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INITIAL SYMPTOMS AND LATE PRESENTATION OF HIV INFECTED PERSONS SEEN IN HIV CLINICS UYO, AKWA IBOM STATE

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ABSTRACT

Background: Recognition of HIV symptoms may be associated with the stage in which HIV infected persons, present at health facilities to seek care, this study aimed at describing the initial symptoms of People living with HIV (PLWHIV) and determine socio demographic characteristics associated with late presentation at the HIV clinics in Uyo.
Methods: This was a cross-sectional descriptive study carried out on PLWHIV at initial visits to either of the two HIV clinics in Uyo. Data was collected using a pre-tested interviewer administered questionnaire, while CD4 and clinical stage were obtained from the patients' folders.
Result: A total of 166 respondents were recruited over a period of four months, 67% of them were females and significantly younger than the males (p value=0.0039). The proportion of late presenters was 60%. Secondary level of education predicted late presentation compared to primary level (OR 5.6 P value= 0.004). PLWHIV whose length of time after diagnosis were between 1 to 3 months and those above 1 year were less likely to present late compared to those that presented within 1 month of diagnosis (OR 0.18, P value 0.03; OR 0.86 P value < 0.0001 respectively). Those who had no perception of illness were not likely to present late (OR 0.6; p value <0.0001). Fever (OR 3.9; P value 0.025), rashes (OR 5.4 P value 0.002) defined late presentation
Conclusion: With the high level of late presentation of PLWHIV to health facilities, Voluntary Counselling and Testing (VCT) need to be intensified at the community level and with the full implementation of the 'test and treat' policy, this situation may improve.

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection is known as the most detrimental infectious disease, with over 36 million people already infected globally;[1] about 70% of people living with the virus live in sub-Saharan Africa.[2] In Nigeria about four million people are living with the virus, which makes Nigeria the country with second highest burden of HIV in the world.[3] The 2013 National HIV/AIDS and Reproductive Health survey reported a national prevalence of 3.4% and 6.8% for Akwa Ibom State.[4] Despite the availability of free voluntary counseling and testing many people are not aware of their serostatus. A report showed that about 50% of people living with HIV (PLWHIV) in sub-Sahara Africa are not aware of their status.[5] Quite often, the fear of stigma and discrimination prevents people from accessing HIV screening service[6] and even the asymptomatic PLWHIVs would prefer to wait till they show symptoms before accessing care.

One of the determinants of treatment success, is the health status of the patient at the point of accessing care. Patients who present late for care are less likely to have good treatment outcomes, leading to high mortality rate among them.[7,8] In HIV infection, viral load increases when there is no treatment, which increases the risk of transmission and thus

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constitutes a huge threat to the society.[9] Symptoms are described as a person's perception of an abnormal physical, emotional and cognitive state and as the main reason why patients seek for health care.[10] The symptoms at the point of initiating care are not specific and they vary among different individuals depending on their level of immunity and the exposure to opportunistic infections.[11,12] Symptoms of advanced disease include persistent fever, oral thrush, persistent diarrhea, persistent rashes, severe weight loss and others symptoms of opportunistic infections.[13]

World Health Organization (WHO) categorized patients into four clinical stages based on the presenting symptoms. The European Consensus definition of late presentation is patients who present with WHO clinical staging 3, 4 or CD4 of less than 350cells/ml irrespective of the stage.[14] The clinical staging is to guide in the management of HIV in resource limited settings like Nigeria and other developing countries.[13] WHO came up with "test and treat all" policy in 2015 to fast track the achievements of HIV targets. The policy requires all individuals who test positive to HIV test should be commenced on antiretroviral treatment irrespective of their CD4 count or clinical stage.[15] WHO set a global target to provide antiretroviral therapy to 90% of all HIV positive individuals.[16] There is no study seen in the literature that had described self-reported symptoms and status of PLWHIV at the point of accessing care in Nigeria. Determining the proportion of HIV positive patients who presented late in our clinics may help health professionals to plan for appropriate care and treatment of advanced disease, and help to advice the program managers in resource allocations. The aim of this study was to identify the common self- reported symptoms of HIV patients at the initial visit to the HIV clinics in our locale and the socio demographic factors associated with late presentation.

