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Non-Alcoholic Fatty Liver Disease and Metabolic Syndrome in Patients with HIV/AIDS and its Correlation with Antiretroviral Therapy and Severity of Disease

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Abstract

Introduction: Metabolic syndrome (MetS) and Non-alcoholic fatty liver disease (NAFLD) are two major causes of morbidity in chronic HIV infected patients on antiretroviral therapy (ART). This study was done on HIV infected individuals by comparing ART naive patients with patients on different ART regimens and evaluating the effect of ART on Metabolic syndrome and NAFLD.

Method: It was a cross-sectional observational study done on 120 HIV infected individuals in a tertiary care centre in New Delhi. All cases with hypertension, diabetes, chronic kidney or liver disease, thyroid disorders or on any drugs except ART were excluded. The risk markers for metabolic syndrome were assessed and compared within groups on different ART regimens.

Results: Metabolic syndrome and NAFLD were found to be significantly more in cases on ART as compared to ART naïve cases. Metabolic syndrome was found to be associated with type of ART protease inhibitors (ATV/r)> nonucleoside reverse transcriptase inhibitors (NNRTI) > no ART] and low CD4 cell counts (p=0.01). In those patients who were on ART, these parameters were found to be more in those on second line ART [i.e., protease inhibitor (PI)(ATV/r) based regimens] as compared to those on first line ART, [i.e., nonnucleoside reverse transcriptase inhibitors (NNRTI) based regimen]. 15% of cases on 2nd line ART (group C) had MetS as compared to 12.5% in those on 1st line ART (group B) and nil in ART naïve cases (group A). One third (34%) of all 120 cases were found to have NAFLD. A significantly higher number of cases (45%) in group C had NAFLD as compared to 32.5% in group B and 25% in group A respectively. Insulin resistance and metabolic risk markers were also significantly higher in cases on ART as compared to ART naïve.

Conclusions: In HIV patients, the use of antiretroviral therapy (ART) is linked to an increase in the prevalence of metabolic risk factors, including insulin resistance, lipoatrophy and dystrophy, dyslipidaemia, and abnormalities of fat distribution. Although care of Opportunistic infections and recently CVD has received a lot of attention, it is equally important to address the metabolic abnormalities such as metabolic syndrome and NAFLD brought on by ART.

Keywords: NAFLD, Metabolic syndrome, HIV

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INTRODUCTION

With the advent of effective antiretroviral therapy, human immunodeficiency virus (HIV) infection has largely become a chronic condition and is increasingly seen in conjunction with metabolic disorders such as dyslipidaemia and insulin resistance. Furthermore, the administration of antiretroviral therapy (ART) itself is associated with an increased incidence of metabolic risk factors namely insulin resistance, lipoatrophy, dyslipidaemia, and abnormalities of fat distribution in HIV infected patients, as observed by Samaras K. et al and Swami A. [1,2]. Thus, further challenges in the management of patients with HIV involve the management of prediabetes/diabetes, metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD). This study was done to evaluate the effect of ART on MetS and NAFLD in Indian patients infected with HIV/AIDS.

MATERIALS AND METHOD

It was a hospital based cross-sectional observational study conducted at the antiretroviral therapy (ART) centre, at Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS), Dr. Ram Manohar Lohia Hospital, New Delhi. The study was approved by the Institutional Ethics Committee, PGIMER, Dr. RMLH Hospital, New Delhi. Consecutive HIV infected patients presenting to the ART centre of this tertiary level hospital over a period of 16 months were offered to participate in the study. Patients aged 18-40 years on ART continuously for atleast 1 year were included in the study. Pregnant or lactating females, patients with hypertension, diabetes, chronic kidney disease, chronic liver disease, hyper or hypothyroidism and patients using any medications (except ART) namely steroids, statins, antiepileptics, aspirin or multivitamins were excluded from the study.

The patients underwent thorough clinical assessment and laboratory investigations. Presence of metabolic syndrome and NAFLD along with metabolic risk assessment was done by various investigations. BECTON-DICKINSON FACS flow cytometer was used to obtain CD4 cell counts. A detailed general physical and systemic examination was conducted including measurement of height, weight, body mass index (BMI), waist circumference and waist hip ratio (WHR).

