Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Scholars Research Library

Archives of Applied Science Research, 2012, 4 (3):1447-1452
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-508X
CODEN (USA) AASRC9

Effects of highly active antiretroviral therapy (HAART) on blood pressure changes and its associated factors in HAART naive HIV-infected patients in North eastern Nigeria

Ballah Akawu Denue[1]; Pharm Jamil Muazu[2]; Wadzani Gashau[3]; Daniel Nkami MBO[4] and Nnenna Anthony Ajayi[5]

[1]Department of Medicine, University of Maiduguri Teaching Hospital, PMB 1414, Maiduguri, Borno State
[2]Department of Pharmaceutical Services , University of Maiduguri Teaching Hospital, PMB 1414, Maiduguri, Borno State
[3]Department of Medicine, University of Maiduguri Teaching Hospital,PMB 1414, Maiduguri
[4]Borno State, Maitama General Hospital, FCDA, Abuja
[5]Federal Medical Centre, Abakaliki, Ebonyi State

ABSTRACT

To examine the impact of highly active antiretroviral therapy (HAART) and associated factors on blood pressure (BP) of naive patients after 2 years of treatment. Observational cohort study of 227 patients initiating their first HAART regimen. We evaluated mean blood pressure (BP) and demographic, epidemiological, clinical, immunologic and biochemical characteristics related to HIV infection prior to HAART and at 2 years. High blood pressure (HBP) [systolic BP (SBP) ≥140mm Hg and/or diastolicBP (DBP) ≥90mm Hg] was defined according to international criteria. Of the 227 patients, 51% were men, majority 81% had AIDS, 26% had HBP and their mean age was 40 years. At 2 years the prevalence of HBP was 31.7%. The corresponding changes in SBP, DBP and pulse pressure (PP) among hypertensive and normotensive group was 3.47±15.21 vs -0.71±16.28 (P=0.08), 1.81±1 0.12 vs 1.0±11.39 (P=0.625) and 1.67±14.14 vs 1.71±12.08 (P =0.982) respectively. Univariate analysis showed that HBP was associated with older age, male gender and higher baseline triglyceride. A linear regressionmodel adjusting for age and sex suggested a significant impact of older age and male gender. We observed high prevalence of hypertension in our cohort, the pattern persisted in an upward trend after 2 years. The increase in BP depended on age, male gender baseline triglyceride. Blood pressure shouldbe periodically measured and treated when necessary in HIV-infected patients on HAART.

Keywords: HAART, HIV, HBP, SBP, DBP hypertension, pulse pressure.

INTRODUCTION

The introduction of a highly active antiretroviral therapy (HAART) in the treatment of HIV diseasehas provided gratifying results, like long-term viral suppression, decrease of opportunistic infections, repair of the immune system and increased CD4 cell counts. As a result, morbidity and mortality of HIV-infected patients continue to decline in developed countries [1]However, chronic non- communicable diseases that may coexist with HIV infection are somewhat neglected in favour of "classic" diseases such as HIV itself and Tuberculosis and malaria[2]The prevalence of systemic hypertension among HIV-infected patients is much higher than that inthe general population: It has been estimated as 20%–25% before the introduction of HAART [3] and as approximately 74% among patients who undergo HAART with protease inhibitorsand who subsequently develop lipodystrophy and metabolic

