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Compliance to Antiretroviral therapy among AIDS patients in Aminu Kano Teaching Hospital, Kano, Nigeria

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ABSTRACT

Background: *Non-compliance with antiretroviral treatment has serious consequences for prognosis and may lead to the development of resistant strains of the virus. This study assessed the level of compliance to antiretroviral treatment, identified factors associated with compliance and reasons for non-compliance among AIDS patients in a Teaching Hospital in Northern Nigeria.*

Methods: *A pre-tested structured interview questionnaire was administered on a cross-section of 263 AIDS patients seen at Aminu Kano Teaching Hospital, Kano. Patient's reported consumption of antiretroviral drugs was compared with the Physician's prescription in the seven-day period preceding the interview.*

Results: *Only 142 (54.0%) of the 263 respondents took at least 80% of the antiretroviral drugs prescribed. Sixty-one (23.2%) did not miss any dose of the drugs. Univariate analysis showed that a significantly higher proportion (58.7%) of patients with formal education were compliant compared to 26.3% of those without formal education (χ^2=13.7 df=1 P<0.01). The educated patient was four times more likely to be compliant [O.R=3.97, 95% CI=1.75-9.24]. In contrast, age and sex variables had no significant influence on compliance among these patients. Main reasons for non-adherence to medication include non-availability of drugs (40.6%), forgetfulness (23.9%) and lack of funds (15.8%).*

Conclusions: *The average compliance observed in this study could be improved by ensuring a steady supply of affordable antiretroviral drugs, better patient-provider communication and enhanced social support for these patients.*

KEYWORDS: *Compliance; Antiretroviral treatment; AIDS patients; Kano.*

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INTRODUCTION

As the worldwide AIDS pandemic continues to gather momentum, an estimated 40 million people infected with HIV face early death unless they receive appropriate life-extending medical care[1]. There have been tremendous gains in survival and quality of life following the introduction of Highly Active Antiretroviral Therapy (HAART)[2,3]. However, low compliance to medication could lead to the appearance of resistant strains of the virus. Compliance can be defined as the degree to which the patient conforms to treatment as prescribed and it is expressed quantitatively as the percentage of prescribed doses that have been taken by the patient[4]. In HARRT therapy, adherence of less than 95% has been linked with treatment failure[5]. Lower adherence rates foster development of virus mutations and the risk of developing resistance has been found to be highest with adherence in the range of 80 to 90%[6]. Compliance can be evaluated in several ways [7]. These include pharmacological measures (determination of serum and urinary concentrations of drugs or using biological markers integrated into the tablets), blood test for viral loads; clinical measures (clinical judgement of the doctor and the use of questionnaires); and physical measures (verifying prescription renewals, counting the remaining pills or pill counting systems). Although, there is no gold standard allowing precise measurement of compliance[8], the electronic pill counter or Medication Event Monitoring System (MEMS) may be considered as the best existing system for measurement of compliance[9]. Pharmacological methods also have a higher sensitivity and specificity[10] but remain difficult to use in practice.

Poor compliance is especially common when a patient has poor knowledge, understanding, and perception of the disease or when a complex drug regime is prescribed[11]. A recent review of compliance to antiretroviral drugs reported figures ranging from 28% to 82% with most studies showing rates between 50 and 80%[12].

Since the official report of HIV/AIDS occurrence in Nigeria in 1986, the prevalence of the infection increased steadily from 1.8% in 1991, 4.5% in 1995 and 5.4% in 2003 [13]. As part of the Nigerian government's response to the epidemic, an accelerated pilot antiretroviral drug initiative was commenced in February 2002. It targeted 10,000 adults and 5,000 children with generic forms of Nevirapine, Lamivudine and Stavudine at $350 per patient per year. Patients pay only $120 per

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annum[14]. Twenty-five centres provide this treatment to patients across the country. Little information is available about compliance of patients to ARV in Northern Nigeria. Therefore, this study assessed AIDS patients' compliance to antiretroviral treatment and identified associated factors and reasons for non-compliance in Aminu Kano Teaching Hospital, Kano, Nigeria.

