

SUBSTANCE ABUSE AND ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG PATIENTS ATTENDING CLINIC AT A SPECIALIST HOSPITAL IN JOS, NIGERIA

¹Suwa G. Goar, ¹Moses D. Audu, ¹Michael .T. Agbir, & ²Bitrus Matawal

¹Department of Psychiatry, Jos University Teaching Hospital, Jos, Nigeria; ²Infectious Disease Unit, Plateau State Specialist Hospital, Jos, Nigeria

ABSTRACT

Substance abuse does not only increase susceptibility to HIV/AIDS through high risk Sexual behaviors but it also hastens the progression of the disease among infected persons than in those who do not abuse drugs. Furthermore, drug use impairs adherence to antiretroviral therapy (ART) leading to reduction in ART effectiveness and ultimately increased HIV-related mortality. In North Central Nigeria there is a dearth of information concerning the influence of substance abuse on adherence to ART which has substantially altered the fate of HIV-infected people. The objectives of this study therefore, were to determine the type of substances abused by HIV-infected patients attending clinic at Plateau State Specialists Hospital (PSSH) and to determine the effect of substance abuse and sociodemographic factors on adherence to ART among these patients. Ethical approval was obtained before the commencement of the study which was cross-sectional in design. The study was carried out at the infectious disease unit of the Plateau State Specialists Hospital, Jos among 160 consecutive patients. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) was used for the assessment of the types of substance abused and AIDS Clinical Trials Group (ACTG) adherence instrument was used to assess reasons for non-adherence. The results showed that 61.9% of the patients did not use any substance of abuse, 38.1% either abused one substance or a combination of substances. Substance abuse were ($p = 0.0001$), alcohol abuse ($p = 0.003$) and educational status ($p = 0.0001$) significantly associated with non-adherence to ART while, age ($p = 0.954$), employment status ($p = 0.924$) and marital status ($p = 0.466$) were not. However, logistic regression revealed that only alcohol abuse ($B = -1.383$, $df = 1$, $p = .002$) predicted non adherence to ART. We recommend the screening of patients on ART for substance abuse and a multi-disciplinary approach to the treatment of HIV/AIDS.

Key words: HIV, substance abuse, medication adherence

INTRODUCTION

The impact of HIV/AIDS will continue to be felt for decade's world over. Sub-Saharan Africa remains the most affected region in the global HIV/AIDS epidemic. More than two thirds (68%) of all people who are HIV positive lived in Sub-Saharan Africa (UNAIDS/WHO/UNICEF, 2011). Similarly, of all AIDS deaths in 2010 more than three-quarters occurred in Sub-Saharan Africa (UNAIDS, 2011).

In recent years efforts have been intensified to increase access to effective treatment and prevention. Fewer than half of Africans are receiving it (UNAIDS/WHO/UNICEF, 2011). However, early confidence recorded with the introduction of antiretroviral therapy (ART) that led to significant reduction in HIV/AIDS associated morbidity and mortality has been compromised. To achieve effective treatment and realize the benefits of treatment, strict adherence to ART instructions is very critical. Adherence to therapy is therefore, an important determinant of clinical and virologic outcomes for patients who have been prescribed ART. Researchers have shown that even modest or occasional non-adherence can lead to emergence of drug resistant viral strains and the transmission of these viral strains in the population (Gifford, 2000; Liu, et al., 2001).

Unfortunately, poor adherence to ART is a common problem with more than half of individuals on combination therapies failing to take their medication with respect to dosage, time and dietary instruction (Murphy et al., 2001; Nieuwkerk et al., 2001). Although there are several reasons for treatment failure among HIV infected patients, co morbid substance abuse contributes significantly to non-adherence. HIV infected drug abusers may among

other factors have mental health problems, medical conditions and sub-optimal support. These have been shown to tamper with adherence to medication (Komiti et al., 2003, Murphy et al., 2004).