1.	Abdominal obesity/waist circumference	Men >102cm and women >88cm
2.	Triglycerides	≥ 150 mg/dL (1.7 mmol/L) or specific treatment for this lipid abnormality
3.	HDL Cholesterol	< 40 mg/dL (1.03 mmol/L) in males & < 50 mg/dL (1.29 mmol/L) in females or specific treatment for this lipid abnormality
4.	Blood Pressure	Systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension
5.	Blood sugar	Raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

Revised NCEP/ATP III definition [3] was used to define metabolic syndrome

The cases were further divided into three groups according to the type of ART i.e., group A (ART naïve cases), group B (cases on 1st line ART) and group C (cases on 2nd line ART) according to different treatment regimens as per the national aids control organization (NACO) guidelines as shown below:

Table 1: List of Antiretroviral Therapy (ART) used in HIV/AIDS patients as per national aids control organization (NACO) till mid-2020.

First line ART	**Second line ART**
Tenofovir 300mg	Tenofovir 300mg
Lamivudine 300mg	Lamivudine 300mg
Efavirenz 600mg	Atazanavir/Ritonavir (ATV/r) 300mg/100mg

Fasting and post prandial (PP) insulin levels were calculated using the VITROS insulin reagent pack and the VITROS insulin calibrator on the VITROS ECI immunodiagnostic system. Insulin resistance (IR) was calculated by homeostasis model assessment of insulin resistance (HOMA-IR). HOMA-IR = Fasting insulin (mU/L) × fasting plasma glucose (mmol/L)/22.5 and HOMA-IR value of >2.8 was used to define IR [4].

The quantitative measurement of apolipoprotein A1 (ApoA1) was performed using the VITROS Chemistry ApoA1 reagent in conjunction with the VITROS Chemistry Products Calibrator Kit 21 and VITROS Chemistry Products FS Diluent Pack 1 (Apo Diluent/UED) on the VITROS 5600 Integrated System. The reportable range was taken as 0.30g/L to 2.40g/L. For the mean concentration of 1.167 the CV%(coefficient of variation) was taken as 2.2 and for the mean concentration of 1.997 the CV% was taken as 2.5. The quantitative measurement of apolipoprotein B (ApoB) was performed using the VITROS Chemistry ApoB reagent in conjunction with the VITROS 5600 Integrated System. The reportable range was taken as 0.35 - 3.00 g/L. For the mean concentration of 1.05 the CV% was 1.3 and for the mean concentration of 1.47 the CV% was 1.2.

Cases were diagnosed as NAFLD by Ultrasonography (USG) by a single observer and graded according to the standard accepted criteria as shown below: [5]

- Grade 1: Slight diffuse increase in the fine echoes. Liver appears bright as compared to the cortex of the kidney. Normal visualization of diaphragm and intrahepatic vessel borders.
- Grade 2: Moderate diffuse increase in the fine echoes. Slightly impaired visualization of the intrahepatic vessels and diaphragm.
- Grade 3: Marked increase in the fine echoes. Poor or no visualization of intrahepatic vessel borders, diaphragm, and the vessels.

Data was analyzed using IBM SPSS software for Windows version 20. Quantitative variables were reported as mean ± standard deviation. For continuous variables, statistical correlation was done by using correlation test and Chi square test and other appropriate statistical tests was used for analyzing categorical variables. P value of < 0.05 was considered significant.

RESULTS

A total of 120 HIV infected individuals were included in the present study out of which 60% of the cases were male and 40% were female. The laboratory and demographic characteristics of all cases (in different groups) is shown in table -2. 67.5% and 2.5% of cases in group C were overweight and obese measured by body mass index (BMI) as compared to 25% and 7.5% in group B and 12.5% and 0% in group A respectively and the difference was found to be statistically significant ($p<0.001$). The waist circumference was not different amongst all three groups, but the waist hip ratio (WHR) was found to be significantly more in group C (65%) as compared to group B (7.5%) and group A (5%) respectively ($p=0.007$). This observation suggests the role of ART (especially PI's) in causing central obesity and lipoatrophy at the hips. The mean HbA1c in group A, group B and