MATERIALS AND METHODS

Study setting

Aminu Kano Teaching Hospital (AKTH) is a 500-bed hospital established in 1988. Located in Kano, the largest commercial centre of northern Nigeria, this hospital receives clients from within Kano, the neighbouring states of Jigawa, Katsina, Kaduna, Bauchi and Zamfara states. The majority of the patients are indigenous Hausa and Fulani, although the Ibos and Yoruba ethnic groups also constitute a substantial proportion of the clientele. Most of the people are traders, farmers, businessmen and civil servants. The hospital operates a multidisciplinary specialist clinic for HIV/AIDS patients once a week. Patients are mostly given a combination of two nucleoside reverse transcriptase inhibitors (NRTI), Lamivudine, Stavudine and one non-nucleoside reverse transcriptase (NNRTI) Nevirapine. Stable patients are usually given monthly appointments. The study population consisted of AIDS patients attending Aminu Kano Teaching Hospital HIV/AIDS specialist clinic. The study was conducted during the month of August 2004.

Study design

The study was cross sectional descriptive in design.

Sample size and sampling technique

The required sample size of 280 was obtained using an appropriate statistical formula for estimating minimum sample size in health studies [$n= Z^2pq/d^2$] [15] and a compliance rate of 80% obtained from a previous study [12]. The multistage sampling strategy was used. In the first stage, the sample size of 280 was divided equally among the 4 clinic days in August 2004. In the second stage, the systematic sampling strategy was used to select patients on each clinic day until the required number of patients was obtained. The random number table was used to locate the starting point and the sampling interval was calculated based on the average attendance.

Instrument description/Data collection

Two hundred and sixty three patients were interviewed using a pre-tested, structured, mostly closed ended questionnaire after obtaining ethical clearance from the hospital and informed consent from the participants. The questionnaire was in three parts. The first part obtained information on socio-demographic variables such as age, place of residence, ethnicity, religion and educational attainment. The second part obtained information about respondent's regularity at follow-up clinic and compliance with treatment. Patients were asked to identify the antiretroviral medications they were presently taking (from samples obtained from the hospital pharmacy). They were also asked to recall the number of times per day they were supposed to take each medication and the number of pills per dose (this was compared with the doctor's prescription). Patients were then asked the number of doses they had missed within the seven-day period preceding the interview. If the patient had reported skipping a dose, the third part inquired about reasons for non-compliance. Multiple responses were allowed in this section. Ten final year Medical students previously trained for the purpose conducted the interviews.

The study instrument was validated during a pilot study on 15 AIDS patients in a similar setting (Abdullahi Wase Specialist Hospital, Kano). Results of the pilot study were used to modify content and wording of the questionnaire.

Data analysis

Data was analysed using Epi-Info version 6.0 statistical software (CDC Atlanta, Georgia, U.S.A). Absolute numbers and simple percentages were used to describe categorical variables. Similarly, quantitative variables were described using measures of central tendency (mean, median) and measures of dispersion (range, standard deviation) as appropriate. The Chi-square test was used in assessing the significance of associations between categorical groups. A *p*-value of 0.05 or less was considered statistically significant.

RESULTS

Out of the 280 patients that were invited to participate, only 263 agreed to the interviews giving a response rate of 94%. There were 167 males and 96 females giving a male: female ratio of 1:1.7. The respondents' age ranged from 19 to 62 years with a mean age of 36.2±3.3 years. Most patients 236 (89.7%) were below 45 years of age. Considered separately, the mean age for male patients was 37.7±1.8 years compared to 32.6±2.7 years for females. This difference was statistically significant

(t=17.3 df=261 $P<0.05$). One hundred and eighty one (68.8%) of the patients resided in Kano, while 82 (31.2%) came from outside Kano.