The effect of alcohol use on adherence to antiretroviral therapy has also been reported in a meta-analysis by Henderhot et al (2009). In this study, approximately 50-60% of alcohol drinkers were found to be less likely adherent to ART compared to abstainers or those who drank relatively less and several variables were found to moderate the alcohol-adherence association. In a related study by Braithwaite et al (2005b) of a temporal and dose response association between alcohol consumption and ART adherence revealed the relative risk of non-adherence associated with alcohol consumption to be 1.5 on non-binge drinking days but 2.7 on binge drinking days. Daily binge alcohol consumption was therefore, found to decrease survival from 28.1 years to 21.4 years which corresponded to a 24 percent decrease.

There is increasing evidence showing that alcohol impacts negatively on HIV disease through various mechanisms namely: HIV transmission, hasten progression and non adherence to ART. Alcohol has been associated with the likelihood of HIV-infected individuals engaging in sexual risk behavior, thereby re-infecting themselves with a different strain and or infecting others (Kalichman et al., 2007). The same holds true for the use of other psychoactive substances. Alcohol hastens HIV disease progression through its action on proteasomes and immune-proteasomes which impede critical immune processes during progressive HIV-1 infection (Haorah et al., 2004). It has also been found that alcohol-exacerbated hepatotoxicity could reduce the efficiency

of the liver. Consequently, it leads to reduction in bioavailability of ART needed to suppress the replication of HIV (Conigliaro et al., 2003). Furthermore, the association between alcohol abuse and HIV disease progression is also caused by non adherence to ART (Samet et al., 2003). For instance, HIV-infected individuals who use alcohol may less likely take their prescribed medication appropriately.

Some studies in Africa have shown high levels of adherence to ART amongst HIV-infected patients. However, recent reviews have shown the need for an increased focus on ART adherence. Hence, it is necessarily important to pay attention to screening of substance use among HIV-infected persons in order to reduce individual's chances of engaging in sexual risk behaviors; reduce the rates of non adherence to ART and slow down the rate of disease progression especially among those who are receiving ART. Therefore, this study was undertaken to assess the types of substances abused and secondly, to determine the effect of substance abuse and sociodemographic factors on adherence to ART among people living with HIV/AIDS receiving treatment at Plateau State Specialist Hospital Jos, Nigeria.

METHOD

The study was carried out at the infectious diseases unit of the Plateau State Specialist Hospital, Jos. Jos is the capital city of Plateau state. It is located in North central Nigeria and has an estimated population of 822,837 as at 2006 (Plateau State Ministry of Information). It offers both specialist and primary care services to in and out patients. This hospital serves as a reference centre for the seventeen

government owned general hospitals spread across the state.

Ethical approval was obtained before the commencement of the study which was cross-sectional in design. A total of 160 patients were recruited for this study. Every consecutive consented patient aged 18 years and above that attended the infectious diseases unit with a diagnosis of HIV-infection was recruited for the study. This was done until the desired sample size of 160 was obtained. A participant must also have been on antiretroviral drugs for at least one month to be qualified for inclusion. Excluded were patients with chronic medical conditions, patients with other psychiatric conditions beside substance abuse, patients with altered sensorium and those who did not consent. Non adherence was assessed using self reported questionnaire. Self reported questionnaire has been used for evaluating adherence to ART in different parts of sub-Saharan Africa (Nwauche et al., 2006). Although self reported outcomes of adherence may have a weakness of reliability, a study by Oyugi et al (2004) found no significant difference between patient-reported and objective measures of adherence. In this study patients were asked if they had missed dosage or timing of ART in the past seven days. They were asked to recall starting from the day of interview if they have taken medication late with 2 hours or missed in the last seven days. Adherence to ART was considered optimal if patients reported no to both questions. Focus was on recent adherence in order to maximize recall and minimize bias.

AIDS Clinical Trials Group (ACTG) questionnaire was used to assess reasons for non-adherence. The Alcohol, Smoking and Substance Involvement Screening

Test (ASSIST) developed by WHO was used for assessing substance abuse in the last one month. ASSIST has been shown to be cross culturally valid and reliable screening test (New come 2005). A score of 11 points and above for alcohol and 4 points and above for all other substances was regarded as harmful use (abuse). Substances in this study are defined broadly to include alcohol, tobacco, illicit drugs and legal pharmaceutical agents that have high dependent potential. A semi-structured questionnaire was used to collect socio-demographic data.

Data was coded and analyzed using statistical package for social sciences SPSS 15. Frequency, cross tabulations and chi square were used to compare variables. The level of significance was set at $p < 0.05$.

