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General Medicine

INSULIN RESISTANCE IN PLHIV ON HAART AND HAART NAÏVE PLHIV: A CROSS-SECTIONAL STUDY

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ABSTRACT HAART (Highly active antiretroviral therapy) has transformed a fatal disease to a chronic, manageable disease. But long term toxicities are emerging after prolonged exposure to antiretroviral therapy(ART). Adverse metabolic effects like dyslipidemia, increased blood pressure, and insulin resistance(IR) have been attributed to HAART. Therefore, the use of HAART raises concerns regarding metabolic disorders and cardiovascular risk in HIV(Human immunodeficiency virus) infected patients.

Objective: To determine the prevalence of insulin resistance in a cohort of HIV infected patients on HAART as compared to HAART naïve PLHIV(People living with HIV)

Methods:A cross sectional study includes 53 subjects, out of which 26 were PLHIV on ART –Group I, 27 were ART naïve PLHIV-Group II was conducted. Insulin resistance was determined by homeostasis model assessment (HOMA-IR) mathematical model. Statistical analysis was performed to assess the association between demographic, clinical characteristics, laboratory results and insulin resistance.

Results: 69.5 % PLHIV on HAART showed IR, as compared to 37 % of ART naïve PLHIV (p= 0.01). MetS(Metabolic Syndrome) was found in 53.8% among PLHIV on ART , compared to 11.1% among ART naïve PLHIV(p= 0.001) .In the multivariate analysis, presence of metabolic syndrome was found to be directly associated with insulin resistance.

KEYWORDS : Metabolic syndrome, PLHIV, Insulin resistance

INTRODUCTION:

Globally, almost 78 million people have been infected with the HIV virus since the beginning of the epidemic and about 39 million people have died of HIV infection. ART improves the survival and quality of life of PLHIV, but long term ART use is associated with metabolic, cardiovascular, hepatic, renal, bone, bone marrow and other complications or toxicities..These complications of ART are variably associated with all major classes of ART regimen. The three most common metabolic abnormalities that are related to ART are dyslipidaemia, lipodystrophy and dysregulation of glucose metabolism[1]leading to metabolic syndrome and increase in cardiovascular comorbodities. The aim of the study was to determine the prevalence of insulin resistance in a cohort of HIV infected patients on HAART as compared to HAART naïve PLHIV

MATERIALS AND METHODS

A hospital based cross-sectional study was conducted at Kalyani J. N. M. Hospital from August 2019 to March 2020. Study subjects comprised of 2 groups: Group I : PLHIV receiving ART ;Group II: PLHIV not receiving ART (i.e. ART naïve) at the time of study enrolment. Participants less than 18 years of age, pregnant women, any subjects with known coronary artery disease, hypertension, diabetes mellitus, hypothyroidism were excluded from the study. A total of 53 participants were taken, 26 in group I, 27 in group II. The study was approved by the ethical committee and written informed consent was taken before study enrolment from the participants.

Clinical records like sex, age, educational status, occupation, socioeconomic status by modified kuppuswamy scale, details of ART, habit of smoking, tobacco chewing, family history of diabetes mellitus, cardiovascular disease, hypertension, stroke, weight, height, BMI, waist circumference, blood pressure were obtained Fasting level of glucose, insulin and lipids were obtained. Fasting blood sugar(FBS) was estimated by glucose oxidase peroxidase method. Similiarly, total cholesterol was estimated by cholesterol oxidase method, HDL(High density cholesterol) and LDL(Low density cholesterol) both were estimated by direct clearance method and triacylglycerol was estimated by GPO-PAP(Glycerine phosphate oxidase peroxidase) method. Serum insulin was estimated by electro chemiluminiscence method.Insulin resistance was calculated by HOMA IR, calculated by dividing the product of the fasting glucose level (mg/dL) and the fasting insulin level (mIU/mL) by 405.

Statistical analysis: The descriptive statistics were presented in frequency and percentages for qualitative variables and as range, means and standard deviations/median & standard error of mean for quantitative variables.The statistical significance of quantative variables was carried out by 't' test/non parametric and Wilcoxon Mann Whitney test and the statistical significance of qualitative variables was determined by Chi Square test and Fischer exact Test.

