

**Research Article****Metabolic Syndrome and Sub Clinical Atherosclerosis: Influence of HIV Status and HAART**Dr. Pradeep Mital<sup>1\*</sup>, Dr. Laxmi Kant Goyal<sup>2</sup>, Dr. Hazari Lal Saini<sup>3</sup>, Dr. Abhishek Agrawal<sup>4</sup>,  
Dr. Renu Saigal<sup>1</sup><sup>1</sup>Professor, Department of Medicine, MG Medical College, Jaipur, India<sup>2</sup>Assistant Professor, Department of Medicine, SMS Medical College, Jaipur, India<sup>3</sup>Resident, Department of Medicine, SMS Medical College, Jaipur, India<sup>4</sup>Associate Professor, Department of Medicine, SMS Medical College, Jaipur, India**\*Corresponding author**

Dr. Pradeep Mital

**Email:** [drpradeepmital@hotmail.com](mailto:drpradeepmital@hotmail.com)

**Abstract:** The aim was to detect and compare metabolic syndrome and sub clinical atherosclerosis in HIV patients on ART/ not on ART and normal population. This one year study was done among 100 HIV patients on ART and 100 HIV patients who were not on ART and 200 control subjects. Metabolic syndrome was diagnosed according to the guidelines from the 2001 National Cholesterol Education Program ATP III. Sub clinical atherosclerosis was detected by carotid colour Doppler studies. Metabolic syndrome was found in 15(7.5%) control subjects (group A), 19(19%) HIV cases who were not on ART (group B) and 21(21%) HIV cases on ART (group C). In metabolic syndrome positive persons; BMI was greater in controls (29.82 + 3.86kg/m<sup>2</sup>) than HIV cases (23.18 + 3.41kg/m<sup>2</sup> in group B and 22.08 + 2.44kg/m<sup>2</sup> in group C) (P<0.05). Waist circumference in control group (98.20 ±9.06cm) was significantly greater than HIV patients who were on ART (89.23±4.70cm) or without ART (89.74±4.09cm) (P < 0.001). But Waist circumference not differ significantly among HIV cases of both groups (P>0.05). SBP was significantly greater in the control group (128.40 + 8.36mm of Hg) as compared with the HIV groups (P <0.05). HIV positive patients on ART had more SBP (125.23 +8.87mm of Hg) than group B (119.58 +10.34 mm of Hg) (P <0.05). In HIV groups FBG were significantly more than the control group (P <0.05). But value not differ significantly among HIV cases (P>0.05). Triglycerides level were significantly increased in HIV cases than the control group (P<0.001) and also significantly higher in HIV group on ART than without ART (P<0.05). HDL was significantly decreased in HIV cases than healthy controls (p <0.05) and in HIV group on ART than without ART (P<0.05). There were no significant difference between all three groups in carotid intima thickness (P >0.05). In conclusion: Compared with controls, HIV patients had a greater frequency of impaired fasting glucose, plasma triglycerides and HDL. Metabolic syndrome might be associated with increased chances of increased carotid intima thickness.

**Keywords:** Metabolic syndrome, HIV, HAART, atherosclerosis**INTRODUCTION**

Human immunodeficiency virus (HIV) was first discovered in 1981. AIDS case in India was detected in 1986 and since then HIV infection has been in all states and union territories.

Highly active anti retroviral therapy (HAART) was introduced in 1996. HAART has resulted in sustained reductions of morbidity and mortality associated with HIV infection. Unfortunately, HAART has also been associated with metabolic complications that may increase patient's risk of cardiovascular disease [2].

For the past 10 years, the association between HIV, HAART and metabolic disorders and/or cardiovascular disease (CVD) has been a major focus of research. Studies of HIV-infected persons have revealed a high prevalence of metabolic syndrome among patients receiving HAART [3]. The metabolic effects of HAART in contributing to increased risk of premature

and accelerated atherosclerosis in HIV infection are recognized [4]. Metabolic syndrome doubles coronary heart disease mortality, after adjustment for age, sex, cholesterol level, physical activity, and smoking [4].