RESULTS

The study showed that 55(34.4%) of the respondents were non-adherents. Table 1 shows that 99(61.9%) of the study sample

Table 1. Frequency and types of substances abused

Variables	Frequency(n)	%
No substance abuse	99	61.9
Substance abuse	66	38.1
Total	165	100
Types of substances	Frequency(n)	%
Alcohol	27	16.9
Antihistamines	5	3.1
Analgesics	7	4.4
Cigarette	3	1.9
Coffee	11	6.9
Others	8	5.0
Total	66	38.1

did not use any substance of abuse while 66(38.1%) either abused one substance or combination of substances. The most abused of all the substances was alcohol 27(16.9%), followed by 11(6.9%) coffee. Others were 7(4.4%) analgesics, 5(3.1 %) antihistamines, 3(1.9%) cigarettes and 8(5.0%) others.

Table 2 shows that slightly greater than half 32(58.2%) of those who abused substances were non-adherents compared to 23(41.8%) who did not abuse substances. Higher proportion, 76(72.4%) of those who did not abuse substances were adherent to medication compared to only 29(27.6%) who abused substances. Those who did not abuse substances were significantly better adherents than those who abused substances ($\chi^2 = 14.292$, $df = 1$, $p = 0.000$). The abuse of alcohol was associated with non adherence to ART ($\chi^2 = 8.916$, $df = 1$, $p = 0.003$). The respondents' age ranged from 18 to 68 years old with a mean of 35.6 ± 8.67 . The peak age group was 25-34 years representing 45% of the study sample. This group had the highest percentage 24(43.6%) of non-adherents. However, there was no significant relationship between age and adherence to medication ($\chi^2 = 0.333$, $df = 3$, $p = 0.954$). There was a preponderance of females 103(64.4%) and only 57(35.6%) were males. Females had higher percentage of both adherents 70(66.7%) and non-adherents 33(60.0%). There was no statistical significance between sex and adherence to medication ($\chi^2 = 0.699$, $df = 1$, $p = 0.403$). The married respondents 56(53.3%) had higher percentage of adherents compared to the singles 49(46.7%) ($\chi^2 = 0.531$, $df = 1$, $p = 0.466$). More 22(40.0%) of the respondents who had no formal education

Table 2. Relationship between substance abuse, alcohol abuse, socio-demographic factors and adherence to ART

Variables	Non adherents	Adherents	Statistic
No substance abuse	23(41.8%)	76(72.4%)	$\chi^2 = 14.292$
Substance abuse	32(58.2%)	29(27.6%)	$df = 1$
Total	55(100)	105(100)	$p = 0.001$
No alcohol use	39(70.9%)	94(89.5%)	$\chi^2 = 8.916$
Alcohol use	16(29.1%)	11(10.5%)	$df = 1$
Total	55(100)	105(100)	$p = 0.003$
Age groups			
15 – 24	5(9.1%)	7(67%)	$\chi^2 = 0.333$
25 – 34	24(43.0%)	48(45.7%)	$df = 3$
35 – 44	17(30.9%)	32(30.5)	$p = 0.954$
45 and above	9(16.4%)	18(17.1%)	
Total	55(100)	105(100)	
Sex			
Male	22(40.0%)	35(33.3%)	$\chi^2 = 0.699$
Female	33(60.0%)	70(66.7%)	$df = 1$
Total	55(100)	105(100)	$p = 0.403$
Marital status			
Single	29(52.7%)	49(46.7%)	$\chi^2 = 0.531$
Married	26(47.3%)	56(53.3%)	$df = 1$
Total	55(100)	105(100)	$p = 0.466$
Employment status			
Unemployed	23(41.8%)	42(33.3%)	$\chi^2 = 0.049$
Employed	32(58.2%)	70(66.7%)	$df = 1$
Total	55(100)	105(100)	$p = 0.924$
Educational status			
No formal education	22(40.0%)	10(9.5%)	$\chi^2 = 25.490$
Primary	9(16.4%)	12(11.4%)	$df = 3$
Secondary	14(25.5%)	36(34.3%)	$p = 0.001$
Post secondary	10(18.2%)	47(44.8%)	
Total	55(100)	105(100)	

were non adherents compared to only 10(18.2%) who had post secondary education. Those who had post secondary education 47(44.8%) were better adherents compared to those with no formal education 10(9.5%). There was a significant relationship between educational level and adherence to medication ($\chi^2 = 25.490$, $df = 3$, $p = 0.001$)