syndrome [4]. The lipodystrophicsyndrome is characterized by peripheral fat wasting in the arms, legs, and buttocks, as well as byincreased fat deposition in the breasts, abdomen, and dorsocervical fat pads. Systemic hypertensionin HIV-positive patients seems to have a significant effect on their risk of premature cardiovasculardisease: Compared with normotensive HIVpositive patients, hypertensive patients havea higher frequency of coronary heart disease (16.1% vs 1.3%) and a higher incidence of myocardial infarction (8.1% vs 0.7%) [5].Reports also suggest that younger HIV-1-infected patients are at a higher risk for developing hypertension compared with the general population, especially if a protease inhibitor was included in the HAART regimen[4,6-8].In view of this strong association between Hypertension and HIV infection, primary preventive measures such as weight andblood profile monitoring including other life style modification [9], and future research into agents such as precursor of L-argenine, nitric oxide (NO) and antioxidants that has a tendency of preventing or reversing atherosclerotic changes in the blood vessels need to be explored [10] Although the association between HAART use and hypertension has been documented elsewhere, to our knowledge it has not been reported in our environment, most previous studies were limited by their cross sectional design [4,6,8,11,12]. The aim of this study was to assess the impact of HAART on the on blood pressure (BP) of treatment-naive patients after 2 years of HAART.

MATERIALS AND METHODS

Patients and Methods

This design was a prospective, observational study of 268 HIV-infected patientswho presented for care at Infectious diseases clinic at university of Maiduguri teaching hospital, who started HAART between January 2007 and October 2008 and remained same regimen for 2 years. HAART was composed of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a nonnucleoside reverse transcriptase inhibitor (NNRTI). The eligibility for HAART were assessed by the attending physician based on CDC 1993 revised classification system for HIV infection and expanded AIDS surveillance case definition for Adolescent and Adult [13]. Patients were excluded if they were pregnant, were breastfeeding, or were current alcohol or illegal drug abusers. Patients who stopped HAART or switched from a PI to a NNRTI or vice versa during the study period were also excluded.

At entry into the study, participants underwent clinical assessment that included history, general physical and gynaecological examination where indicated. Anthropometric measurements were carried out for all subjects.Smokers were considered to be those who smoked one or more cigarettes a day. BP, measured with a mercury sphygmomanometer, was taken with the patient sitting in a relaxed, upright position and remaining silent. Patients had been resting for at least 5 min before BP was measured. Two measurements were made at 30 s intervals and the mean BP was calculated. High blood pressure (HBP) [systolic BP (SBP) ≥140 mm Hg and/or diastolic BP (DBP) ≥90 mm Hg] was defined according to international criteria[11] and a high pulse pressure (HPP) was defined as a pulse pressure (PP) >50 mm Hg.[12] Blood was drawn after a 12-h fast for the measurement of plasma lipids. Fasting blood glucose, serum total cholesterol, triglycerides, HDL, LDL, urea, creatinine serum enzyme ALT were estimated by automated clinical chemistry autoanalyzer (Hitachi 902 Roche Diagnostic GmbH, Mannhein Germany). The CD4+T lymphocyte cell count was estimated by cyflow counter (Partec GmbH, Gorlitz Germany). Blood was drawn after a 12-hour fast for the measurement of plasma lipids. Diagnosis of dyslipidaemia was based on cholesterol levels≥5.18mmol/L and triglyceride levels 1.69mmol/L.

Patient data were collected in a computerized database for later statistical analysis with SPSS®, version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were analysed with the $\chi 2$ test and Yates' correction or Fisher's exact test when necessary. Comparison of quantitative variables prior to starting HAART and at 2 years of HAART was performed with the paired Student's t-test or the Mann Whitney U-test for variables that did not follow a normal distribution. Quantitative variables for hypertensive and normotensive patients were compared with Student's t-test or the Mann Whitney U-test for variables that did not follow a normal distribution. The change in SBP compared with baseline was defined as the outcome variable. Pearson correlation coefficients between this variable and continuous variables were determined, and a linear regression model adjusting for age and gender, with the variables correlated with the change in SBP, was used to investigate which variables better explained the increase in SBP. Statistical significance was set at $p<0.05$.

RESULTS

Demographic data and clinical characteristics of the study population

A total of 268 HIV-1 seropositive patients were enrolled in this prospective study. Seven patients died due to complications unrelated to cardiovascular disease and 34 were excluded for lack of follow-up. A study population of 227 patients was, thus, observed and included in the analysis. Heterosexual was the presumed risk factor in majority of the patients. Mean duration of diagnosed HIV infection was 56.7±52.6 months 81% had AIDS by clinical or

immunological criteria. Participants that had clinical AIDS had a lower BP than others (SBP 113.9 vs 135.4; DBP 72.6 vs 88.3.2mmHg; P<0.001). The demographic data and clinical characteristics are shown in Table 1.

