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Study of metabolic syndrome, diabetes, and cardiovascular risk in patients with HIV at a tertiary hospital

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ABSTRACT

Background: Metabolic syndrome (MetS), a cluster of interrelated cardio-metabolic abnormalities, is associated with increased risk of cardiovascular events and deaths. HIV infection and ART can induce lipodystrophy, insulin resistance and dyslipidemia which are risk factors of metabolic syndrome. Present study was aimed to study of metabolic syndrome, diabetes, and cardiovascular risk in patients with HIV at a tertiary hospital. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in patients > 18 years, previously or newly diagnosed HIV positive patients (ART and Pre-ART). Participants having three or more of the NCEP-ATP3 2005 revision criteria were considered to have MetS. **Results:** During study period 500 PLHIV were considered for this study. Metabolic syndrome was labelled in 49 cases, incidence was 9.8 %. Mean age, gender & addictions were comparable among both groups. In MetS group majority had HIV duration 12-24 months, reduced CD4 count, use of HAART was noted more as compared to No MetS group & difference was statistically significant. According to National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP3) 2005 revision criteria[10] $\geq$ 3 criteria were noted in 49 cases (9.8 %). All 5 criteria were noted in 5 cases (1 %) & 4 criteria were noted in 9 cases (1.8 %). Higher values of Weight, Waist, BMI, Systolic BP, Diastolic BP, Total Cholesterol, Triglycerides & FBS in MetS groups as compared to no MetS group, difference was statistically significant. While height, HDL cholesterol & LDL cholesterol were comparable among both groups & difference was not significant statistically. **Conclusion:** High prevalence of components of metabolic syndrome in PLHIV warrants regular screening and monitoring of metabolic syndrome with the view to offer treatment early to reduce the risk of cardiovascular disease in HIV patients on HAART.

Keywords: Metabolic syndrome, hypertension, cardiovascular diseases, PLHIV, diabetes

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Introduction

Metabolic syndrome (MetS), a cluster of interrelated cardio-metabolic abnormalities, is associated with increased risk of cardiovascular events and deaths.[1,2] HIV infection is known to cause derangements in lipid metabolism through a variety of mechanisms, particularly the combination of elevated triglycerides and reduced high-density lipoprotein (HDL).[3]

Improved methods of detection of HIV, earlier diagnosis, and better management have helped in improving the survival of these patients. The availability of, and access to, potent retroviral and anti-infective therapy has translated into lesser acute morbidity and mortality, and thus, a

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longer lifespan.[4] Although the medical management of HIV has been revolutionized by the use of ART, drug-related metabolic complications continue to constitute a major challenge to clinicians in the management of HIV/AIDS. A complex interaction between the host's advancing age, virus, inflammatory process, and ART use has been described as the underlying mechanism for the increased CVD risk among HIV-infected patients.[5]

HIV infection and ART can induce lipodystrophy, insulin resistance and dyslipidemia which are risk factors of metabolic syndrome.[6] Apart from cardiovascular disease and type 2 Diabetes, individuals with metabolic syndrome are susceptible to other conditions, notably polycystic ovarian syndrome, fatty liver, cholesterol gall stones, asthma, sleep disturbances and some forms of cancers. Present study was aimed to study of metabolic syndrome, diabetes, and cardiovascular risk in patients with HIV at a tertiary hospital.

Material And Methods

Present study was single-center, prospective, observational study, conducted in Department of General Medicine, at Anti-Retroviral treatment center of Vilasrao Deshmukh Government Medical College & Hospital, Latur, India. Study duration was of 2 years (January 2020 to December 2021). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients > 18 years, previously or newly diagnosed HIV positive patients (ART and Pre-ART), willing to participate in present study

Exclusion criteria

- Withdrawal of combination ART
- Evidence of clinical signs of active AIDS in the 3 months before entry Because of their possible impact on anthropometric and laboratory parameters.
- Pregnant women and anyone who switched ART combination regimen for any reason.