Reasons given for non-adherence to ART

As shown in Table 3, the most prominent reasons for non-adherence were: simply forgot (13.8%), avoid side effects (12.5%), away from home (10.0%) and being busy (7.5%). The results of logistic regression analysis reported in Table 4 show that only alcohol abuse predicted non-adherence to ART ($B = -1.383$, $df = 1$, $P = 0.002$)

Table 3. Reasons for non-adherence to antiretroviral drugs

Variables	Frequency (n)	%
Avoid side effects	20	12.5
Overwhelmed	6	3.8
Many pills	3	1.9
Not want others to know	3	1.9
Drug toxic	6	3.8
Simply forget	22	13.8
Away from home	16	10.0
Being busy	12	7.5
Change in routine	6	3.8
Slept off	6	3.8
Specific time	2	1.3
Felt sick	5	3.1
Total	107	100

DISCUSSION

The prevalence rate of non-adherence in this study was 34.6%. This is in agreement with earlier studies done in this country (Erah and Arute., 2008), other parts of Africa (Kalichman et al., 2007) and in the Western countries (Mills et al., 2006).

High prevalence of substance abuse (39.1%) with alcohol being the most abused was found in this study. This concurs with several other studies that have

demonstrated high prevalence of alcohol abuse among individuals with HIV/AIDS (Chander et al., 2008, Galvan et al., 2002). People with substance related problems are more likely to contract HIV because they tend to engage in behavior that places them at risk (Malow et al., 2001; Audu et al., 2010). They are also more likely to abuse substances either as an expression of maladaptive coping strategy or due to the presence of other co-morbid psychiatric conditions which are prevalent in patients with HIV/AIDS (Olley et al., 2003; Pence et al., 2008).

A significant relationship between alcohol abuse and non-adherence to ART was found. This is in agreement with a study done by (Hendershot et al., 2009) that showed that HIV infected patients with co-morbid alcohol abuse contribute significantly to non-adherence. There are variety of ways by which drinking can compromise ART adherence. For instance, intoxication impairs memory, planning, organizational skills and other cognitive abilities that can result in missed doses or timing of medication (Aloisi et al, 2002; Braithwaite et al, 2007). Recently, a study revealed that patients who take ART and abuse alcohol had intentionally stopped taking their medication based on the belief that mixing alcohol and ART

Table 4. Logistic regression analysis showing association between non-adherence to ART and predictors

Variables	B	S.E	Wald	df	Sig	Exp(B)
Alcohol use	-1.383	.454	9.270	1	.002	.251
Agegrp	.081	.229	.124	1	.725	1.084
Marital status	.283	.407	.485	1	.486	1.328
Employstatus	.043	.380	.013	1	.911	1.044
Edustatus	-.557	.402	1.923	1	.166	.573
Sex	.114	.388	.086	1	.770	1.120
Constant	.871	.887	.964	1	.326	2.390

is very toxic to the liver (Kalichman et al., 2012). It has also been shown to exacerbate emotional distress in HIV positive individuals which has the capacity to tamper with adherence to ART (Komiti et al., 2003). Additionally, HIV infected drug abusers may among other factors have mental health problems, medical conditions and sub-optimal social support that have been found to interfere with adherence to medication (Chesney et al., 2000).

However, aside alcohol abuse there are other several factors that have been associated with non-adherence to active anti-retroviral treatment among HIV patients. These include individual characteristics such as gastro-intestinal conditions that interfere with response to medication, existing resistance to medication and to inability to adhere to treatment. Optimal adherence ($\geq 85\%$) to antiretroviral regimen is required to achieve viral suppression in people living with HIV. In spite of this, there are often approximately 80% of patients with undetectable viral loads (Peterson et al., 2000). This is even more critical in Nigeria where majority of the people live below the poverty line and have to travel long distances to treatment centers that have poor facilities.