Persons with metabolic syndrome have a faster rate of progression of carotid and coronary atherosclerosis and, hence, have an increased risk of cardiovascular morbidity and mortality [5]. Measurement of carotid artery intima-media thickness (IMT) with high-resolution B-mode ultrasound is a well accepted, non invasive method of assessing atherosclerosis and tracking its progression [5]. Carotid IMT measurements correlate well with pathological measurements and are potent predictors of myocardial infarction and stroke, even after adjustment for other risk factors. [5] Progression of carotid IMT can be measured reliably over time and has been used as an end point in clinical trials in which treatment reduced both carotid IMT progression and cardiovascular events.

The studies in developed countries show an increase prevalence of metabolic syndrome in HIV infected individuals. However there is very limited data in the literature documenting the association between carotid atherosclerosis and metabolic syndrome in HIV-infected patients. Further in the Indian population we are observing that the patients of HIV are much emaciated. This observation coupled with the paucity of studies in the Indian population has promoted us to undertake this study.

## MATERIAL AND METHODS

This prospective and cross sectional study was done in department of medicine, SMS medical college and hospital, Jaipur from November 2010 to August 2011. In this study metabolic syndrome and sub clinical atherosclerosis was assessed and compared in HIV patients on ART/ not on ART and normal population.

We included 100 HIV patients on ART and 100 HIV patients who were not on ART. In control population, 200 subjects were taken who were age and sex matched. The subjects were randomly selected from indoor and outdoor (ART clinic, medical outdoor) department of SMS medical college and hospital and their consent taken. All subjects were above 18 years old. All HIV cases had HIV infection for more than six months. ART included in this study were 1st line therapy –NRTI+NNRTI; and 2nd line therapy or alternative therapy which included protease inhibitors alone or protease inhibitors combined with 1st line therapy. Patients who had any evidence of coronary artery disease, hypertension, diabetes mellitus, pregnancy, atherosclerosis (cause other than HIV) or metabolic syndrome (cause other than HIV) were excluded from the study.

HIV results were obtained by three type rapid method for detection of antibodies to HIV-1 & HIV-2 in serum/plasma [SD-bioline-(immunochromatography), Preeksak -(immunofiltration) and Combaids -solid phase immunosorbent assay (SPIA) in immuno-dot test format]. CD4 assay was done by flow cytometer -the BD FACS caliber system. Blood investigations results were obtained from central laboratory of SMS hospital after 12 hours fasting.

Metabolic syndrome was diagnosed according to the guidelines from the 2001 National Cholesterol Education Program Adult Treatment Panel (ATP III). According to ATP III, any three of the following traits in the same individual meet the criteria for the metabolic syndrome [6]. Abdominal obesity: a waist circumference over 102 cm (40 in) in men and over 88 cm (35 inches) in women., serum triglycerides 150 mg/dl or above, HDL cholesterol 40mg/dl or lower in men and 50mg/dl or lower in women, blood pressure of 130/85mm of mercury column or more, fasting blood

glucose of 110 mg/dl or above. Blood pressure measurements were taken in right arm sitting after 10 minutes of rest with mercury sphygmomanometer. Waist circumference was taken at maximum diameter at hips.

Sub clinical atherosclerosis was detected by colour Doppler studies of carotid vessels. The patients were examined by ultrasonography of carotid vessels using latest generation power colour doppler with 7.5 MHz probes. The patients were placed in a supine position for at least 10 minutes in a comfortable room for acclimatization. The common carotid, its bifurcation and at least the first 2 cm of the internal and external carotid vessels were examined bilaterally in the short and long axis using strong magnification; this helped correctly distinguish the real lumen from plaques, which were markedly hypo echoic with power colour doppler methods. Pathological findings were defined as the presence of plaques (focal echogenic structure with an  $IMT \geq 0.9mm$  [7].

## Statistical analysis

Continuous variables were expressed as mean  $\pm$  sd. Pairs of groups were compared using student's 't' test for a normally distributed continuous distribution. ANNOVA test was applied to compare more than two samples. Statistical significance was set at  $p < 0.05$ . Microsoft Excel and SPSS 20.0 for Windows were used for data storage and analysis.

## RESULTS

400 persons were included in our study. 100 were HIV positive on ART (group C), 100 were HIV positive without ART (group B) and 200 were control healthy subjects (group A).

Metabolic syndrome was found in 15(7.5%) healthy control subjects, 19(19%) HIV cases who were not on ART and 21(21%) HIV cases on ART.