Table 2: Laboratory and demographic characteristics of all cases in different groups

Laboratory and demographic characteristics	**Group A (n=40) Mean ± SD**	**Group B(n=40) Mean ± SD**	**Group C(n=40) Mean ±SD**
Age (years)	33.85 ± 8.84	37.8 ± 3.3	36.38 ± 7.95
BMI (kg/m^2)	21.87 ± 2.84	23.4 ± 3.5	25.95 ± 2.22
SBP (mmHg)	131.75 ± 7.72	131.8 ± 8.9	131.75 ± 8.88
DBP (mmHg)	81.1 ± 6.90	82.3 ± 6.6	82.3 ± 6.7
Waist hip ratio	0.83 ± 0.03	0.9 ± 0.02	0.9 ± 0.02
Creatinine (mg%)	0.86 ± 0.86	1.2 ± 1.8	0.79 ± 0.28
Aspartate aminotransferase (IU/L)	48.13 ± 30.52	52.1 ± 32.3	37.35 ± 11.61
Alanine transaminase (IU/L)	49.6 ± 41.71	57.9 ± 48.2	49.28 ± 30.21
Alkaline phosphatase (IU/L)	131.4 ± 128.63	158.5 ± 147.8	161.75 ± 78.87
Fasting blood sugar (mg%)	86.4 ± 8.80	88.9 ± 18.2	90.48 ± 21.98
Post prandial blood sugar (mg%)	125 ± 43.76	135 ± 38.9	143.43 ± 42.69
Fasting insulin (IU/L)	10.78 ± 6.97	14.5 ± 7.6	15.45 ± 6.61
Post prandial insulin levels (IU/L)	21.8 ± 19.63	24.5 ± 24.6	35.01 ± 22.62
HOMA-IR	2.33 ± 1.56	3.2 ± 1.8	3.38 ± 1.52
Lactate dehydrogenase (IU/L)	391.25 ± 208.92	265.8 ± 109	216.39 ± 101.84
Apolipoprotein-A	103.11 ± 41.88	83.3 ± 42.3	78.08 ± 37.30
Apolipoprotein-B	74.04 ± 25	74 ± 27.1	75.27 ± 21.27
HbA1C	5.36 ± 0.64	5.5 ± 0.6	6.04 ± 0.69
Cholesterol (mg%)	138.13 ± 36.88	145.3 ± 44.4	164.08 ± 47.56
HDL (mg%)	49.30 ± 26.64	34.9 ± 13.1	33.4 ± 11.95
LDL (mg%)	81.65 ± 23.13	88.2 ± 26.6	92.4 ± 28.75
VLDL (mg%)	27.75 ± 13.55	29.7 ± 15.4	30.1 ± 18.44
Triglycerides (mg%)	144.98 ± 80.18	150.7 ± 93.1	157.82 ± 143.47
CD4 cell counts/mm^3	505.25 ± 268.97	341.5 ± 240.7	373.25 ± 199.72

group C was 5.36±0.64, 5.54±0.6 and 6.42±0.69 respectively. The mean HbA1c and serum cholesterol were found to be significantly higher in group C as compared to group A and group B ($p<0.001$, $p<0.022$ respectively).

BMI- Body Mass Index, SBP- Systolic Blood Pressure, DBP- Diastolic Blood Pressure, HDL- High-density lipoprotein, LDL- Low-density lipoprotein, VLDL- Very low-density lipoprotein , CD4 - cluster of differentiation 4, HOMA-IR - Homeostatic Model Assessment of Insulin Resistance**.** The average fasting insulin levels in group A were found to be 10.78±6.97 mg/dl as compared to 14.53±7.64 mg/dl in group B and 15.45±6.61 mg/dl in group C and the difference was found to be statistically significant (P=0.01).

Similarly, the mean postprandial insulin (2H) was significantly lower in group A i.e., 21.80±9.63 IU/L as compared to 24.52±24.58 IU/L in group B and 35.01±22.62 IU/L in group C ($p<0.025$). Insulin resistance as calculated by HOMA-IR was found to be 2.33±1.56, 3.21±1.79 and 3.38±1.52 in group A, group B and group C respectively, and was found to be significantly higher in group C as compared to group B and group A ($p<0.005$, $p<0.001$) and group B as compared to group A ($p<0.005$) respectively.