Systemic hypertension was present in 26.4% of HIVinfected patients in our cohort (60 of 227 patients).Hypertension showed a male preponderance of 35.4% than 17.12% in females (p=0.002). No significant difference was observed between hypertensive and normotensive subjects in terms of risk factor for HIV acquisition. Diagnosis of hypertension was known for the first time in 46 of the participants at initial assessment of those evaluated. Twenty-eight subjects (60.9% of hypertensives) received antihypertensive therapy during the study period. While 14 patients already had antihypertensive treatment prior to study entry, five patients were started on antihypertensive therapy during the follow-up.These patients are included as hypertensive patients at the end of the study, and we used their BP at the moment they initiated treatment withantihypertensive drugs to calculate SBP changes.

Comparison of demographic and clinical data between hypertensive and normotensive patients
The mean SBP in the hypertensive group at study entry was 130.38±18.91mmHg and the mean DBP was 86.80±12.31mmHg compared with 117.83±15.61 and 78.04±8.80mmHg in the normotensive group, respectively (P<0.0001). At the end of follow-up, the corresponding increase SBP in hypertensive and normotensive group was 3.47±15.21 and-0.71±16.28, p=0.084 respectively, while the change in DBP in hypertensive and normotensives was 1.81±10.12 and 1.0±11.39 (p=0.625) respectively. The frequency of hypertensives increased to 72 (31.72%) in comparision to 60 (26.40%) at baseline. (p=0.147).

Taking age and gender into account the hypertensive group was an average of 12 years older than the normotensive group (46.0±9.10 vs 34±12.74 years; P<0.0001). Accordingly, age >50 years was associated with 4 times risk of developing hypertension (OR: 5.73; 95% CI: 2.81–14.63; P<0.0001). The proportion of males were significantly higher in the hypertensive group than normotensive 61.10% vs 38.90% (p=0.000). The BMI between the hypertensive and normotensives was similar. Prevalence of diabetes mellitus was similar in the hypertensive group and normotensive group (8.1% vs 7.8%; p=0.889).No significant differences were observed in frequency of chronic infection with hepatitis B or C as shown in Table 2.

Comparison of some laboratory tests between at study end point
Baseline mean CD4 lymphocyte counts were slightly lower in the hypertensive individuals than in the normotensive group (244.79±153.58 vs 247.19±174.88 cells/mm3; P=0.925). After 2years of HAART there was similar increase in CD4 count in both group (p=0.624).

No significant difference in the mean values for metabolic and renal parameters in the two groups were noted at baseline. The level of Triglycerides significantly higher in hypertensives than normotensives (P = 0.002),while total cholesterol, LDL- or HDL–cholesterol serum creatinine, urea, ALT and FBGwere similar between the two groups. Univariate analysis showed that HBP was associated with older age, male gender and higher baseline triglyceride. A linear regressionmodel adjusting for age and sex suggested a significant impact of older age and male gender (Table 3).