MATERIALS AND METHODS

This was conducted in uyo, the capital city of Akwa Ibom State which is one of the oil producing states in the southern part of Nigeria; it has a population of 305,961 based on 2006 census.[17] There are two health facilities that offer comprehensive antiretroviral services in Uyo. These are University of Uyo Teaching Hospital (UUTH), a tertiary level health institution and St Luke Hospital Anua (SLHA), a public private secondary level facility. Most Primary health facilities and eight private hospitals in Uyo offer voluntary counseling and testing (VCT) and Prevention of Mother to Child transmission (PMTCT) services within the city.

This was a descriptive cross-sectional study of newly enrolled HIV positive patients, who presented in the HIV clinics of University of Teaching Hospital and St Luke Hospital, Anua. The minimum sample size calculated using the percentage of late presentation from a previous study 67%,[18] was adjusted to 165, based on 320, which was the estimated number of new patients seen over four months (71 and 9 new patients seen every month in SLHA and UUTH respectively). The adjusted sample size was proportionally allocated to UUTH and SLHA at a ratio of 1:8. All new patients who presented to both clinics were recruited consecutively over the period of four months, provided they gave informed written consent. However, patients with previous history of taking antiretroviral drugs and those with known history of tuberculosis, diabetes, hypertension and cancers were excluded from the study.

Data were collected by trained research assistants (Nurses and HIV volunteers working in the clinics), using a pre-tested interviewer administered structured questionnaire taken from WHOQOL-HIV BRIEF tool,[19] this study was a part of Quality of Life of HIV patients' study. The baseline CD4 count and the clinical staging of the patients were extracted from their folders as documented by the clinician after their enrolment into care. The data were entered, cleaned, verified and analyzed using Stata version 10.

The outcome variables

The clinical presentation was categorized into early and late using European Consensus Definition of Late Presentation. Early presentation was WHO Clinical stages 1 and 2 with CD4 above 350cells/ml, while late presentation was WHO Clinical stages 3 and 4 and /or CD4 count below 350cells/ml. The categorical variables were described using proportions while mean and standard deviation were used to summarize continuous variables. The proportions of the patients who presented with each symptoms was also determined. Chi square test was

used to determine association between variables while multivariate analysis was done for variables with p value< 0.2 at bivariate level

Ethical consideration:

Ethical clearance and approval were obtained from Ethical Review Committee of University of Uyo Teaching Hospital as well as the review committee of Akwa Ibom State Ministry of Health. Recruitment into the study was voluntary and the decision not to participate did not affect their treatment in any way. The participants were interviewed individually within an enclosure in the clinics for privacy, names of the respondents were not documented on the questionnaire to ensure confidentiality. A written Informed consent was obtained from each respondent.

TABLE 1: THE DISTRIBUTION OF THE SOCIO DEMOGRAPHIC CHARACTERISTICS AND SOME PARAMETERS OF THE RESPONDENTS

Variables	Sex n (%)		Total n (%) (n=166)	Statistical inference
	Male (n=55)	Female (n=111)		
Age (years)				
Less than 20	0 (0.0)	10 (9.0)	10 (6.0)	Df=4
21-30	20 (36.4)	57 (51.4)	77 (46.4)	P value=0.011+*
31-40	21 (38.2)	27 (24.3)	48 (28.9)	
41-50	13 (23.6)	15 (13.5)	28 (16.9)	
Above 50	1 (1.8)	2 (1.8)	3 (1.8)	Df=164 Ttest=2.9279
Mean Age (SD)	34.7 (7.6)	30.5 (9.2)	31.9 (8.9)	P value= 0.004+
Educational status				
No and Primary	14 (25.4)	36 (31.5)	50 (30.1)	Df=2
Secondary	26 (47.3)	34 (30.6)	60 (36.1)	χ^2=4.4308
Post-secondary	15 (27.3)	41 (36.9)	56 (33.7)	p value=0.109
Marital status				
Single	21 (38.2)	55 (49.6)	76 (45.8)	Df= 4
Married	27 (49.1)	40 (36.0)	67 (40.4)	Pvalue= 0.305*
Cohabiting	2 (3.6)	2 (1.8)	4 (2.4)	
Separated	1 (1.8)	7 (6.3)	8 (4.8)	
Widowed	4 (7.3)	7 (6.3)	11 (6.6)	
Length of time since diagnosis				
Less than 1 month	28 (50.9)	67 (60.4)	95 (57.2)	Df=3
Btw 1 and 3 months	12 (21.8)	25 (22.5)	37 (22.3)	χ^2=2.5425
Between 3 months and 1 year	11 (20.0)	13 (11.7)	24 (14.5)	p value=0.450
Above 1 year	4 (7.3)	6 (5.4)	10 (6.0)	
Median length of time in wks (range)	3 (2-22)	2 (2-4)	3 (2-10)	
Possible route of transmission				
Sexual intercourse	44 (80.0)	96 (86.5)	140 (84.3)	Df=3
Blood and blood products	6 (10.9)	9 (8.1)	15 (9.0)	p value=0.596*
Other means	1 (1.8)	2 (1.8)	3 (1.8)	
Unknown	4 (7.3)	4 (3.6)	8 (4.8)	
Felt Ill				Df=1
Yes	41 (74.6)	77 (69.4)	118 (71.1)	χ^2=0.4749
No	14 (25.5)	34 (30.6)	48 (28.9)	p value=0.489
CD4 at presentation Mean (SD)	297.1 (34.7)	303.3 (17.4)	301.2 (16.3)	Df=164 Ttest=-0.1793 P value= 0.859