The mean APO-A in group A, group B and group C was 103.11±41.88 mg/dL, 83.20±42.27 mg/dL and 78.08±37.30 mg/dL respectively. Serum levels of Apo-A and high-density lipoproteins (HDL) were found to be significantly lower in both group B and group C as compared to group A ($p<0.002$).

Table 3: Prevalence of insulin resistance (HOMA-IR) in different HIV groups

HOMA-IR value	**Patient status**	**Group A (n=40)**	**Group B (n=40)**	**GroupC (n=40)**
<2.5	No Insulin resistance	25(62.5%)	16(40%)	13(32.5%)
2.5 or above	Insulin resistance present	15(37.5%)	24(60%)	27(67.5%)

The mean APO-B in group A, group B and group C was 74.04±25.00 mg/dL, 74.05±27.06 mg/dL and 75.27±21.27 mg/dL respectively, the difference being insignificant. This suggests a significantly higher prevalence of dyslipidaemia and MetS, and hence future high CVD risk amongst cases on ART (especially 2nd line ART).

Metabolic syndrome was observed more frequently in cases in group C as compared to group B (15% vs 12.5% respectively), ($p<0.05$) and significantly lesser in group A (0%) ($p<0.001$). This observation indicates that not only the type of ART but ART by itself is associated with increased incidence of metabolic syndrome, and 2nd line ART i.e., ATV/r is associated with a higher chance of this complication.

Apart from that MetS was found to be associated with low CD4 cell counts ($p=0.01$). Amongst all the individual parameters of MetS, elevated fasting blood sugar levels, hypertension and low HDL levels were found to be significantly more common in group C and group B as compared to group A ($p<0.01$). BMI, Waist circumference and triglyceride levels did not differ between separate groups.

Table 4: Prevalence of individual components of metabolic syndrome in different ART groups

Index	Group A (n=40)	GroupB (n=40)	GroupC (n=40)
Waist circumference >102 cm in male and >88cm in female	0(0%)	0 (0%)	0 (0%)
Blood Pressure ≥130/85 mm hg	9 (22.5%)	11 (27.5%)	15 (37.5%)
Fasting blood sugar (FBS) >100 mg/dl	1 (2.5%)	7 (17.5%)	9 (22.5%)
Triglycerides >150 mg/dl	13 (32.5%)	11 (27.5%)	14 (35%)
HDL < 40 mg/dl in male, <50 mg/dl in female	16(40%)	27(67.5%)	29(72.5%)
Metabolic syndrome	0(0%)	5(12.5%)	6(15%)

Approximately 34% of all cases were found to have ultrasonographically (USG) documented NAFLD. A significantly higher percentage of cases (45%) in group C had NAFLD as compared to 32.5% in group B and 25% in group A ($p<0.001$). Amongst all 120 HIV positive cases, 30 (25%) patients had grade 1 fatty liver, 9 (7.5%) had grade 2 and two cases (1.67%) (all in group C) had grade 3 NAFLD.

The prevalence and severity of NAFLD was significantly more in cases on 2nd line ART as compared to those on 1st line ART or ART naïve individuals ($p<0.01$).

Table 5: Prevalence of fatty liver in different HIV groups

Index	**Group A(n=40)**	**Group B(n=40)**	**Group C(n=40)**
Fatty Liver total	10(25%)	13(32.5%)	18(45%)
Grade 1	8(20%)	10(25%)	12(30%)
Grade 2	2(5%)	3(7.5%)	4(10%)
Grade 3	0(0%)	0(0%)	2(5%)

DISCUSSION

ART has been seen to be associated with significantly higher risk of Metabolic syndrome and NAFLD in people infected with HIV/AIDS. To elucidate the fact, especially in Indian patients, 120 HIV infected individuals were recruited in the present study and subdivided into group A (ART naïve), group B (patient on first line ART) and group C (patients taking second line ART). They were evaluated for the presence of NAFLD, metabolic syndrome and associated metabolic risk markers.