DISCUSSION

As the quality and life expectancy of HIV-1-infected patients improves, long-term complications of the HIV infection and antiretroviral therapy is expected. Controversial and conflicting association between chronic infection and/or chronic antiretroviral therapy and systemic hypertension have been documented elsewhere. While some authors documented normal BP in HIV-infected patients [11,12] others found that hypertension was common in HIV-infected patients [4,6,8,16-18]. To the best of our knowledge, this is the first prospective study to analyse the influence of HAART on BP in our environment. Systemic hypertension was present in 26.4% of HIV infected patients in our cohort higher than the national prevalence of hypertension of 14.5% determined earlier [19,20]. The prevalence of hypertension remained high after 2 years on HAART. The participants were around 40 years of age, with a high prevalence of AIDS patients. Clinical AIDS patients had significantly lower BP, in agreement with other studies, we found no correlation between hypertension, duration of HIV infection and CD4-cell count [4,6,17]. Seaberg et al [21] analyzed BP in the Multi-centre AIDS Cohort Study and found that, while the risk of systolic hypertension in men on HAART was similar to that in HIV-negative men during the first 2 years following initiation of HAART, a longer duration on HAART carried a substantially increase risk of systolic hypertension; no change was seen in DBP. In our series, the time of exposure to HAART was limited to 2 years. Groups of hypertensive and normotensive patients had similar risk factor for HIV, proportion of AIDS and duration of infection, but patients with systemic hypertension had slightly low CD4 lymphocyte counts. As in the general population, our hypertensive subjects were older but had similar BMI with normotensive patients. Moreover, age and male gender were found to be independent risk factors for the development of hypertension in this population. In contrast, BMI was found not

to be an independent risk factor, this finding is at variance with previous study that reported linear relationship between BMI and Pack cell volume with blood pressure level normal population [9],as changes in BMI in hypertensives and normotensives were insignificant, hence changes in BMI observed in the cohort might be attributable to the age-related increase in bodyweight and the HAART-induced improvement in the general state of health of these patients. The hypothesis of an increased risk for the development of hypertension in HIV-infected patients is based mainly on a few studies investigating the effects of PIs, in particular with regard to indinavir, and lipodystrophy on blood pressure as well as on observational data [4,6-8], however our cohort had no PI as part of their HAART regimen. A few cross-sectional analyses and cohort studies have examined the effects of HAART on blood pressure. Bergensen et al. compared the prevalence of hypertension in HIV-infected patients naïve to HAART or receiving HAART and HIV-negative controls in a cross-sectional analysis. They reported the prevalence of hypertension to be 13% in HAART-naïve patients, 21% in those individuals receiving HAART, and 24% in HIV-negative individuals. They concluded that the prevalence of hypertension in patients receiving HAART was not statistically different from that of the HIV-negative controls or treatment-naïve patients[12].Gazzaruso et al. looked at the prevalence of hypertension in relation to the metabolic syndrome in 287 HIV-positive patients receiving HAART and 287 age- and gender-matched controls. Compared to the control group, there was an increased prevalence of hypertension (34.2% vs. 11.9%, $p < .0001$) and metabolic syndrome (33.1% vs. 2.4%, $p < .0001$) in the patients on HAART [6].Seaberg et al. examined a cohort of 5,578 patients (84,813 person-visits) over approximately 20 years; 58.80% were HIV negative and 41.25% were HIV positive. Of the HIV-positive patients, 35.0% were using antiretroviral therapy and 37.1% of those were using HAART. The investigators concluded that the prevalence of systolic and diastolic hypertension was not significantly different in patients receiving HAART compared to HIV-negative controls when used for less than 2 years. After 2 years, the prevalence of systolic hypertension increased from 2 to 5 years (odds ratio [OR] 1.51, 95% CI 1.25–1.82), and again at 5 years (OR 1.70, 95% CI 1.34–2.16) [21].In a another study Crane et al. followed a cohort of 444 HAART-naïve, HIV-positive patients initiating treatment. The mean age was 35 years, and 84% were male. Treatment regimens were evenly divided between those receiving PI-based regimens and NNRTI regimens. The cohort experienced a significant increase in mean SBP after initiating HAART (124.6 vs. 121.6 mmHg, $p \leq .001$). The researchers found no significant difference between classes of drugs on blood pressure elevation; however, they concluded that patients receiving a liponavir/ritonavir-based regimen had a two-fold increased risk of developing elevated blood pressure (OR 2.4, 95% CI 1.0–5.6, $p = .04$), which was partly mediated by an increase in BMI (OR 1.4, 95% CI 1.0–1.8, $p = .02$). Further, patients with a CD4+ count of ≤50 were twice as likely to develop elevated blood pressure (OR 2.4, 95% CI 1.2–4.8, $p = .02$).[23] Thus, there are conflicting reports of elevations in blood pressure with the use of HAART.