Mean age of subjects having metabolic syndrome in HIV positive on ART was  $36.76 \pm 6.51$  years, in HIV positive without ART  $38.00 \pm 10.04$  years and in control group  $38.53 \pm 6.99$  years. HIV positive groups on ART had no significant age difference than other groups ( $P > 0.05$ ). There was no statistically significant difference in mean age among the studied groups ( $P > 0.05$ ).

Alcohol had effect on metabolic syndrome. In HIV positive on ART having metabolic syndrome alcoholic habit was seen in 15 (71.43%) subjects, as compared to HIV cases not on ART 8 (42.11%) and control subjects 7 (46.67%). We did not find any statistically significant difference for alcohol habits among the studied groups ( $P > 0.05$ ). So alcohol habit did not confound our study.

Table No.1 - Characteristics of study subjects having metabolic syndrome

		Group-A Healthy control n (%)	Group-B HIV positive without ART n(%)	Group-C HIV positive on ART n (%)	P value
N		200	100	100	
Metabolic syndrome		15 (7.5%)	19(19%)	21 (21%)	
Age of subjects having metabolic syndrome (yrs)		38.53 ± 6.99	38.00 ±10.04	36.76 ± 6.51	>0.05 NS
Alcohol		7 (46.67)	8 (42.11)	15 (71.43)	>0.05 NS
Smoker		14 (93.33)	18 (94.74)	17 (80.95)	>0.05 NS
Mean BMI (kg/m <sup>2</sup> )		29.82 ± 3.86	23.18 ± 3.41	22.08 ± 2.44	P<0.05 Sig
BMI	Under Weight <18.5	0 (0.00)	1 (5.26)	1 (4.76)	
	Normal	1(6.67)	15 (78.95)	18 (85.72)	
	Pre obese BMI ≥25– 29.9 kg/m <sup>2</sup>	8(53.34)	2 (10.53)	2 (9.52)	
	Obese BMI >30 kg/m <sup>2</sup>	6 (40.00)	1 (5.26)	0 (0.00)	
Waist circumference(cm)		98.20 ±9.06	89.74 ±4.09	89.23 ±4.70	>0.05 NS
SBP(mm of Hg)		128.40±8.36	119.58 ±10.34	125.23 ±8.87	
FBG(mg/dl)		103.2 ± 12.28	113.11 ± 10.03	114.86 ±17.57	P<0.05 Sig
TG(mg/dl)		158.71 ± 13.43	211.53 ± 81.96	297.29 ± 133.07	P<0.05 Sig
HDL(mg/dl)		41.67 ±4.42	41.42 ± 9.88	39.33 ±7.30	P<0.05 Sig
Carotid intima thickness (mm)	Rt	0.86 ± 0.07	0.88 ± 0.07	0.86 ± 0.19	>0.05 NS
	Lt	0.90 ± 0.09	0.89 ± 0.07	0.85 ± 0.20	>0.05 NS

Table No. 2 - Parameters in various groups of metabolic syndrome.

Parameter	Group B	Group-C	P-value
Duration of HIV (years)	2.63 ± 0.53	3.27 ± 0.79	>0.05 NS
CD 4 (cells/mm <sup>3</sup> )	335.42±180.51	290.95±221.17	> 0.05 NS

Table No.-3- Correlation between components of metabolic syndrome and CD4 among various groups.

		r-value	P-value	Significance
FBG	Group –B	- 0.183	>0.05	NS
	Group-C	+ 0.007	> 0.05	NS
HDL	Group –B	- 0.200	> .05	NS
	Group-C	- 0.090	> .05	NS
TG	Group –B	- 0.118	> 0.05	NS
	Group-C	+ 0.198	> 0.05	NS
WC	Group –B	+0.043	> 0.05	NS
	Group-C	+0.190	> 0.05	NS
SBP	Group –B	+0.187	> 0.05	NS
	Group-C	+0.241	>0.05	NS

Smoking has direct impact on metabolic syndrome. Smoking habits were more common in healthy control persons 14 (93.33%) as compared to HIV positive groups (18, 94.74% in group B, 17, 80.95% in group C). But there was no statistically significant difference exist for smoking habits among the studied groups ( $P > 0.05$ ). So smoking did not confound our study.

In metabolic syndrome positive persons; BMI was greater in healthy control persons ( $29.82 \pm 3.86 \text{ kg/m}^2$ ) than HIV positive groups ( $23.18 \pm 3.41 \text{ kg/m}^2$  in group B and  $22.08 \pm 2.44 \text{ kg/m}^2$  in group C) ( $P < 0.05$ ). BMI was not different statistically among group B and group C subjects ( $P > 0.05$ ).