The majority of the patients 165 (62.7%) were married, 50 (19.0%) were single and 12 (4.6%) were widowed. Most of the patients 85 (32.3%) were Hausa or Fulani, closely followed by Igbo 75 (28.5%) and Yoruba 20 (7.6%). The rest were from other Nigerian tribes including Tiv, Edo and Kanuri. Regarding educational status, most patients either had tertiary education 95 (36.1%) or secondary school education 90 (34.2%). Forty (15.2%) had primary school education, 20 (7.6%) had Qur'anic education and the remaining 18 (6.8%) were illiterate. One hundred and fifty one (57.4%) of the patients belonged to the Christian faith whereas 112 (42.6%) were Muslims.

Table II shows that only 142 (54.0%) of the 263 patients interviewed took 80% or more of the prescribed antiretroviral drugs in the seven-day period preceding the interview. Sixty-one (23.2%) of the patients did not miss any dose of the drugs. Univariate analysis showed that a significantly higher proportion (58.7%) of patients with formal education were compliant compared to 26.3% of those without formal education (χ^2=13.7 df=1 $P<0.01$). The educated patient was four times more likely to be compliant [O.R=3.97, 95% CI=1.75-9.24] as shown in Table III. Similarly, a higher proportion (55.7%) of male respondents were compliant with antiretroviral medication compared to (51.0%) of female patients. Furthermore, 54.8% of respondents aged 40 years or more were adherent to their medication compared to 53.5% of their younger colleagues. These differences were, however, not statistically significant.

Table IV shows in order of frequency the reasons proffered by patients for non-compliance with antiretroviral therapy. The commonest reasons include; non-availability of drugs (40.6%), forgetfulness (23.9%) and lack of funds (15.8%).

Table II. Compliance with antiretroviral drugs among AIDS patients in Aminu Kano Teaching Hospital, 2004

Compliance	Frequency No.(%) Males	Females	Total
Compliant	93 (55.7)	49 (51.0)	142 (54.0)
Not compliant	74 (44.3)	47 (49.0)	121 (46.0)
Total	167 (100.0)	96 (100.0)	263 (100.0)

Table I. Age distribution of AIDS patients in Aminu Kano Teaching Hospital, Kano, 2004

Age(years)	Frequency No.(%) Males	Females	Total
15-24	28 (16.8)	41 (42.7)	69 (26.2)
25-34	64 (38.3)	21 (21.9)	85 (32.3)
35-44	55 (32.9)	27 (28.1)	82 (31.2)
45-54	14 (8.4)	6 (6.3)	20 (7.6)
55-64	6 (3.6)	1 (1.0)	7 (2.7)
Total	167 (100.0)	96 (100.0)	263 (100.0)

Table III. Effect of educational status on compliance to antiretroviral drugs among AIDS patients in AKTH, Kano

Educational status	Compliant	Not compliant	Total
formal education	10 (26.3)	28 (73.7)	38 (100.0)
Formally educated	132 (58.7)	93 (41.3)	225 (100.0)
Total	142 (54.0)	121 (46.0)	263 (100.0)

χ^2=13.7 df=1 $P<0.01$ Significant

Table IV. Reasons for non-compliance to antiretroviral drugs among AIDS patients in AKTH, Kano

Reasons for non-compliance	Frequency No. * (%)	Rank order
Non-availability	126 (40.6)	1
Forgetfulness	74 (23.9)	2
Lack of funds	49 (15.8)	3
Busy schedule	28 (9.0)	4
Exhaustion of drugs	15 (4.8)	5
Absence of symptoms	10 (3.2)	6
Fear of side effects	8 (2.6)	7

*Multiple responses recorded. Percentages represent proportion of responses obtained

DISCUSSION

Patient's self reported consumption of antiretroviral drugs was compared with the doctor's prescription to assess compliance. Although there is a risk of over-estimation, this method was used for its simplicity and low-cost. It has also been used

elsewhere[16,17]. Patients ingesting 95% or more of the prescribed drugs in the seven-day period preceding the interview were considered compliant[16,18].

The male preponderance among the patients may be explained by selection factors since hospital care is not yet free, and men have economic advantage over women, particularly in our study population[19]. In Nigeria, the highest infection rates have been reported in the 20-24 year age group[13], and since those infected may become symptomatic later, that could explain the clustering of patients in the 25-45 years age bracket. The younger age of female patients could be due to the earlier sexual debut among females coupled with the dominant role of heterosexual transmission in the developing countries[20]. Although the centre's catchment population are mainly Hausa Muslims, Christians outnumbered Muslims among the patients. The pooling of patients from outside the hospital's usual catchment area due to limited treatment centres could explain this anomaly.