We also observed lower but insignificant CD4 lymphocyte counts in hypertensive in comparison to normotensive patients. This might be attributable to the higher mean age in the hypertensive group, as CD4 lymphocyte counts lower with age and recovery of CD4 cells in response to antiretroviral therapy is impaired in older subjects, making a more intensive antiretroviral therapy necessary [24]. However, it is difficult to establish a clear link between immune status and hypertension from our data. In our cohort 4.7% normotensives develop high blood pressure within 2 years, suggesting that antiretroviral therapy has a significant direct impact on blood pressure. This is in sharp contrast to some workers that reported no effect of antiretroviral therapy on blood pressure [6,8]. In our study, we observed no statistical difference between hypertensive and normotensive patients when comparing current as well as total duration of specific antiretroviral drugs or combination regimen. In this study, 12 different antiretroviral agents are available for the combination therapy of HIV disease, the number of patients in our study might be too small to show significant differences in regards to specific antiretroviral drugs. We demonstrated a positive correlation between serum triglycerides and blood pressure elevation. Sattler et al [4], in a case–control study, reported that SBP correlated with lipodystrophy and with fasting triglycerides in all HIV-infected patients. These findings are consistent with those of another group and our observations showing elevated triglycerides in hypertensive as compared with normotensive patients [6]. Although we cannot predict from this study what changes in BP might occur later, given the remarkable increase in BP during the 2 years year on HAART, it would be interesting to assess the pattern of longer-term prevalence of hypertension in these patients. Factors associated with the increase in BP at 2 years in our cohort were age, male gender and hypertriglycerinaemia,

In summary, we observed high prevalence of hypertension in our cohort, the pattern persisted in an upward trend after 2 years. Age, male gender and hypertriglycerinaemia were associated with hypertension. Longer follow-up of patients on HAART and case–control studies will reveal more information about the true role of HAART and its metabolic consequences for high BP. The observation of high prevalence of hypertension, a known cardiovascular risk factor and additional to the risk factors of metabolic disorders related to HAART is worrisome [25-31], so should be monitored periodically and treated when necessary.

Table 1.Clinical and epidemiological characteristics of the 227 patients and study parameters before antiretroviral therapy

Variable	
Sex (n(%))	
Male	116 (51%)
Female	111(49%)
Age (years)	40.26±9.30
Smokers (n(%))	12(5.3%)
HIV risk (n(%))	
Heterosexual	204 (89.9%)
Parenteral drug abuser	0
Homosexual	0
unknown	23(10.1%)
HIV time (months)	56±53
AIDS (n (%)	184(81.05%)
Hepatitis B (n(%))	19(18.40%)
Hepatitis C infection (n(%))	01(0.40%)
ARV (n (%))	
2 NRTI	227(100%)
1 NNRTI	227(100%)
PI	0
Body mass index (kg/m^2)	24.72±8.22 (6.00-49.32)
Systolic blood pressure (mmHg)	123.29±18.17
Diastolic blood pressure(mmHg)	81.89±11.33
High blood pressure (n(%))	60(26.43%)
Males (n(%)	41(35.35%)
Females(n(%)	19(17.12%)
Total cholesterol (mmol/L)	4.57±1.39
HDL cholesterol (mmol/L)	1.45±0.75
LDL cholesterol (mmol/L)	2.63±1.26
Triglyceride (mmol/L)	2.28±1.22
Creatinine (umol/L	87.98±32.92
Urea (mmol/L)	4.13±1.87
ALT (mmol/L)	34.49±36.88
CD4+ Count (cells/µl)	246.43±168.08