Obesity was one of the important components of metabolic syndrome. Obese 6 (40%) and pre obese 8 (53.34%) were more common in healthy control persons while in HIV groups maximum patients either were of normal weight or underweight.

Waist circumference in control group with metabolic syndrome had mean value ( $98.20 \pm 9.06 \text{ cm}$ ). This was significantly greater than HIV patients who were on ART ( $89.23 \pm 4.70 \text{ cm}$ ) or without ART ( $89.74 \pm 4.09 \text{ cm}$ ) ( $P < 0.001$ ). But Waist circumference not differ significantly among HIV cases of both groups ( $P > 0.05$ ).

SBP was significantly greater in the control group ( $128.40 \pm 8.36 \text{ mm of Hg}$ ) as compared with the HIV groups ( $P < 0.05$ ). HIV positive patients on ART had more SBP ( $125.23 \pm 8.87 \text{ mm of Hg}$ ) than those who were not on ART ( $119.58 \pm 10.34 \text{ mm of Hg}$ ) ( $P < 0.05$ ).

In HIV groups either on ART or not ART fasting blood glucose value were significantly more than the control group ( $P < 0.05$ ). But fasting blood glucose value not differ significantly among HIV cases taking ART or not taking ART ( $P > 0.05$ ).

Lipid profile abnormalities were most commonly observed in both HIV groups either on ART or without ART. The abnormalities were increased triglycerides and decreased HDL level. Triglycerides level were significantly increased in HIV cases than the control group ( $P < 0.001$ ). Triglycerides level were also significantly higher in HIV group on ART than cases of HIV without ART ( $P < 0.05$ ).

HDL was significantly decreased in HIV cases than healthy controls ( $p < 0.05$ ). HDL level were also significantly lower in HIV group on ART than cases of HIV without ART ( $P < 0.05$ ).

We observed that in control population group A out of 15 persons having metabolic syndrome, 9 persons were having right carotid intima thickness  $\geq 0.9 \text{ mm}$  and 12 persons had left carotid intima

thickness  $\geq 0.9 \text{ mm}$ . In group B HIV positive without ART, out of 19 patients of metabolic syndrome, 15 patients had right carotid intima thickness  $\geq 0.9 \text{ mm}$  and 13 patients had left carotid intima thickness  $\geq 0.9 \text{ mm}$ . In group C HIV positive on ART, out of 21 patients of metabolic syndrome there were 15 patients had right carotid intima thickness  $\geq 0.9 \text{ mm}$  and 15 patients had left carotid intima thickness  $\geq 0.9 \text{ mm}$ . The mean value of carotid intima thickness on right side was  $0.86 \pm 0.07 \text{ mm}$  in group A subjects,  $0.88 \pm 0.07 \text{ mm}$  in group B cases and  $0.86 \pm 0.19 \text{ mm}$  in group C cases. The mean value of carotid intima thickness on left side was  $0.90 \pm 0.09 \text{ mm}$  in group A subjects,  $0.89 \pm 0.07 \text{ mm}$  in group B cases and  $0.85 \pm 0.20 \text{ mm}$  in group C cases.

There were no significant difference between all the three groups carotid intima thickness, either right or left in all metabolic syndrome patients ( $P > 0.05$ ).

#### Duration of HIV positivity and CD4 count (Table 2)

In our study we observed that the average duration in both groups either on ART or not ART for metabolic syndrome is more than 2 years. Also there was no significant difference between both the groups for the duration of the illness ( $P > 0.05$ ).

Though CD4 counts were less in HIV positive group on ART ( $290.95 \pm 221.17$ ) than not on ART ( $335.42 \pm 180.51$ ) but metabolic syndrome and CD4 cell count had no significant difference in both HIV positive groups ( $P > 0.05$ ).

#### Correlation between components of metabolic syndrome and CD4 (Table 3)

In our study; we did not found significant correlation between fasting blood sugar and CD4 count, HDL and CD4 count, TG and CD4 count, waist circumference and CD4 count and systolic blood pressure and CD4 count of all HIV cases who had metabolic syndrome ( $p > 0.05$ ).

## DISCUSSION

### Prevalence of Metabolic Syndrome

In our study metabolic syndrome was found in 21/100 (21%) patients who were HIV positive taking ART, 19/100 (19%) HIV positive patients were not taking ART and 15/200 (7.5%) normal healthy subjects.