Fifty four percent of the patients were compliant with antiretroviral (ARV) therapy and only 61 (23.1%) of the patients took all prescribed ARV drugs in the preceding week. This moderate compliance rate is comparable to reports from Ivory Coast[21] (58%) and Spain[7] (58.8%). It is however, much lower than the rates observed in Lagos[14] (92% at 3 months and 88% at 18 months), Senegal[20] (91%), South Africa[22] (87.2%) and the United States[16] (63%). The higher compliance rate among literate patients was also reported by other researchers[12]. This could be due to better comprehension of instructions in addition to the economic advantage they have over their illiterate counterparts. In contrast with other reports[7,22], patient's gender or age did not influence compliance in this study.

Reasons proffered by patients for their inability to adhere to their prescriptions include non-availability of drugs, lack of funds, exhaustion of drugs, forgetfulness and busy schedule. Other reasons were absence of symptoms and fear of side effects. Similar reasons were reported by Ekong *et. al*[14] among AIDS patients in Lagos. They reported that forgetfulness, adverse effects, feeling of well being, pill load, stigmatisation and sharing of drugs with others were some of the reasons for non-compliance among their patients. In addition, some of the patients sold the drugs.

In another report from Sagamu in South West Nigeria, the commonest reason for non-adherence was lack of funds to purchase drugs[23]. Non-availability of drugs and exhaustion of drugs are health services related factors, whereas forgetfulness, busy schedule and fear of side effects could result from communication gaps regarding antiretroviral therapy.

The inconsistent adherence to medication as observed in almost half of the patients at this centre has serious consequences. Patients may not benefit fully from the treatment and may become resistant to other medications as observed elsewhere[11,18]. Similarly, development of resistance has implications for the broader public health, because inadvertent transmission of multi-drug resistant strains of HIV has been demonstrated[11]. Currently in industrialised countries, up to 23% of incident infections are with virus strains resistant to one or more drugs[11]. Some experts argued that the best way to deliver highly active antiretroviral drugs treatment (HAART) is likely to be through directly observed therapy (DOT), so called DOHAART[24] in order to support adherence. But, treatment completion rates for tuberculosis using DOTS also vary from as low as 37% in Central African Republic to moderate rates of 78% in Kenya and Tanzania[24]. Furthermore, Senegal, Malawi and South Africa have achieved high and sustainable adherence rates for antiretroviral drugs without directly observed treatment[24]. Unavailability of drugs and lack of funds are unlikely to be improved by directly observed treatment. On the contrary, the additional cost of transportation to health facilities for supervised intake of medication may further increase the financial burden on patients. It is therefore necessary to study the effectiveness of adherence strategies in resource poor settings and identify reasons for non-compliance at each centre before applying appropriate strategies to overcome them.

At this centre, only about half of the patients complied with their therapy. Non-compliance was due to lack of funds, non-availability of drugs and forgetfulness. Educated patients were more likely to be compliant with medication. Therefore, to improve adherence, the important factors seem to be the provision of a steady supply of affordable antiretroviral drugs, better provider-patient communication and improved social support for these patients.

REFERENCES

1. UNAIDS. AIDS epidemic update: December 2003. Available at http://www.unaids.org/worldaidsday/2003/Press/update2003_en.doc
2. Palella FJ, Delaney KM, Moorman AC, *et al.* Declining morbidity and mortality among patients with advanced

human immunodeficiency virus infection. N Engl J Med 1998; 338: 853-60.