Quantitative variables are expressed as the mean±standard deviation (SD).
HBV, hepatitis B virus; ARV, antiretroviral therapy; PI, protease inhibitor; NNRTI, Non-nucleoside reverse transcriptase inhibitors; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Table 2.Univariate analysis of patients with high blood pressure (n=72) versus patients without high blood pressure (155) after 2 years of HAART

Variable	High blood pressure	Non-high blood pressure	p-value
Age (years)	46±9.10	34±12.74	0.000*
% male sex	61.10	38.90	0.000*
% smokers	8(11.1%)	4(2.5%)	0.000*
HIV time (months)	58.3±53.4	54.8±57.4	0.928
AIDS (n (%)	14(19.40%)	29(18.71)	0.896
Baseline SBP (mm Hg)	130.38±18.91	117.83±15.61	0.000*
Baseline DBP (mm Hg)	86.80±12.31	78.04±8.80	0.000*
Baseline PP (mm Hg)	26.39±21.45	31.54±21.14	0.108
Δ SBP (mm Hg)	3.47±15.21	-0.71±16.28	0.084
Δ DBP (mm Hg)	1.81±10.12	1.0±11.39	0.625
Δ PP (mm Hg)	1.67±14.14	1.71±12.08	
Baseline BMI (kg/m^2)	24.22±8.13	24.95±8.29	0.557
BMI (kg/m^2)	26.42±7.10	25.94±9.95	0.732
ΔBMI(kg/m^2)	2.20±4.83	1.00±6.41	
Baseline TC (mmol/L)	4.51±1.30	4.59±1.43	0.704
% baseline TCH	14(19.44%)	28(18.10%)	0.999
% baseline HTG	21(29.20%)	13(8.40%)	0.000*
Baseline LDL (mmol/L)	2.57±1.35	2.67±1.22	0.597
Baseline HDL (mmol/L)	1.44±0.73	1.46±0.75	0.858
Baseline TG (mmol/L)	2.23±1.16	2.38±1.34	0.442
Baseline Cr (umol/L)	88.49±31.84	87.74±33.51	0.880
Baseline Urea (mmol/L)	4.28±1.86	4.05±1.88	0.416
Δ Cr (umol/L)	-2.57±42.67	-5.65±31.46	0.556
Δ Urea (mmol/L)	0.64±2.30	0.74±3.40	0.833
Baseline CD4+ Count(cells/µl)	244.79±153.58	247.19±174.88	0.925
Δ CD4+ Count (cells/µl)	183.99±261.71	205.16±295.13	0.624

**Statistically significant.*
Quantitative variables are expressed as the mean±standarddeviation(SD).HBV, hepatitis C virus; PIs, protease inhibitors; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; Δ, increase; BMI, bodymass index, TC, total cholesterol; HCT, hypercholesterolaemia (TC> 5.18 mmol/L); HTG, hypertriglyceridaemia; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

Table 3.Comparision of some immunological and biochemical parameters after 2 years of HAART

Parameter	Hypertensive group (n=72)	Normotensive group (n=155)	p-value
Δ Cr (umol/l)	-2.57±42.67	-5.65±31.46	0.542
Δ Urea(mmol/l)	0.64±2.30	0.74±3.40	0.856
Δ CD4 Count(cells/µl)	193.99±261.71	205.16±295.13	0.784
Δ T chol(mmol/l)	0.65±1.27	0.60±1.85	0.836
Δ HDL chol(mmol/l)	0.01±0.90	0.17±0.97	0.238
Δ LDL chol (mmol/l)	0.51±1.51	0.55±1.42	0.847
Δ TG (mmol/l)	0.50±1.61	-0.22±1.63	0.002*
Δ Fasting Glu (mmol/l)	0.63±2.19	0.42±1.86	0.456

**Statistically significant. Δ, change; Cr, Creatinine; T chol, Total cholesterol; HDL chol, high density lipoprotein, LDL, low density lipoprotein, TG, triglyceride, Glu, glucose.*