Metabolic syndrome (MetS) was found in 0(0%),5(12.5%) and 6(15%) of cases in group A, B and C respectively. Significant associations were observed with type of ART and low CD4 cell counts. Theengh D.et al, Estrada V et al, and Drelichowska J. et al also showed higher metabolic and body fat abnormality in HIV-infected adults specially those who were taking ART and HIV-associated lipodystrophy was found to be associated with several host, disease, and drug factors [6-8]. While prevalence of lipoatrophy increased with the use of indinavir and stavudine (now out of use and banned in many countries), lipoaccumulation was associated with duration as well as type of ART specially protease inhibitors. The normal prevalence in general population of Metabolic syndrome is 20-25% whereas in our study it was much less. The reason is that we already excluded all cases who were hypertensive, diabetic or dyslipidemic, and hence were apparently metabolically inert. Despite that, the prevalence of Metabolic syndrome from 12.5-15% of cases on ART is a serious concern.

In our study we found that amongst cases in group B and group C the fasting insulin levels, HbA1c and insulin resistance (HOMA-IR) were found to be significantly higher as compared to cases in group A ($p=0.03$, $p=0.04$ respectively) and were alarmingly higher in those having concomitant Metabolic syndrome. This can be explained by the fact that the most important etiopathogenic factors for Metabolic syndrome are inflammation, insulin resistance and hyperinsulinemia [8]. Viral and ART related factors related to inflammation, endothelial dysfunction, cytokines and differences in body composition between the groups may be an additional reason for this observation. Insulin resistance based on HOMA values and fasting insulin levels were found to have a positive correlation with Metabolic syndrome, thereby reiterating its pivotal role in the pathogenesis of this condition. In the context of high usage of nucleoside reverse transcriptase inhibitors in our ART regimes, such results appear alarming. The mean HbA1C in group C was significantly higher as compared to group B and group A. Although the difference in HbA1C between group A and B was not significant, the difference in HbA1C between group A and C and between group B and C was found to be highly significant ($p<0.001$ and <0.001 respectively). It has been proven in previous studies that higher levels of HbA1C are present in patients on ART as compared to ART naïve patients. Therefore, the future risk of developing diabetes, insulin resistance, metabolic and cardiovascular disease is more in HIV infected patients on ART, and protease inhibitors (2nd line ART) are found to be the main culprit amongst all. NNRTI and NRTI have also to some extent been implicated in published literature [9-11]. Estrada V et al concluded that HIV infected patients on ART have higher prevalence of metabolic syndrome, and these patients show a reduced plasma adiponectin (AD)-to-leptin ratio, increased BMI, increased IR (HOMA) and increased plasma fasting insulin levels [7]. Our study also showed that Metabolic syndrome was present most frequently in cases in group C, with least prevalence in group A. Insulin resistance based on HOMA-IR was found to be highest in group C (67.5%) followed by group B (60%), and lowest in group A (37.5%). HIV infected patients taking ART have significant

metabolic abnormalities such as lipodystrophy, glucose intolerance, and high BMI [12], which are important factors associated with insulin resistance and Metabolic syndrome. Blood pressure (systolic and diastolic both) was found to be significantly higher in cases in group C having MetS and can be a direct effect of ART, as protease inhibitors are known to cause abnormal body fat distribution and endothelial dysfunction, further hampering blood pressure homeostasis in HIV infected individuals [13]. Although the difference in waist circumference between the three groups was not significant. WHR was higher in group C and group B (0.90±0.02) as compared to 0.82±0.02 in group A, suggesting that ART has some impact on abnormal body fat distribution causing lipoatrophy at hips and reduction of parietal i.e., subcutaneous fat, with simultaneous increase in central abdominal fat causing increasing WHR but normal waist circumference.