3. Mocroft A, Ledergerber B, Katlama C, *et al.* Decline in the AIDS and death rates in the EuroSIDA study: an observational study. Lancet 2003; 362: 22-9.
4. Ferreira MT, Monreal D, Venancio da Cunha R, Aparecida LT. Compliance to antiretroviral medication as reported by AIDS patients assisted at University Hospital of the Federal University of Mato Grosso do Sul. Braz J Infect Dis 2002; 6:1-7.
5. Hsu J. Adherence. Johns Hopkins Point of Care Information Technology 2005;24:4-6. Available at www.hopkins-hivguide.org.
6. Sethi AK. Adherence and HIV drug resistance. The Hopkin's HIV Report. 2004. Available at www.hopkins-aids.educ/publications/report/jan 04 04.html.
7. Riera M, La Fuente Ld L, Castanyer B, *et al.* Adherence to antiretroviral therapy measured by pill count and drug serum concentrations. Variables associated with a bad adherence. Med Clin (Barc) 2002; 119 (8): 286-92.
8. Mallion JM, Schmitt D. Patient compliance in the treatment of arterial hypertension. European Society of Hypertension Scientific Newsletter 2001; 2:7.
9. Eisen SA, Woodward RS, Miller D, Spitznagel E, Windham CA. The effect of medication compliance on the control of hypertension. J Gen Intern Med 1987; 2(5): 298-305.
10. Bittar N. Maintaining long-term control of blood pressure: the role of improved compliance. Clin Cardiol 1995; 18: III12-III16.
11. Stevens W, Kaye S, Corrah T. Antiretroviral therapy in Africa. BMJ 2004; 328: 280-2.
12. Puigventos F, Riera M, Delibes C, *et al.* Adherence to antiretroviral drug therapy. A systemic review. Med Clin (Barc) 2002; 119 (4): 130-7.
13. FMOH/NACA. Situation analyses report on STI/HIV/AIDS in Nigeria, Federal Ministry of Health and National Action Committee on AIDS, Abuja 2003: 15-18.
14. Ekong E, Idemyor V, Akinlade O, Uwah A. Challenges to Antiretroviral (ARV) drug therapy in resource-limited settings-progress and challenges in the Nigerian Initiative. 11th Conference on Retroviruses and Opportunistic Infection, San Francisco, U.S.A February 8-11, 2004 Poster number: 596.
15. Lwanga S, Lemeshow S. Sample Size Determination in health Studies: a Practical Manual. Geneva: World Health Organization, 1991:23-30.
16. Singh N, Squier C, Sivek C, *et al.* Determinants of compliance with antiretroviral therapy in patients with human immunodeficiency virus: prospective assessment with implications for enhancing compliance. AIDS Care 1996; 8:261-9.
17. Pires VR, Santana AC, Monteiro MD. Adherence to antiretroviral treatment: experience in Maceio, Brazil. Braz J Infect Dis 1999; 3(Suppl 2): S65
18. Rodriguez-Rosado R, Jimenez-Nacher I, Soriano V, Anton P, Gonzalez-Lahoz J. Virological failure and adherence to antiretroviral therapy in HIV-infected patients. AIDS 1998; 12:1112-3.
19. Iliyasu Z, Arotiba JT, Babashani M. Sociodemographic characteristics and risk factors among HIV/AIDS patients in Kano, Northern Nigeria. Niger J Med 2004; 13(3): 267-71.
20. Laniece I, Ciss M, Desclaux A, *et al.* Adherence to HAART and its principal determinants in a chort of Senegalese adults. AIDS 2003; 17 (Suppl 3): S103-8.
21. Gourvellec G, Anglaret X, Toure S, *et al.* Compliance in HIV infected adults: Study of opportunistic infection prophylaxis with Cotrimoxazole in Ivory Coast. Presse Med 2004; 33:595-600.
22. Orrell C, Bangsberg DR, Badri M, *et al.* Adherence is not a barrier to successful antiretroviral therapy in South Africa. AIDS 2003; 17 (9): 1369-75.
23. Daniel O, Olusoji J, Odusoya A. Adherence pattern to antiretroviral drugs among HIV/AIDS patients in Sagamu, Nigeria. Fourth National conference on HIV/AIDS, Abuja, Nigeria. May 2-5, 2004.
24. Furber AS, Hodgson IJ, Desclaux A, *et al.* Barriers to better care for people with AIDS in developing countries. BMJ 2004; 329:1281-3.