Studies on the relationship between medication adherence and socio-demographic factors have not been consistent. Some researchers have demonstrated that male sex, older age, higher income and higher education correlate with better adherence (Ickovics et al., 2002; Nwauche et al., 2006). It has also been found that adherence increases with age (Ghidei et al., 2013) except in the most elderly (those aged over 75 years). This may be because the elderly usually have more complex medical regimens and more co-morbidity, such as visual, hearing or

memory impairment. On the contrary, Barclay et al, (2007) found that the rate of poor adherence was twice as high among younger patients (68%) than with older individuals (33%).

Although in our study there was a higher percentage of non-adherence in the younger age groups 25-34 and 35-44 years, it was not statistically significant. The non-adherence may have been influenced by the higher rate of substance abuse in the younger age groups which have been shown to compromise adherence to ART.

There was a preponderance of female participants in this study which reflects the fact that the rate of HIV infection is higher in women than men. However, there was no significant association between gender and medication adherence. This finding is in contrast to the study that was carried out in Port Harcourt, Nigeria by Nwauche, (2006) and in United States by Berg et al, (2004) who found that gender has influence on adherence to anti-retroviral therapy.

In this study the percentage of the non adherents in the unemployed was more than the employed. There was no significant relationship between employment status and adherence to medication. This finding is in agreement with study done by Erah and Arute (2008). This may be explainable by the fact that antiretroviral drugs are free. Furthermore, it has also been shown that the positive effect of free treatment is often offset by indirect transportation costs in areas where patients live far away from health facilities (Mills et al., 2006). In addition, researchers had found that health services fees and cost of transportation are associated with lower adherence to ART (Mills et al., 2006).

High levels of education have been associated with increased adherence to ART (Peltzer and Pengpid, 2013; Stone., 2004) This was replicated in this study, people with higher level of education generally have greater access to information and are more likely to stick to informed decisions.

Some common reasons for missing medications have been simply forgot 66%, being busy 53%, away from home 57% and change in routine (Chesney et al., 2000, Talam et al., 2008). In this study we found simply forgot (13.8%) avoiding side effects 12.5%, away from home 10% and being busy 7.5%, were the common reasons. These reasons may have been associated with improved in health and patients may likely be working away from home and or lack of social support and cognitive impairment from substance abuse (Gonzalez et al, 2004).

In conclusion, this study underscores the critical importance of establishing a comprehensive therapeutic alliance between clinicians and patients to assess and address factors that tamper with treatment adherence. Most especially, in scarce resource countries where the second line treatment regimen is not readily available if resistance is developed to the first line regimen. Fortunately, most of these factors are amenable to medical and behavioral intervention once they are identified. Therefore, it is necessarily important to screen all patients on ART for substance abuse and to give clear instructions about regimen and it should be tailored to fit the individual lifestyle in order to achieve optimum benefits.

The study has several limitations most especially the sample size which was small and may not be a true reflection of what is happening and in other centers

across the state. A diagnostic rather than screening instrument would have given clearer clinical picture of the magnitude of the problem. Furthermore, confounding variables such as psychosocial factors were not controlled which may have influenced the association between substance use and adherence to ART.

We suggest that further study in this area should look at psychosocial factors and the temporal relationship between substance misuse and adherence to ART in our environment.

ACKNOWLEDGEMENTS

We want to specially register our gratitude to the record staff of infectious diseases unit of Plateau State Special Hospital in ensuring that all eligible consented individuals participated in the study.

REFERENCES

- Aloisi, M.S.; Arici, C.; Balzano, R. et al (2002). Behavioral correlates of non adherence to antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndrome*, 31(3), 145-148.
- Barclay, T.R., Hinkin, C.H., Castello, S.A., et al (2007). Age-associated predictors of medication adherence in HIV positive adults: health beliefs, self-efficacy and neuro-cognitive status. *Health Psychology*, 26(1), 40-49.
- Berg, K.M.; Demas, P.A.; Howard, A.A.; Schoenbaum, E.E.; Gourevitch, M.N. & Amsten, J.H. (2004). Gender differences in factors associated with adherence to antiretroviral therapy. *Journal of General Internal Medicine* 19(11), 1111-1117.

