prevalence in North-Central Nigeria, and the factors associated with HIV-1 differed widely across the different study sites. Although some factors have been associated with the prevalence of HIV-1 in North-Central

Nigeria, the factors responsible for differences in prevalence in this geopolitical area as opposed to others cannot be inferred. This is because data are not available on the risk factors associated with HIV in other geopolitical zones. Thus, we suggest that similar studies should be carried out in other geopolitical zones. Furthermore, this study suggests identifying and addressing risk factors and factors associated with HIV-1 at the community level as the best way to control the high HIV prevalence in North-Central Nigeria, instead of the national health care policies that are not able to put individual community peculiarities into consideration.

Acknowledgements

HOA was supported by grants from Ahmadu Bello University Board of Research and the HIV Research Trust. The authors would like to thank the antenatal clinic clients who participated. This study involved the work of several people, including health care staff and laboratory technicians; the authors thank them for their dedication and hard work.

Ethical considerations: The study was approved by the institutional ethics review board of the Ahmadu Bello University Teaching Hospital, Zaria, Nigeria and the ethics boards/committees of the various facilities involved. Informed consent was received from each participant to have data and blood samples taken for this study.

Conflict of interest: None of the authors have any conflicts of interest to declare.

^a Significant at 0.05 level.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijid.2012.09.020.

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