RESULTS:

A total of 53 subjects were enrolled in the study, of them 26 were PLHIV on ART –Group I, 27 were ART naïve PLHIV-Group II .The demographic information, family and social history are presented in table 1. Higher proportions of the study participants were males, in the age group of 31-40 years, from the upper lower socioeconomic class, had history of smoking in the PLHIV groups. Participants with or without ART were not statistically different with regards to age (p = 0.238) and sex composition (p = 0.595).

Table 1: Baseline Characteristics Of The Study Participants

Variables		PLHIV on ARTNumber =26,(%)	ART naïve PLHIVNumber =27,(%)
1.sex	Male	17 (65.4%)	21 (77.8%)
	Female	9 (34.6%)	6 (22.2%)
2.age	<30 years	3 (11.5%)	9 (33.3%)
	31-40 years	17 (65.4%)	12 (44.4%)
	>40 years	6 (23.1%)	6 (22.2%)
3.socioeconomic class (modified kuppuswamy scale)	Lower	0	2 (7.4%)
	Lower middle	7(26.9%)	4 (14.8%)
	Upper lower	19(73.1%)	21 (77.8%)
	Upper middle	0	0
4.family history of cardiovascular disease risk	PRESENT	5 (19.23%)	11 (40.74%)
	ABSENT	21(80.76%)	16 (59.25%)
5.smoking	PRESENT	15 (57.7%)	18 (66.7%)
	ABSENT	11 (42.3%)	9 (33.3%)

Details of ART is given in table 2. The mean duration of ART in group I subjects was 6.55±3.54 year. Mean duration of HIV among study subjects of Group I was 8.1 year. The mean CD4 count of the study participants in group I was 399.15±285.30 cells /mm^3 (70 – 1174 cells/mm^3) whereas, the mean CD4 count of the study participants in group II was 281.81± 205.90 cells/mm^3 (range 17-838 cells/mm^3). Out of 26 study subjects in group I most (65.38%) of the subjects were on non protease inhibitor (PI) therapy (TDF-3TC-EFV) regimen.

Table 2: Details Of Art

	PLHIV on ART (Group I)	ART naïve PLHIV (Group II)
Duration of ART		

1-5 YEARS	42.30	
5-10 YEARS	30.76	
>10 YEARS	27.92	
Duration of HIV		
≥5 year	80.8	0
<5 year	19.2	100
ART Regimen		
Non PI regimen	65.38	
PI regimen	34.61	
Adherence		
<95%	30.76	
≥95%	69.23	

Mean BMI(Body mass index) of the study subjects of group I was 21.23 ± 4.61kg/m^2 , group II was 20.32 ± 3.58 kg/m^2 .The difference in BMI between Group I and Group II was not significant (p= 0.42). Similiarily, the difference in waist circumference between Group I and Group II was not significant (p=0.128) . Although SBP(systolic blood pressure), DBP(diastolic blood pressure) was in higher range in PLHIV on ART, compared to ART naïve PLHIV ,they are not statistically significant.FBS, total cholesterol, HDL, LDL were significantly higher in PLHIV receiving ART compared to those ART naïve (p=0.003, 0.025, 0.011, 0.010) respectively.Clinical characteristics and laboratory parameters are given in table 3.

TABLE 3: Clinical characteristics and laboratory parameters

	PLHIV on ART (Group I)	ART naïve PLHIV (Group II)
BMI	Number=26,(%)	Number=27,(%)
<18.5	7(26.9%)	8(29.6%)
18.5-24.9	14(53.8%)	15(55.6%)
>25-29.9	5(19.2%)	4(14.8%)
	Mean±SD	Mean±SD
Waist circumference (cm)	84.78 ±12.07	80.25 ± 9.08
SBP (mm Hg)	113.92 ±13.23	107.63 ± 9.73
DBP (mmHg)	76.15 ±10.11	72.37 ± 9.01
FBS(mg/dl)	102.69±48.28	87.56±25.68
Triglyceride(mg/dl)	149.77±107.06	110.44±53.32
LDL(mg/dl)	104.11±33.86	79.82±34.04
HDL (mg/dl)	40.23±17.40	30.07±14.54
Total cholesterol(mg/dl)	164.92±50.153	135.67±43.83
Insulin level (mIU/ml)	9.652±6.80	9.44±12.23

The prevalence of IR in PLHIV on ART is 69.5 %, compared to 37 % among ART naïve PLHIV (p= 0.01)) is depicted in Fig 1MetS using the NCEP ATPIII(National Cholesterol Education Program Adult Treatment Panel III)criteria was found in 53.8% among PLHIV on ART , compared to 11.1% among ART naïve PLHIV(p= 0.001) The most frequent components of MetS were hypertriglyceridemia (p= 0.00. OR 1.014), high SBP (p =0.001; OR 1.11), DBP (p = 0.000, OR 1.18) and increase FBS (p = 0.003,OR 1.1).