- Braithwaite, R.S., McGinnis, K.A., Conigliaro, J. et al (2005b). A temporal and dose-response association between alcohol consumption and medication adherence among veterans in care. *Alcoholism Clinical and Experimental Research*, 29:7;1190-1197.
- Braithwaite, R.S.; Kozal, M.J.; Chang, C.C. et al (2007). Adherence, virological and immunological outcomes for HIV-infected veterans starting combination antiretroviral therapies. *AIDS* 21:12; 1579-1589
- Chander, G., Lau, B., Moore, R.D. (2006). Hazardous alcohol use: a risk factor for non-adherence and lack of suppression in HIV infection. *Journal of Acquired Immune Deficiency Syndrome* 1:43-44; 411-417.
- Chesney, M.A. (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases* 30:171-176.
- Conigliaro, J.; Gordon, A.J.; McGinnis, K.A. & Rabeneck, L. (2003). How harmful is hazardous alcohol use and abuse in HIV infection: do health care providers know who is at risk? *Journal of Acquired Immune Deficiency Syndrome* 33:521-525.
- Erah, P.O., Arute, J.E. (2008). Adherence of HIV/AIDS patients to antiretroviral therapy in a tertiary health facility in Benin City. *African Journal of Pharmacy and Pharmacology* 2:7; 145- 152.
- Galvan, F.H., Bing, E.G., Fleishman, J.A., et al (2002). The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: results from the HIV cost and services utilization study. *Journal on Studies of Alcohol* 63:2; 179-186.
- Ghidei, L.; Simone, M.J.; Salow, M.J.; Zimmerman, K.M. et al (2013). Aging, antiretrovirals and adherence: A meta-analysis of adherence among older HIV-infected individuals. *Drugs Aging* 30:10; 809-819.
- Gifford, A. L., Bormann, J. E., Shively, M. J., Wright, B. C., Richman, D. D., Bozzette, S. A. (2000). Predictors of self reported adherence and plasma concentrations in patients on multi drug antiretroviral regimes. *Journal of Acquired Immune Deficiency Syndromes* 23: 386-395.
- Gill, C.J., Hames, D.H., Simon, J.L., Thea, D.M., Sabin, L.A. (2005) No room for complacency about adherence to antiretroviral therapy in Sub-Saharan Africa. *AIDS* 19:1243-9
- Gonzalez, J.S., Penedo, F.J., Antoni, M.H. et al (2004). Social support, positive state of mind and HIV treatment adherence in men and women living with HIV/AIDS. *Health Psychology* 23:4; 413-418.
- Haorah, J.; Heilman, D.; Diekmann, C.; Osna, N. et al (2004). Alcohol and HIV decrease proteasomes and immunoproteasome function in macrophages: implications for impaired immune function during disease. *Cellular Immunology* 229:2; 139-148.
- Hendershot, C.S., Stoner, S.A. Pantalone, D.W., Simoni, J.M. (2009). Alcohol use and antiretroviral adherence: review and meta-analysis. *Journal of Acquired Immune-deficiency Syndromes*, 52:2; 180-202.
- Ickovics, J.R., Mende, C.S. (2002). Adherence to HAART among patients with HIV: breakthroughs and barriers. *AIDS Care* 14:309-18.
- Kalichman, S.; Simbayi, L.C.; Kaufman, M.; Cain, D. & Jooste, S. (2007). Alcohol use and sexual risks for HIV/AIDS in Sub-Saharan Africa: Systematic