- Fischer's exact test + significant P value

TABLE 2: DISTRIBUTION OF RESPONDENTS ACCORDING TO THEIR SOCIO DEMOGRAPHIC CHARACTERISTICS AND CLINICAL STAGE OF PRESENTATION

Variables	Presentation n (%)		Statistical indices
	Early (n=66)	Late (n=100)	
Age (years)			
Less than 20	5 (62.5)	3 (37.5)	Df=4
21-29	31 (44.9)	38 (55.1)	χ^2=7.2251
30-39	14 (28.6)	35 (71.4)	P value=0.168
40 and above	16 (40.0)	24 (60.0)	
Mean (SD)	31.5 (9.5)	32.2 (8.4)	Df=164
			tt=-0.5394
			P value=0.5903
Sex			Df=1
Male	19 (34.5)	36 (65.5)	χ^2=0.9335
Female	47 (42.3)	64 (57.7)	P value=0.334
Educational status			
No/Primary education	23 (46.0)	27 (54.0)	Df=2
Secondary education	18 (30.0)	42 (70.0)	χ^2=3.7566
Post-secondary education	25 (44.6)	31 (55.4)	P value=0.153
Marital status			
Single	28 (36.8)	48 (63.2)	Df=3
Married /cohabiting	34 (47.9)	37 (52.1)	χ^2=5.0943
Separated	2 (25.0)	6 (75.0)	p value=0.165
Widowed	2 (18.2)	9 (81.8)	
Felt Ill			Df=1
Yes	34 (28.8)	84 (71.2)	χ^2=20.4122
No	32 (66.7)	16 (33.3)	p value< 0.0001+
Possible route of transmission			
Sexual intercourse	53 (37.9)	87 (62.1)	Df=3
Blood and blood prods	4 (26.7)	11 (73.3)	χ^2=9.8046
Other routes	2 (66.7)	1 (33.3)	P value= 0.020+*
Unknown	7 (87.5)	1 (12.5)	
Length of time since diagnosis			
Less than 1 month	26 (32.1)	55 (67.9)	Df=3
Btw 1 and 3 months	25 (49.0)	26 (51.0)	χ^2=5.1854
Between 3 months and 1 year	6 (35.3)	11 (64.7)	P value=0.159
Above 1 year	9 (52.9)	8 (47.1)	
CD4 at presentation			Tt=-119.27
Mean (SD)	487.8 (18.5)	178.1 (14.2)	Df=164
			P value=0.000+

*fischer's exact test +significant P value

RESULTS

A total 166 respondents were successfully recruited for the study, out of which 67% (111) were females. The respondents aged 18 to 58 years, with a mean ± SD of 31.9±8.9 years. Forty-six percent of the respondents (77/166) were within age group 21-30 years and the females were significantly younger than the male (P=0.0039). A total of 116 (69.8%) had at least secondary level of education and more than 50% of them were living alone. The mean CD4 was 301.2 ± 16.3 cells/ml, these were similar in both sexes

More than half (60.2%) of the respondents presented late to clinics for HIV care. About 57% presented within 1 month of being aware of their HIV serostatus. The median interval of presentation from the time of diagnosis was 3 weeks. At the time of presentation, less than one-third (29%) of them