NAFLD was found to be significantly more in cases on ART i.e., group B and group C. Out of the total 120 HIV positive cases, 30 (25%) had grade 1 NAFLD, 41(34%) had grade 2 NAFLD and 2 (5%) cases had grade 3 fatty liver. At this point it is worth mentioning that we had already excluded all cases with hypertension, diabetes etc. and hence our cases were amongst the apparently healthy HIV infected population, and yet NAFLD was quite frequent. NAFLD may be due to higher insulin resistance, metabolic syndrome or dyslipidaemia associated with ART (PI and NNRTI) per se in cases in group B and group C, or it may be due to HIV itself as mentioned previously in published literature [14]. It has been postulated that, the virus might promote hepatic steatosis by interacting with sterol regulatory element-binding-protein 1 and peroxisome proliferator-activated receptor γ, which are key regulators of lipogenesis and insulin signaling, respectively [15]. HIV influences the activation of hepatic stellate cells, and thus causes hepatic collagen deposition and fibrogenesis [16,17]. While there have been significant advances in treating HIV, HBV and HCV, there has also been a dramatic increase in the metabolic syndrome in those living with HIV, which suggests that NAFLD will become an increasing problem in this patient population, especially those on protease inhibitors and NNRTI based regimens. Grade-3 NAFLD was seen exclusively (5%) in group C further reinforcing the fact that protease inhibitors may be a strong inhibitor of HIV but are associated with serious metabolic complications.

The difference in levels of total cholesterol, HDL and triglycerides between group A and C was found to be statistically significant and difference in HDL levels between group A and B was also found significant while no difference was found in levels of LDL and VLDL between all three groups. This may again be reiterated by the fact that PI's cause insulin resistance, NAFLD, and metabolic syndrome and hence may have more effect on TG and HDL rather than other components of lipid profile. The difference in levels of Apo-A between group A and B, and between group B and C were not significant (p=0.708, p=0.834) while difference in levels of Apo-A between group A and C was found to be significant (p=0.018). While the difference between Apo B levels in all three groups was not found to be significant. This characteristic dyslipidaemia can again be attributed to the type of ART i.e., PI based in group C causing lipodystrophy, lipid irregularity, more NAFLD, metabolic syndrome and prediabetes and hence alteration of lipid parameters.

The limitation of the study was that it was only a cross sectional observational study with a small sample size. Prospective studies with larger sample size would help elucidate these observations and could help establish causal associations. Viral load was not done in this study, hence the direct effect of HIV infection itself on metabolic syndrome and NAFLD cannot be conclusively commented upon. The exact duration of first line and second line ART was not taken into account, therefore further detailed study exploring the association with metabolic syndrome is warranted.

CONCUSSION

The administration of antiretroviral therapy (ART) itself is associated with an increase in the incidence of metabolic risk factors (namely insulin resistance, lipoatrophy and dystrophy, dyslipidaemia, and abnormalities of fat distribution) in HIV patients. A lot of focus has been on the management of OI's and lately CVD, likewise the subtle metabolic irregularities induced by ART have to be addressed.

Thus, further challenges in the management of HIV patients include the management of metabolic syndrome and associated diseases specially NAFLD which although does not cause acute complications, but in the long run may be a major key factor for morbidity and mortality. Early switch from NNRTI's and PI's to dolutegravir based regimen is the need of the hour.

Author declaration

Author contributions
All authors have contributed to the study including the conception, the acquisition, analysis, interpretation of data, as well as drafting, editing and approval of the version to be published. All the authors have contributed to the study and are responsible for its content.