Study was explained to patients in local language & written consent was taken for participation & study. Details including sociodemographic characteristics and behavioural factors such as diet, tobacco, and alcohol consumption were collected. Detailed history and clinical examination were carried out and an 8 h fasting venous blood sample was collected for enzyme‐linked immunosorbent assay for HIV, CD4 T‐cell count, fasting blood glucose (FBS), serum cholesterol, high‐density lipoprotein (HDL) cholesterol & serum triglycerides in all the study patients.

Anthropometric measures such as weight (kg), height (cm), and waist circumference (cm) were measured. Body mass index (BMI) was computed and classified based on Indian classification. Two blood pressure (BP) readings were taken through a digital sphygmomanometer, in sitting position in the right arm, 10 minutes apart, and an average of two readings was considered. Hypertension was defined as SBP/DBP of ≥140/90 for those aged <60 years and ≥150/90 for individuals aged above 60 years.[8] Diabetes was defined as fasting plasma glucose (FPG) ≥126 mg/dl and or postprandial plasma glucose ≥200 mg/dl.[9]

National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP3) 2005 revision criteria[10] were used to define MS which were as follows:

1. Abdominal obesity (waist circumference ≥ 90 cm for Asian men or ≥80 cm for Asian women),
2. Fasting triglycerides (TG) ≥ 150 mg/dl or drug treatment for elevated triglycerides
3. HDL cholesterol (HDL-C) ≤ 40 mg/dl for men or ≤50 mg/dl for women or on drug treatment for reduced HDL-C,
4. Systolic/diastolic blood pressure (SBP/DBP) ≥ 130/85mmHg or receiving drug treatment,
5. FPG ≥ 100 mg/dl or drug treatment for elevated glucose.

Participants having three or more of the above criteria were considered to have MS. All findings were noted. Data was collected and compiled using Microsoft Excel, analysed

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using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

During study period 500 PLHIV were considered for this study. According to National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP3) 2005 revision criteria[10] metabolic syndrome was labelled in 49 cases, incidence was 9.8 %. Mean age, gender & addictions were comparable among both groups. In MetS group majority had HIV duration 12-24 months, reduced CD4 count, use of HAART was noted more as compared to No MetS group & difference was statistically significant.

Table 1: Baseline characteristics

Characteristics	Total	No MetS	MetS	p value
Number (%)	500	451 (90.2 %)	49 (9.8 %)	<0.001
Mean age (years)	37.0 ± 9.1	36.6 ± 8.4	39.1 ± 8.9	0.35
Sex				
Males	311 (62.2 %)	289 (57.8 %)	22 (4.4 %)	0.52
Females	189 (37.8 %)	162 (32.4 %)	27 (5.4 %)	
HIV Duration (months)				
12-24	231 (46.2 %)	210 (42 %)	21 (4.2 %)	0.037
25-48	127 (25.4 %)	114 (22.8 %)	13 (2.6 %)	
>48	142 (28.4 %)	127 (25.4 %)	15 (3 %)	
CD4 count/mm3	545 ± 134	556 ± 250	405 ± 150	0.001
Use of HAART				
Yes	392 (78.4 %)	350 (70 %)	42 (8.4 %)	<0.0001
No	108 (21.6 %)	101 (20.2 %)	7 (1.4 %)	
Addictions				
Smokers	68 (13.6 %)	57 (11.4 %)	11 (2.2 %)	0.45
Alcohol consumption	127 (25.4 %)	114 (22.8 %)	13 (2.6 %)	0.38

According to National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP3) 2005 revision criteria[10] ≥ 3 criteria were noted in 49 cases (9.8 %). All 5 criteria were noted in 5 cases (1 %) & 4 criteria were noted in 9 cases (1.8 %).