TABLE 3: LOGISTIC REGRESSION OF FACTORS ASSOCIATED WITH LATE PRESENTATION OF HIV PATIENTS AT THE CLINICS IN UYO

Variable	Odd ratio	95%CI	P value
Age (years)			
Less than 20	Ref		
20-29	3.49	0.44-27.90	0.238
30-39	7.83	0.82-75.10	0.078
40-49	2.02	0.16-25-60	0.588
Sex			
Male	Ref		
Female	0.85	0.34-2.14	0.738
Educational status			
Primary education and below	Ref		
Secondary education	5.6	1.71-18.38	0.004+
Post-second. Education	2.06	0.68-6.29	0.202
Marital status			
Single	Ref		
Married /cohabiting	0.91	0.31-2.70	0.867
Separated	0.69	0.07-6.53	0.749
Widowed	4.99	0.26-96.26	0.287
Felt Ill			
Yes	Ref		
No	0.6	0.02-0.23	<0.001+
Possible route of transmission			
Sexual intercourse	Ref		
Blood and blood prods	2.98	0.53-16.74	0.214
Other routes	0.21	0.02-2.93	0.247
Unknown	0.19	0.01-2.70	0.221
Length of time since diagnosis			
Less than 1 month	Ref.		
Btw 1 and 3 months	0.18	0.06-0.56	0.003+
Between 3 months and 1 year	0.86	0.16-4.46	0.855
Above 1 year	0.06	0.01-0.29	<0.001+

+significant P value

went to the clinics despite not being ill. Sexual intercourse was the most important possible route of HIV transmission (84.3%) among the respondents (Table 1)

At bivariate level, possible route of transmission and being ill, showed significant association with late presentation. The mean CD4 for the late presenters was 178.1 (14.2) cells/ml. (Table 2). At the multivariate analysis, secondary level of education, being ill and short length of time from the point of diagnosis were the predictors of late presentation (Table 3)

Fever, cough and rashes were the most common symptoms at presentation, 21%, 18.7% and 16.9% respectively. Fever, rashes and frequent stooling were significantly associated with late presentation at the bivariate level with p value of 0.002, 0.003 and 0.012 respectively.(Table 4)

Multivariate analysis showed that PLWHIV who presented with Fever were over 3 times more likely to present at a late stage of the disease, compared to those without fever (P value= 0.025) and those with rashes were over 5-fold more likely to present as a late stage of the disease than those without rashes (P value = 0.025). (Table 5)

TABLE 4: DISTRIBUTION OF INITIAL SYMPTOMS OF THE RESPONDENTS ACCORDING TO THE CLINICAL STAGE AT PRESENTATION TO THE CLINICS IN UYO

Complaints	Presentation n (%)		Total n (%) (n=166)	Statistical indices
	Early (n=66)	Late (n=100)		
Fever				Df=1
Yes	6 (12.7)	29 (29.0)	35 (21.1)	χ^2=9.471
No	60 (87.3)	71 (71.0)	131 (78.9)	p value= 0.002+
Cough				Df=1
Yes	8 (12.1)	23 (23.0)	31 (18.7)	χ^2=3.0983
No	58 (87.9)	77 (77.0)	135 (81.3)	p value=0.078
Weakness				Df=1
Yes	5 (7.6)	8 (8.0)	13 (7.8)	χ^2=0.0099
No	61 (92.4)	92 (92.0)	153 (92.2)	p value=0.921
Pains				Df=1
Yes	11 (16.7)	13 (13.0)	24 (14.5)	χ^2=0.4322
No	55 (83.3)	87 (87.0)	142 (85.5)	p value=0.511
Rashes				Df=1
Yes	4 (6.1)	24 (24.0)	28 (16.9)	p value=0.003*+
No	62 (93.9)	76 (76.0)	138 (83.1)	
Stooling				Df=1
Yes	0 (0.0)	9 (9.0)	9 (5.4)	p value=0.012*+
No	66 (100)	91 (91.0)	157 (94.6)	
Weight loss				Df=1
Yes	4 (6.1)	4 (4.0)	8 (4.8)	χ^2=0.3680
No	62 (93.9)	96 (96.0)	158 (95.2)	p value=0.544*
Internal heat				Df=1
Yes	5 (7.6)	3 (3.0)	8 (4.8)	p value=0.267*
No	61 (92.4)	97 (97.0)	158 (95.2)	
Others				Df=1
Yes	4 (6.1)	10 (10.0)	14 (8.4)	P value= 0.398*
No	62 (93.9)	90 (90.0)	152 (91.6)	
No symptom				Df=1
Yes	25 (38.0)	14 (14.0)	39 (23.5)	χ^2=12.6127
No	41 (62.0)	86 (86.0)	127 (76.5)	p value<0.0001+
Symptoms count				Df=2
No symptom	25 (37.9)	14 (14.0)	39 (23.5)	χ^2=13.2108
1-2 symptoms	37 (56.1)	81 (81.0)	118 (71.1)	p value<0.0001+
Above 2 symptoms	4 (6.1)	5 (5.0)	9 (5.4)	