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REFERENCES

1. Samaras K, Wand H, Law M et al. Prevalence of Metabolic Syndrome in HIV Infected Patients Receiving Highly Active Antiretroviral Therapy Using International Diabetes Foundation and Adult Treatment Panel III Criteria Associations with insulin resistance, disturbed body fat compartmentalization, elevated C-reactive protein, and hypo adiponectinemia, Diabetic care 2007;30:113-19. https://doi.org/10.2337/dc06-1075
2. Swami A. Metabolic syndrome and HIV infection, Journal of HIV and retrovirus, 2016; 2:1-5. https://doi.org/10.21767/2471-9676.100014
3. Grundy SM, Cleeman JI, Daniels S R, et al. Diagnosis and management of the metabolic syndrome – An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation, 2005;112:2735-52. https://doi.org/10.1161/01.atv.0000189155.75833.c7
4. Singh Y, Garg MK, Tandon N, et al. A Study of Insulin Resistance by HOMA-IR and its Cut-off Value to Identify Metabolic Syndrome in Urban Indian Adolescents. Journal of Clinical Research in Pediatric Endocrinology, 2013;5(4):24551. https://doi.org/10.4274/jcrpe.1127
5. Roti Agrawal, Sunita Mishra, VK Dixit &, Sweta Rai. Association of non-alcoholic fatty liver disorder with obesity. Indian J Prev Soc Med, 2008; 39:13-16. https://doi.org/10.1111/obr.12271
6. Theengh D, Yadav P, Jain A, Nandy P. Assessment of metabolic syndrome in HIV-infected individuals. Indian Journal of Sexually Transmitted Diseases and AIDS, 2017;38(2):152-55. https://doi.org/10.4103/ijstd.ijstd_55_16
7. Estrada V, Martínez-Larrad MT, González-Sánchez JL et al. Lipodystrophy and metabolic syndrome in HIV-infected patients treated with antiretroviral therapy. Metabolism, 2006;55(7):94045. https://doi.org/10.1016/j.metabol.2006.02.024
8. Drelichowska J, Kwiatkowska W, Knysz B, Witkiewicz W. Metabolic syndrome in HIV-positive patients. HIV & AIDS Review, 2015;14(2):3541. https://doi.org/10.1016/j.hivar.2014.09.002
9. Honnapurmath V, Patil V. Antiretroviral therapy-induced insulin resistance and oxidative deoxy nucleic acid damage in human immunodeficiency virus-1 patients. Indian Journal of Endocrinology and Metabolism, 2017;21(2):316-21. https://doi.org/10.4103/2230-8210.202029
10. Tien PC, Schneider MF, Cole SR et al. Antiretroviral therapy exposure and insulin resistance in the Womens interagency HIV study. J Acquir Immune Defi Syndr 2008; 49:36976 https://doi.org/10.1097/qai.0b013e318189a780
11. Arama V, Tiliscan C, Streinu-Cercel A et al. Insulin resistance and adipokines serum levels in a Caucasian cohort of HIV-positive patients undergoing antiretroviral therapy: A cross sectional study. BMC Endocr Disord 2013;13(4). https://doi.org/10.1186/1472-6823-13-4.
12. Bala B, Majumdar B, Pal J, Datta S et al. Study of metabolic complications after 1 year of antiretroviral therapy in HIV-infected patients in a tertiary care center in North Bengal. Annals of Tropical Medicine and Public Health, 2016;9(2):97-101. https://doi.org/10.4103/1755-6783.177376
13. Stein JH, Klein MA, Bellehumeur JL, et al. Use of human immunodeficiency virus-1 protease inhibitors is associated with atherogenic lipoprotein changes and endothelial dysfunction. Circulation 2001; 104:257-62 https://doi.org/10.1161/01.cir.104.3.257
14. Guaraldi G, Squillace N, Stentarelli C, et al. Nonalcoholic Fatty Liver Disease in HIV-Infected Patients Referred to a Metabolic Clinic: Prevalence, Characteristics, and Predictors. Clinical Infectious Diseases,2008;47(2):250-57. https://doi.org/10.1086/589294
15. Lemoine M, Barbu V, Girard PM, et al. Altered hepatic expression of SREBP-1 and PPARγ is associated with liver injury in insulin-resistant lipodystrophic HIV-infected patients. AIDS 2006; 20: 387–95. https://doi.org/10.1097/01.aids.0000206503.01536.11
16. Gupta D, Rani M, Khan N, Jameel S. HIV-1 infected peripheral blood mononuclear cells modulate the fibrogenic activity of hepatic stellate cells through secreted TGF-β and JNK signaling. PLoS One 2014: 9. https://doi.org/10.1371/journal.pone.0091569
17. Renga B, Francisci D, Schiaroli E, et al. The HIV matrix protein p17 promotes the activation of human hepatic stellate cells through interactions with CXCR2 and syndecan-2. PLoS One 2014; 9. https://doi.org/10.1371/journal.pone.0094798