Prabhakaran *et al.* [13] recently reported prevalence of metabolic syndrome in general population as 24.6% from Delhi while Gupta *et al.* [12] reported 31% prevalence in Jaipur and Ramachandran *et al.* [11] reported 41% in Chennai. In CURES [10] the prevalence of metabolic syndrome was 25.8%.

Compared to the Indian studies of metabolic syndrome in general population our study has low

prevalence of metabolic syndrome in all the three groups but MS was more frequent in HIV-infected patients than control group in our study. Our findings support earlier studies by Signe W. Worm *et al.* [14] DAD study who also demonstrated increased prevalence of the metabolic syndrome in HIV positive patients with or without ART than the control group. Previous studies of HIV-infected persons also revealed a high prevalence of metabolic syndrome among patients receiving HAART [3,8]. A Spanish study demonstrated MS prevalence in HIV at 17%, while a US study described a prevalence of 26% [9].

### Metabolic Syndrome

In our study, out of 15 subjects in group A, 11(73.33%) subjects have 3 components of metabolic syndrome, 4 (26.67%) subjects have 4 components of metabolic syndrome. In group B out of 19, 17 (89.47%) patients had 3 components of metabolic syndrome, 2 (10.53%) patients had 4 components of metabolic syndrome. In group C out of 21, 15 (71.53%) patients had 3 components of metabolic syndrome, 6 (28.57%) patients have 4 components of metabolic syndrome.

In the Spanish study, of the total 710 study patients (both ART-treated and -naïve), one criteria of metabolic syndrome was fulfilled by 69.3%, two by 35.8%, three by 17%, four by 4.5%, and all five criteria were seen only in one patient [3].

Obese (40.00%) and pre obese (53.33%) were more common in healthy control subject in keeping with the lean fat Indian phenotype with central obesity [16]. In HIV groups maximum patients were either of normal weight or underweight. HIV-infected patients had a significantly smaller waist circumference compared with the subjects from the control. The main difference in metabolic syndrome components in the present study as compared with other studies (with HIV-infected or uninfected subjects) was the low prevalence of abdominal obesity. In a population with a higher prevalence of obesity, such as in the United States, the effects of HAART-related lipodystrophy could be more evident on subcutaneous fat, leading to the significant difference between HIV-positive subjects and controls found by Mondy *et al.* [17]. However this was not observed in our study.

Fasting blood glucose values were high in 12/19 patients without ART, in 16/21 patients on ART suggests a high proportion of patients with dysglycemia. In HIV groups either on ART or not, fasting blood glucose value were significantly more than the control group (p value <0.05). A recent study also reported a high prevalence of diabetes in men receiving HAART [18].

In our study SBP was significantly greater in control group than HIV groups. HIV positive on ART

had more SBP than who were not on ART (P value <0.05). DBP had no significant relationship in all the three groups (P value >0.05). It signifies that ART and HIV itself increase systolic blood pressure in both groups.

### Lipid Profile Abnormality

In our study, hypertriglyceridemia and low HDL cholesterol were the most observed parameter, whereas in the Spanish study, hypertriglyceridemia was the most commonly recognized. Despite this difference, the dyslipidemia observed in our patients is concordant with HIV associated dyslipidemia which is a confirmed risk factor for macrovascular disease [19].

In our study we found that presence of high triglyceride levels, a low HDL level, hypertension and hyperglycemia carried a significantly more likely association with metabolic syndrome than waist circumference in HIV groups.

### Cd4 Counts–Haart and Duration of HIV

Lower CD4 cell count and increased viral load is associated with metabolic syndrome or increased cardiovascular risk [8].

In our study CD4 cell count had no significant relationship with metabolic syndrome in both HIV positive groups (P value is >.05) however CD4 counts were less in HIV positive group on ART than not on ART. This may be because of selection bias because HIV positive patients without ART already have CD4 counts more than HIV positive patients on ART.

Lack of independent effects of HAART on metabolic syndrome, support the notion that the traditional risk factors (i.e., hypertension, hyperglycemia, and dyslipidemia) may be important than HAART related factors for the prediction of metabolic syndrome and cardiovascular disease risk.