*Fischer's exact test, + significant P value

TABLE 5: MULTIVARIATE ANALYSIS OF INITIAL SYMPTOMS IN ASSOCIATED WITH LATE PRESENTATION OF HIV PATIENTS AT INITIAL VISITS TO THE CLINICS IN UYO

Symptoms	Odd ratio	95%CI	P value
Fever			
No	Ref		
Yes	3.92	1.56-8.65	0.025+
Rashes			
No	Ref		
Yes	5.42	1.96-19.19	0.002+
Cough			
No	Ref		
Yes	2.39	0.94-6.08	0.068

+ Significant P value

DISCUSSION

The socio demographic characteristic of the PLWHA at initial visits showed that 67% of them were females. This was a little above 60% which was reported in south Eastern Nigeria,[15] and has grave implications on mother- to child transmission of the disease, since HIV infected women who are pregnant are more likely to transmit the infection to their children. The mean age was 31.[9] years and the females were significantly younger than the males, findings which are similar to what was reported in Ekiti.[20] The most common age group at presentation was 21-30 years, (46%). This was a much younger population compared to the national figure of 35-40 years.[4] This age group may help to maintain HIV transmission in the society, since many may still be single and more likely to be sexually active, considering the fact that sexual intercourse was the most perceived route of transmission in the study by more than eighty percent of the respondents.

In the present study, out of the 81 respondents that were recently diagnosed (less than 1 month prior to the study), about 68% of them presented late. Seventy-one percent perceived they were ill at presentation, and this perception was a predictor for late presentation. It can be inferred that until PLWHIV perceived that they were ill, they would not access HIV screening service and that may explain why majority presented within one month of diagnosis. The implication of this is that the risk of transmission will be high within the population, much so when one considers the high prevalence of HIV in Akwa Ibom State. Though several studies have shown that patients presented late in developing countries, the proportion ranged from 40- 55% depending on their definition of late presentation.[21,22,23] Studies done in Lagos and Jos using CD4 below 350 cells/ml similar to this study, reported prevalence of 67.4%[18] and 85.6% respectively[24], which were much higher than the 60.2% found in the present study.

The mean CD4 among the late presenters of 178.1 +/- 16.2 which was less than 200cells/ml, CD4 of less than 200 cells/ml has been described as advanced HIV disease in 2007.[13] CD4 is the numerical estimations of the level of immunity of the patients, the lower it is the more susceptible an individual becomes to a wide range of infections.[25] A study done in Jos showed that CD4 less than 200cells/ml was a predictor of morbidity and mortality.[26]

The present study also showed that those with secondary level of education were about 5 fold more likely to present late compared to those with primary education, no other study was seen to show any relationship. One would expect that the higher the level of education the more the uptake of healthcare services, possibly at this level of education the respondents were more aware of the disease and more conscious of stigmatization. Socio demographic characteristics like age and sex did not affect the clinical stage of presentation of the respondents. This is in contrast to a study done in Northern Nigeria where male gender and those above 35 years were more likely to present late to the clinic.[26]

At presentation, 76% of the respondents were symptomatic, and came with one or two complains. A study done in Cape Town reported nausea, pain and vomiting as the most frequently reported symptoms[27] while in the present study fever, cough and rashes were the topmost symptoms. Fever and rashes were strong predictors of late presentation among the respondents, this is supported by the fact that persistent fever of more than 30 days had been described by WHO as AIDS defining.[13]

This study was limited by the fact that it depended on patients' self-reporting of symptoms, no detailed history taking was done to elucidate other symptoms the patients might have had at presentation, also, most factors such as socio economic and environmental factors associated with late presentation were not considered in this study.

In conclusion, symptoms like fever and rashes were the predictors of late presentation of HIV in this setting. It is hoped that test and treat policy will help to reduce the high proportion of late presentation. This will be achieved with high level of awareness on screening at the community level.

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