Table-2: Metabolic syndrome criteria distribution

Number of Criteria	Frequency	Percent	Cumulative Percent
0	153	30.6	30.6
1	181	36.2	66.8
2	117	23.4	90.2
3	35	7	97.2
4	9	1.8	99
5	5	1	100

In present study, we noted higher values of Weight, Waist, BMI, Systolic BP, Diastolic BP, Total Cholesterol, Triglycerides & FBS in MetS groups as compared to no MetS group, difference was statistically significant. While height, HDL cholesterol & LDL cholesterol were comparable among both groups & difference was not significant statistically.

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Table 3: Statistical correlation of various parameters

	Patients with MetS (n=23)	**Patients without MetS (n=93)**	**p value**
Weight (in kg)	68.93 ± 11.45	57.02 ± 10.51	<0.001
Height (in cms)	163.9 ± 11.92	162.4 ± 11.35	0.73
Waist (in cms)	92.66 ±7.24	84.5 ± 8.02	<0.001
BMI (kg/m2)	24.33 ± 3.38	22.63 ± 3.34	0.001
Systolic BP (mm Hg)	126.35 ± 15.52	108.23 ± 18.34	<0.001
Diastolic BP (mm Hg)	86.44 ± 11.91	74.45 ± 9.36	<0.001
Total Cholesterol (mg/dl)	191.63 ± 34.38	167.33 ± 56.35	0.045
HDL cholesterol (mg/dl)	39.33 ± 8.02	41.48 ± 8.14	0.56
LDL cholesterol (mg/dl)	92.47 ± 28.43	94.35 ± 39.33	0.58
Triglycerides (mg/dl)	311.72 ± 232.37	171.56 ± 134.67	<0.001
FBS (mg/dl)	116.34 ± 29.74	86.47 ± 11.62	<0.001

Discussion

Metabolic syndrome (MetS) is a useful construct to identify patients in whom there is a greater overall risk of mortality and, specifically, a greater risk of dying from cardiovascular-related causes or diabetes.[11] Increased rates of MetS (33–45%) among PLHIV have been reported by some investigators, while other studies showed rates comparable to those found in the general population (11–26%).[12,13,14]

These differences are due to population heterogeneity across the studies regarding clinical and demographic features, and factors related to HIV infection itself, as well as to the set of criteria used to diagnose MetS. Dietary and lifestyle choices and a combination of genetic, cultural and environmental factors may contribute to the differences in this observed prevalence.[15]

It is now recognized that HIV-induced immune activation, chronic inflammation and the higher prevalence of traditional CVD risk factors like diabetes, hypertension and smoking among PLWH, all contribute to increased CVD risk.[16,17] Antiretroviral therapy (ART) regimes in the past had increased risk of lipodystrophy and the chronic inflammatory nature of the disease make patients of HIV more prone to MetS. Estimates on prevalence of MetS in people living with HIV/AIDS (PLHA) have ranged from 7% to 30%. A recent meta-analysis of HIV and MetS calculated an overall prevalence of 16.7%.[18]

According to the Global Burden of Disease Study, 29% of all deaths in India are attributable to CVD, which also occur at an earlier age.[19] In India, 52% of these deaths occur before the age of 70 compared with 23% in those with European ancestry.[20] This difference has been explained by genetic factors as well as the clustering of traditional risk factors at a younger age.

Risk factors contributing to the development of metabolic syndrome in PLHIV patients include advancing age, male gender, longer duration of HIV infection, low CD4 count, high viral burden, high body mass index, greater waist circumference or waist- to hip ratio, lower socioeconomic class, and certain ethnic backgrounds or culture.[21,22] The U.S. National Cholesterol Education Program Adult Treatment Panel III (ATPIII) report identified MetS as a multifaceted risk factor for CVDs.[23] An international cross-sectional study that used a well-characterized cohort of 788 HIV-infected adults recruited at 32 centers reported that the prevalence of MetS was 14% according to the International Diabetes Federation (IDF) criteria and 18% by the U.S. ATPIII criteria.[24]

Jyothi I et al.,[25] noted a high prevalence of metabolic syndrome was observed in patients with HIV (16/60), and was more prevalent in the ART-treated group (13/30; P = 0.028). Similarly, insulin resistance was also noted to be high (24/60), and of these patients, 15 were on ART.