REFERENCES

[1] Palella, F.J, Jr, Delaney KM, Moorman AC. *N Engl J Med***1998**; 338:853–860.
[2] Daniel M, Edinah M, Caston S, Peter M, Philimon N, Shadreck D. *Achieves of Applied Science Research*, **2001**, 3(1):333-342.
[3] Aoun S, Ramos E.*CurrHypertens Rep***2000**;2:478–481.
[4] Sattler FR, Qian D, Louie S,*AIDS***2001**;15:2001–2010.
[5] Jung O, Bickel M, Ditting T. *Nephrol Dial Transplant***2004**;19:2250–2258.
[6] Gazzaruso C, Bruno R, Garzaniti A. *J Hypertens***2003**; 21:1377–1382.
[7] Chow D, Souza S, Richmond-Crum S, Shikuma C. *Antiviral Ther***2000**; 5 [Suppl 5]: S31.
[8] Cattelan AM, Trevenzoli M, Sasset L. *AIDS***2001**; 15: 805–807.
[9] Akinjide M A, Olubayode B, Ijeoma CC. *Annals of Biological Research*, **2011**, 2(2):65-71.
[10] Vincent M, Yamini S, Mithum SR, Akhilesh V, Tejas DS, *Des Pharmacia Lettre***2010**,2(2):244-257.
[11] Mattana J, Siegal FP, Sankaran RT, Singhal PC. *Am J Med Sci***1999**;317:232-237.
[12] Bergersen BM, Sandvick L, Dunlop O, Birkeland K, Bruun JN. *Eur J ClinMicrobiol Infect Dis***2003**;22:731-736.
[13] Centers for Disease Control and prevention. *JAMA***1993**; 269: 729 – 730.
[14] Joint National Committee. *Arch Intern Med***1997**; 157: 2413–2446.
[15] Kannel WB, Vasan RS, Levy D. *Hypertension***2003**; 42: 453–456.
[16] Hadigan C, Meigs J, Corcoran C. *Clin Infect Dis***2003**; 32: 130–138.
[17] Chow DC, Souza SA, Chen R, Richmond-Crum SM, Grandinetti A, Shikuma C. *HIV Clin Trials***2003**; 4: 411–416.
[18] Friis-Moller N, Weber R, Reiss P *AIDS***2003**; 17: 1179–1193.
[19] Cooper R, Rotimi C, Ataman S, McGee D, Osotimehin B, Kadiri S, *Am J Public Health* **1997**;87(2):160-8.
[20] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluationand Treatment of High Blood Pressure (The JNC 7 Report). *JAMA***2003**;289(19):2560-2572.
[21] Seaberg EC, Mun˜ oz A, Lu M. 10th Conference on Retroviruses and Opportunistic Infections. Boston, MA: February, **2003** [Abstract 744].
[22] Seaberg EC, Munoz A, Lu M,.*AIDS*.**2005**;19(9):953–960.
[23] Crane HM, Rompaey SE, Kitahata MM. *AIDS*. **2006**;20:1019–1026
[24] Viard JP, Mocroft A, Chiesi A. *J Infect Dis***2001**; 183: 1290–1294
[25] Carr A, Cooper DA. *Lancet***2000**; 356: 1423–1430.
[26] Hicks C, Currier J, Sax P, Sherer R, Wanke C. *AIDS Patient Care STDs***2003**;17: 221–233.
[27] Currier JS. *J Acquir Immune DeficSyndr***2002**; 31: S16–S32.
[28] Rhew DC, Bernal M, Aguilar D, Iloeje U, Goetz MB. *Clin Infect Dis***2003**; 37: 959–972.
[29] Carr A, Samaras K, Burton S. *AIDS***1998**; 12: F51–F58.
[30] Tsiodras S, Mantzoros C, Hammer S, Samore M.*Arch Intern Med***2000**; 160: 2050–2056.
[31] Palacios R, Santos J, Ruiz J, Gonza´lez M, Ma´rquez M. *AIDS***2003**; 17: 933–935.