- review of empirical findings. *Prevention Sciences* 8:2; 141-151.
- Kalichman, S.C.; Grebber, T.; Amaral, C.M.; McNereg, M. et al (2012). Intentional non adherence to medications among HIV positive alcohol drinkers: prospective study of interactive toxicity beliefs. *Journal of General Internal Medicine* 28:3;399-405.
- Komiti, A., Judd, F., Grech, P., et al (2003). Depression in people living with HIV/AIDS attending primary care and out patients clinics. *Australian New Zealand Journal of Psychiatry* 37:70-77.
- Liu, H., Golin, C. E., Miller, L. G., Hony, R.S., Beck, C.k., Sanudaji, S. et al (2001). A comparison study of multiple measures of adherence to HIV protease inhibitors. *Annals of Internal Medicine* 134: 968- 977
- Mills, E.J., Nachega, J.B., Buchan, I., Orbinski J., Attaran, A., Singh, S. (2006). Adherence to Antiretroviral Therapy in sub-Saharan Africa. A meta-analysis. *Journal of the American Medical Association* 296: 679-690.
- Murphy, D.A., Marelich, W.D., Hoffman, D., Steers, W.N. (2004). Predictors of Antiretroviral Adherence. *AIDS Care* 16:4; 471-484
- Murphy, E. L., Collier, A. C., Kalish, L. A., Assman, S. F., Para, M. R., Flanigan, T. et al (2001). Highly active antiretroviral decreases mortality and morbidity in patients with advanced HIV disease. *Annals of Internal Medicine*, 135:17-26 and North America: A meta-analysis. *Journal of the American Medical Association* 296: 679- 690.
- Nachega, J.B., Stein, D.M., Lehman, D.A., Hlatshwayo, D., Mothopeng, R., Chaisson., R.E. et al (2004). Adherence to antiretroviral therapy in HIV- infected adults in Soweto South Africa. *AIDS Research in Human Retroviruses* 20:1053-6.
- Newcombe, D.A., Humenuk, R.E., Ali R. (2005). Validation of the World Health Organization Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). Report of result from Australia Site. *Drug and Alcohol Research* 24:3; 217- 26.
- Nieuwkerk, P.Y., Sprangers, M.A., Burger, D.M., Hoetelmans, R.M., Hugen, P.W., Danner, S.A. et al (2001). Limited patients Adherence To Highly Active Antiretroviral Therapy for HIV- I Infection Observational cohort. *Archives of Internal Medicine* 161:1962- 1968.
- Nwauche, C.A., Erhabor, O., Ejele, O.A., Akani, C.I, (2006) Adherence to Antiretroviral Therapy among HIV- infected subjects in resource limited setting in the Niger Delta of Nigeria. *African Journal of Health Sciences* 13: 34; 13-7.
- Olley, B.O., Gxamba, F., Seedat, S. et al (2003). Psychopathology and coping in recently diagnosed HIV/AIDS patients: The role of gender. *South African Medical Journal*, 93:12; 928-931.
- Oyugi, J.H., Byakika-Tusiime, J., Charleboes, E.D. et al (2004). Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. *Journal of Acquired Immune Deficiency Syndromes* 36:5; 1100-1102.
- Peltzer, K. & Pengpid, S. (2013). Socioeconomic factors in adherence to HIV therapy in low and middle income countries. *Journal of Health, Population and Nutrition*, 31:2; 150-170.
- Pence, B.W., Thiemann, N.M., Whitten, J.O. et al (2008). Coping strategies and patterns of alcohol and drug use

- among HIV infected patients in the United States Southeast. *AIDS Patient Care and STDs* 229:11; 869-877.
- Peterson, D.L., Swindles, S., Mohr, J. et al (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine* 133:21-30.
- Samet, J.H.; Horton, N.J.; Traphagen, E.T.; Lyon, S.M. & Freedberg, L. (2003). Alcohol consumption and HIV disease progression: Are they related? *Alcoholism Clinical and Experimental Research* 27:5; 862-867.
- UNAIDS/ WHO/UNICEF (2011). *AIDS Epidemic Update* UNAIDS, World Health Organization Geneva.
- UNAIDS (2011). *AIDS epidemic update* Geneva Switzerland.
- Stone, V.E (2004). Optimizing the care of minority patients with HIV/ AIDS. *Clinical Infectious Diseases* 38:3; 400-404.
- Tucker, J.S., Orlando, M., Burman, M.A., Sherbourne, C.D., Kung, F.Y., Clifford, A.L. (2004). Psychosocial mediators of Antiretroviral non-adherence in HIV positive adults with substance use and mental health problems. *Health Psychology* 23: 363-370.
- Talam, N. C., Gatongi, P., Rotich, J., Kimaiyo, S. (2008). Factors affecting antiretroviral drug adherence among HIV/AIDS adult patients attending HIV/AIDS clinic at Moi Teaching and Referral Hospital, Eldoret, Kenya. *East African Journal of Public Health* 5:2; 74-78.