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Seventy-five percent of patients with metabolic syndrome had insulin resistance. Diabetes was diagnosed in 1 patient who was ART-naïve and in 6 patients who were on ART. They noted an increased prevalence of metabolic syndrome, insulin resistance, and diabetes mellitus in ART-treated patients.

Sneha DM et al.,[26] studied 182 adults aged ≥ 18 years, prevalence of MS was 40.1% (95% CI = 33.0%–47.2%). About 24.7% of the participants had at least a single criterion for MS. Age >45 years (adjusted odds ratio (AOR) = 2.3; 95% CI = 1.1–4.9, $p < 0.018$) and body mass index (BMI) > 23 kg/m2 (AOR = 6.4; 95% CI = 3.1–13.1, $p < 0.001$) were positively associated with MS, whereas daily consumption of high sugar items was inversely associated (AOR = 0.2; 95% CI = 0.1–0.5, $p < 0.001$). More than 50% of the participants were found to have moderate or high 5-year CVD risk.

Theengh DP et al.,[27] studied 116 HIV positive patients, high prevalence of MS was observed in HIV positive patients (ATP III – 19.8% and IDF – 25.9%). The prevalence of MS was higher in the anti‑ retroviral therapy (ART) group (ATP III – 33.3% and IDF – 36.4%) than ART‑ naïve group (ATP III – 2% and IDF – 12%).

Ang LW et al.,[28] studied 2,231 PLHIV, 93.9% were men, and the median age at latest follow-up was 48 years. The median duration of HIV infection and duration of exposure to ART was 6.8 years and 5.7 years, respectively. All had been exposed to nucleoside reverse transcriptase inhibitors (NRTIs) as the first line of treatment, 93.9% to non-NRTIs, 28.6% to protease inhibitors (PIs) and 12.8% to integrase strand transfer inhibitors. The most common metabolic abnormality among PLHIV was HDL hypocholesterolemia (60.2%) followed by hypertriglyceridemia (45.5%). 68.8% had at least one component of MetS. The overall prevalence of MetS was 23.6% (95% confidence interval 21.9%–25.4%). Of the 526 with MetS, the most common combination was HDL hypocholesterolemia, hypertriglyceridemia and hypertension (51.0%), followed by HDL hypocholesterolemia, hypertriglyceridemia, hypertension and diabetes (25.1%). Compared with PLHIV without MetS, a significantly higher proportion of those with MetS were ever on protease inhibitors (33.5% vs. 27.1%).

HAART regimes have been classified in different therapeutic groups according to their mechanisms of action: nucleoside reverse transcriptase inhibitors (NRTIs), nonnucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, entry inhibitors and integrase strand transfer inhibitors (InSTIs).[29] The role of HAART in promoting atherosclerosis and CVDs has been extensively reviewed;[30] HAART is associated with increase of total cholesterol (CHO), low-density lipoprotein (LDL) and triglycerides (TG) and reduced values of high-density lipoprotein (HDL).[31]

HIV patients on metformin should be educated about the symptoms of lactic acidosis, including fatigue, weight loss, nausea, abdominal pain, dyspnea, and arrhythmia. Liver-related symptoms such as tender hepatomegaly, edema, ascites and encephalopathy may occur, but jaundice is uncommon.[32] A sincere effort should always be made to detect MS in HIV positive patients particularly those who are on HAART as it is well known that MS is a significant, multifaceted and modifiable risk factor for CVD, especially in Indian subcontinent where there is a genetic predisposition to cardiovascular risk.

Conclusion

Metabolic syndrome (MS) is a clustering of insulin resistance, abdominal obesity, hypertension (HTN) and dyslipidemia, all are known risk factors for cardiovascular diseases. High prevalence of components of metabolic syndrome in PLHIV warrants regular screening and monitoring of metabolic syndrome with the view to offer treatment early to reduce the risk of cardiovascular disease in HIV patients on HAART.

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