Stavudine use may also contribute to hypertriglyceridemia and numerous studies have implicated PIs as important risk factors for cardiovascular disease [20]. The individual contribution of drugs could not be assessed in our study due to inadequate number of patients, though 5 out of 21 patients on PI'S based regimes had metabolic syndrome, where as in alternative regimen 2 out of 16 patients had metabolic syndrome. These findings suggest that patients on protease inhibitors in our ART-treated group had greater effect on metabolic syndrome.

In current study, no significant notable difference was observed between ART-treated and without ART treated patients, in the duration of disease. However, this bias cannot be fully eliminated as it may

be unethical to hold therapy in patients whose CD4 counts fall to recommended levels to commence therapy.

#### **Carotid Intima Thickness-Subclinical Atherosclerosis and Cardiovascular Risk**

In our study we observed that in control population group A out of 15 persons having metabolic syndrome, 9 persons were having right carotid intima thickness  $\geq 0.9$ mm and 12 persons had left carotid intima thickness  $\geq 0.9$ mm. In group B HIV positive without ART, out of 19 patients of metabolic syndrome, 15 patients had right carotid intima thickness  $\geq 0.9$ mm and 13 patients had left carotid intima thickness  $\geq 0.9$ mm. In group C HIV positive on ART, out of 21 patients of metabolic syndrome there were 15 patients had right carotid intima thickness  $\geq 0.9$ mm and 15 patients had left carotid intima thickness  $\geq 0.9$ mm. These finding suggest that metabolic syndrome is associated with subclinical atherosclerosis.

HIV infection itself is associated with an increased cardiovascular risk, probably as a consequence of the activation of inflammatory pathways. HIV can directly activate endothelial cells, changing their phenotype from anti to prothrombotic [21], so increased carotid intima thickness.

#### **Limitations**

In the present study, the association between individual antiretroviral drug exposure and the metabolic syndrome was not evaluated. The use of specific anti-retroviral over a long period of time may have had long lasting, irreversible metabolic effects that were not captured in this analysis.

By using fasting glucose values alone for diagnosis rather than prospective follow up we underestimated prevalence of insulin resistance the contribution of diabetes mellitus to the risk of the metabolic syndrome among the study subjects.

As we used waist circumference as a component of the metabolic syndrome, this may have resulted in over estimated effects compared with BMI because BMI includes total fat mass.

#### **CONCLUSIONS AND SUMMARY**

The prevalence of metabolic syndrome and its components is more in ART treated 21% (21/100) than untreated HIV-positive patients 19 % (19/100) as compared with the general population 7.5 % (15/200).

Healthy subjects with metabolic syndrome had carotid intima thickness in subclinical atherosclerosis range in (13/15)86.67%, in HIV patients without ART (16/19)84.21% had carotid intima thickness in subclinical atherosclerosis range and in HIV patients on ART (18/21)85.71% had carotid intima thickness in

subclinical atherosclerosis range. These findings suggest that metabolic syndrome might be associated with increased chances of increased carotid intima thickness.

Compared with controls, HIV-infected patients had a greater prevalence of the impaired fasting glucose, increased plasma triglycerides, and reduced high-density lipoprotein cholesterol components.

Despite the limitation of the small number of patients in our study, there is an increase in metabolic syndrome in patients on ART in India. However, in metabolic syndrome risk-prone Indian population, the additional burden conferred by ART/ HIV-induced metabolic syndrome needs to be evaluated at a large scale involving greater numbers of patients and multicentre trials. If proven, this will have implications on future drug policies for HIV-infected patients.

#### **REFERENCES**

1. 'United Nations (2011) 'Personal Declaration on HIV/AIDS: Intensifying our Efforts to Eliminate HIV/AIDS'. United Nations General Assembly; Agenda item 10: 65<sup>th</sup> session: 8 June 2011.
2. Hadigan C, Meigs JB, Corcoran C, Rietschel P, Piecuch S, Basgoz N *et al.*; Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. *Clin Infect Dis* 2001; 32(1):130–139.
3. Jericó C, Knobel H, Montero M, Ordoñez-Llanos J, Guelar A, Gimeno JL *et al.*; Metabolic syndrome among HIV-infected patients: prevalence, characteristics, and related factors. *Diabetes Care*, 2005; 28(1): 144–149.
4. Depairon M, Chessex S, Sudre P, Rodondi N, Doser N, Chave JP *et al.*; Swiss HIV Cohort Study , Premature atherosclerosis in HIV-infected individuals—focus on protease inhibitor therapy. *AIDS*, 2001 ;15: 329–334.
5. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Bonadonna RC *et al.*; Carotid atherosclerosis and coronary heart disease in the metabolic syndrome: prospective data from the Bruneck study. *Diabetes Care*, 2003; 26: 1251–1257.
6. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C; National Heart, Lung, and Blood Institute *et al.*; Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Assoc. Conference on Scientific Issues Related to Definition. *Arterioscler Thromb Vasc Biol.*, 2004; 24(2): e13-e18.
7. Mangili A, Jacobson DL, Gerrior J, Polak JF, Gorbach SL, Wanke CA; Metabolic Syndrome