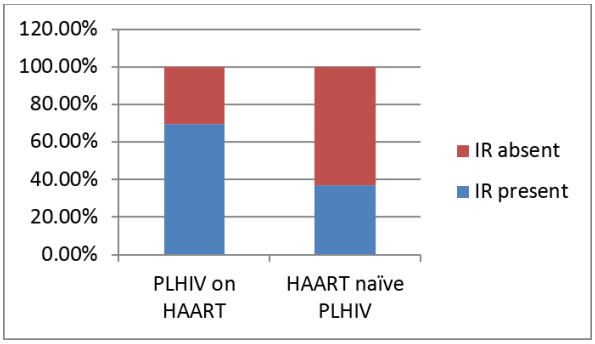

Figure1: Bar diagram showing prevalence of Insulin resistance

DISCUSSION

The results of our study show that there is an increased prevalence of insulin resistance in patients treated with ART. In our study, the overall prevalence of IR in PLHIV on ART was 69.5%, as compared to 37% among ART naïve PLHIV. The reported prevalence rates of IR among HIV patients on ART ranges from 24.1% to 62.9% [2-6].The HOMA-IR cutoff taken was 1.93 for Indian population, which was based on a previous study conducted[2].The cut off is lower than the usual western standard value of 2.1[4]. The disparities observed between the various studies may be partly due to the method used to assess insulin resistance. In fact although the general trend is towards using the HOMA – IR index, there is no current consensus on which method should be used for insulin resistance evaluation among PLHIV. Moreover even when using indirect assessment tools like HOMA -IR, the main difficulty remains the threshold to consider in defining insulin resistance, since the threshold may vary depending on race, gender and even some pathologies. Through multivariate analysis, only presence of metabolic syndrome was found to be associated with the development of insulin resistance. Though variables like hypertriglyceridemia , high SBP, DBP, high FBS are associated with increase in the incidence of MetS , they are not directly found to be associated with IR in our study. Our study find a prevalence of 55.55% of IR among the PLHIV on protease inhibitors containing regimen, but it was not found to be statistically significant,in contrast to the other reports which showed a clear association[7,8] this may be explained by the small number of patients using PI as a part of HAART regimen in our study The prevalence of IR was also not found to be statistically significant among patients who were 1 year on HAART , as compared to those who were on less year to treatment. But IR was found to be higher among patients with HIV duration ≥ 5 years of the infection (p= 0.007) as compared to less than 5 years of HIV.The prevalence of MetS in our study was found to be 53.8% among PLHIV on ART , compared to 11.1% among ART naïve PLHIV(p= 0.001), which is higher than the reported prevalence of 17.0% to 45.4%[9-11].With regards to component of MetS in our study, hypertriglyceridemia (p= 0.00, OR 1.014) , high SBP (p =0.001, OR 1.11), DBP (p = 0.000, OR 1.18), increase FBS (p = 0.003,OR 1.1) are associated with increase in the incidence of MetS.

Limitations

Firstly, the study subjects were limited in number, due to the nature and constraints of the study. Also, the definitions of MetS, IR are largely derived from epidemiological studies based on white, Caucasian populations that are very different from Indian subjects demographically, clinically and metabolically. In, addition CD4 count, viral load were omitted. These variables were found to be associated with IR in some studies[12]. Therefore; these two variables must be included in future studies.

CONCLUSION:

In conclusion, this study shows a significant percentage of PLHIV on HAART was insulin resistant. Factor directly found to be associated with IR was presence of MetS, and hypertriglyceridemia, high SBP, DBP, high FBS are associated indirectly IR. Detection of IR and its risk factors will allow for the assessment of metabolic risk of each PLHIV and will promote to modify such risk to prevent the future development of Type 2 diabetes and cardiovascular disease. Based on our results, we suggest routine test for plasma glucose, lipids during followup and control the traditional risk factors for cardiovascular disease among PLHIV.

Conflict of interest: None

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