- and Subclinical Atherosclerosis in Patients Infected with HIV. *Clin Infect Dis.*, 2007; 44(10): 1368–1374.
8. Palella F, Wang Z, Chu H, Riddler S, Visscher B, Dobs A *et al.*; Correlates and prevalence of the metabolic syndrome over time in the Multicenter AIDS Cohort Study (MACS) [abstract TuPe2.2B18]. In Program and abstracts of the 3<sup>rd</sup> IAS Conference on HIV Pathogenesis and Treatment (Rio de Janeiro, Brazil) 2005.
  9. Friis-Moller N, Reiss P, El-Sadr W, et al. Exposure to PI and NNRTI and risk of myocardial infarction: Results from the D:A:D study. Program and abstracts of the 13th Conference on Retroviruses and Opportunistic Infections; February 5-8, 2006; Denver, Colorado.
  10. Deepa M, Farooq S, Datta M, Deepa R, Mohan V; Prevalence of metabolic syndrome using WHO, ATP III and IDF definitions in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-34). *Diabetes Metab Res Rev.*, 2007; 23(2): 127–134.
  11. Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V; Metabolic syndrome in urban Asian Indian adults – a population study using modified ATP III criteria. *Diabetes Res Clin Pract.*, 2003; 60(3): 199–204.
  12. Gupta R, Deedwania PC, Gupta A, Rastogi S, Panwar RB, Kothari K; Prevalence of metabolic syndrome in an Indian urban population. *Int J Cardiol.*, 2004; 97(2), 257–261.
  13. Prabhakaran D, Chaturvedi V, Shah P, Manhapra A, Jeemon P, Shah B *et al.*; Differences in the prevalence of metabolic syndrome in urban and rural India: a problem of urbanization. *Chronic Illn.*, 2007, 3(1): 8–19.
  14. Worm SW, Friis-Moller N, Bruyand M, D'Arminio Monforte A, Rickenbach M, Reiss P *et al.*; High prevalence of the metabolic syndrome in HIV-infected patients: impact of different definitions of the metabolic syndrome. *AIDS*, 2010; 24: 427–435.
  15. Mancia G, Facchetti R, Bombelli M, Polo Friz H, Grassi G, Giannattasio C *et al.*; Relationship of office, home, and ambulatory blood pressure to blood glucose and lipid variables in the PAMELA population. *Hypertension*. 2005; 45(6): 1072-1077.
  16. Yusuf S, Ounpuu S; Tackling the global epidemic of cardiovascular disease in South Asia. *J Am Coll Cardiol.* 2001; 38(3):688–690.
  17. Kristin Mondy, Edgar Turner Overton, Jessica Grubb, Shao Tong, Warren Seyfried, William Powderly *et al.*; Metabolic Syndrome in HIV-Infected Patients from an Urban, Midwestern US Outpatient Population. *Clinical Infectious Diseases*, 2007; 44(5): 726–734.
  18. Brown TT, Cole SR, Li X, Kingsley LA, Palella FJ, Riddler SA *et al.*; Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Intern Med.* 2005; 165(10): 1179–1184.
  19. Oh J, Hegele RA; HIV-associated dyslipidaemia: pathogenesis and treatment. *Lancet*, 2007; 7(12): 787–796.
  20. Gallant JE, Staszewski S, Pozniak A, et al. Efficacy and safety of tenofovir df vs stavudine in combination therapy in antiretroviral-naïve patients. *JAMA*, 2004; 292:191–201.
  21. Lafon ME, Steffan AM, Royer C, Jaeck D, Beretz A, Kirn A *et al.* HIV-1 infection induces functional alterations in human liver endothelial cells in primary culture. *AIDS*, 1994; 8(6): 747-752.