IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 6 Ver. 14 (June. 2018), PP 69-77
www.iosrjournals.org

Study of Metabolic Syndrome in HIV Individuals

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Abstract:
BACKGROUND:
As Prevalence of metabolic syndrome in HIV infected people is inreasing& the risk for cardiovascular diseases will be more in people with hiv infection. The metabolic complications may result from HIV diseases, Highly active anti retroviral therapy & its complications and opportunistic infections.
AIMS
OBJECTIVES:
To compare the prevalence of metabolic syndrome in HIV patients and non HIV controls whitch includes fasting blood sugar, serum triglyceride levels, HDL level,blood pressure & central obesity in patients who attended the outpatient department of Dermatology, Venereology, and Leprosy, Governament General Hospital, Vijayawada.(A.P)
METHODS:
The present study was conducted in patients who attended the outpatient department of Dermatology, Venereology and leprosy, Government General Hospital, Vijayawada. 100 HIV patients were compared with age & sex matched on non HIV controls to know the prevalence of metabolic syndrome.
RESULTS:
Out of 100 HIV patients, 64(64%) are males. The prevalence of metabolic syndrome is high in HIV patients compare to Non HIV controls (40% vs 25%). Serum triglycerides, low HDL levels, hypertention are more in HIV patients, The prevalence of metabolic syndrome was high in HIV patients using 2nd line ART regimen.
CONCLUSION:
The prevalence of metabolic syndrome is high in HIV patients compare to non HIV population ,which increases the risk of cardiovascular morbidity in HIV patients.

Keywords: *HIV Metabolic syndrome, Highly active antiretroviral therpy, Waist circumference, Serum HDL cholesterol & triglycerides.*

Date of Submission: 14-06-2018 Date Of Acceptance: 01-07-2018

I. Introduction:

The introduction and widespresd use of highly active antiretroviral therpy (HAART) in the mid 1990's has led to dramatic improvement in HIV patients the decline in morbidity & mortality.As a results life expectancy increased and contributing to the occurrence of obesity, diabetes mellitus (DM) and cardiovascular diseases.

Metabolic syndrome is a complex inter related risk factors for Cardiovascular diseses(CVD) and diabetes. These factors include dysglycemia, raised blood pressure, elevated triglyceride levels, low high density lipoprotein cholesterol levels and obesity (particularly central adiposity).

NHANES (National health and nutritional examination survey) data 2003-2012 have shown a prevalence rate of 18.3% among those aged 20 to 39 years which increased to 46.7% among those aged 60 years or older with a higher incidence noted among women.[2-9]

Adipose tissue in the abdomen is known to be metabolically active and produce a variety of cytokines-adipocytokines whitch includes glycerol, Free Fatty Acids (FFA), proinflammatary mediators(Tumour Necrosis Factor Alfa (TNFα) and Interlukin-6 (IL-6), Plasminogen Activator Inhibitor-1 (PAI-1), and C-Reactive Protein(CRP).[11] Increased production of free fatty acids, inflammatory cytokines, and adipokines and mitochondrial dysfunction contribute to impaired insulin signaling, decreased skeletalHI muscle glucose uptake, increased hepatic gluconeogenesis , and β cell dysfunction leading to hyperglycemia. In addition insulin resistence leads to the development of hypertention by impairing vasodilatation induced by nitric acid.

The initial description of MeTS was found in HIV patient few years after initiation of protease inhibitor chiefly ritonavir plus saquinavir combination based antiretroviral therpy. Prevalence of MeTs in HIV population regarded as high, ranging from 11.2% up to 45.4%.[14] Cytokines like hS-CRP,tumor necrosis factor,IL-6,IL-1β,urokinase plasminogen activator receptor(suPAR) and IL-6 are increased in the initial stage of HIV infection and these not only contribute to viral replication but also initiates the earliest changes leading to development of metabolic syndrome in future.[15]Some genes responsible for suppressing inflammation like tyrosine kinase RON are downregulated in HIV infection leading to continuous inflammatory response and increased HIV transcription (16). Even after institution of HAART(Highly Active Antiretroviral Therpy) with HIV levels below detectable range , the blood levels of these cytokines remain elevated. In the SMART trail, participants bearing ≤400 copies /mL of HIV RNA also had elevated hsCRP and IL-6 levels in 38% and 60%, respectively, in comparison to normal individual form cohrts for cardiovascular outcomes [(17)](Fig-1).

As the disease progresses, LDL-C decreases followed by an increase in triglycerides, apolipoprotein levels and VLDL in the advance course of the disease. Hypertriglyceridemia may be due to decreased clearance of triglycerides and increased production of VLDL.[18]

Insulin resistance can occur in HIV patients on therapy, but probably the mechanism is different from general population. Studies have shown that PIs selectively inhibit glucose transport in adipocytes without affecting early insulin-signaling events or translocation of intracellular GLUT4 transporters to the cell surface.[20] (figure- 2) [21].

Fat Distribution and Metabolic Syndrome:

The most visible effect of metaboli syndrome in HIV patient is the development of lipodystrophy which includes facial lipoatrophy (fat loss), increased upper trunk fat(Buffalo hump),lipoatrophy of arms and legs ,and abdominal obesity[22.29](Fig-3).

Hypertension:

Some reports have implicated protease inhibitors as the cause.[24].Increase in BMI after effective antiretroviral therapy has been postulated as the cause of hypertension.

II. Materials & Methods

The present study was conducted in patients who attended the outpatient department of Dermatology, Venereology, and Leprosy, Governament General Hospital, Vijayawada.

STUDY DESIGN: Case control study.

INCLUSION CRITERIA:

100 patients of HIV on Highly Active Anti Retroviral Therapy aged more than 25 years. Age & sex matched HIV negative controls.

EXCLUSION CRITERIA:

Pregnant women

Severe and acutely ill patients

METHOD:

HIV infected patients attending outpatient department of DVL & ART center Government General Hospital, Vijayawada were included in the study. Informed consent was taken prior to doing investigations. Ethical consideration was taken from institutional ethical committee , consent was taken from each patient & confidentiality was maintained.

General data regarding age, sex, complaints & duration of disease, h/o treatment, smoking ,alcohol, family history, of cardiovascular disease and cerebrovascular disease were collected.

Controls were selected among patients referred for dermatological conditions without HIV. The sources for cases and controls was same.

Cases and age sex matched controls were screened for presence of metabolic syndrome as defined by National cholesterol Education Program Adult treatment Panel III 2001.

1. Waist circumference was determined by placing the measuring tape at the upper most part of hip bone around abdomen, horizontally & tape measure was snug but did not cause compression on the skin.
2. Blood pressure was recorded as the average of two measurements after asking patients to sit for 5 minutes.
3. Serum samples were taken the subjects had fasted over night (at least for 8hrs)
4. Serum HDL cholesterol & triglycerides were measured with enzymatic procedure.
5. Plasma glucose was measured by using glucose oxidase method. (FiG-1)

III. Observation, Results And Discussion :

Hiv disease is caused by Human Immunodefiency virus. The metabolic complications may complicate HIV disease in many ways. Metabolic dysfunction may result HIV disease, Highly Active Anti RetroviralTherpy &it's complications and opportunistic infections, with introduction of Highly Active Anti RetroviralTherpy (HAART), HIV related morbidity and mortality have declined and survival and quality of life have improved inHIV infected patients.

Highly Active Anti RetroviralTherpy has transformed a preaviously fatal disease to a chronic , manageble infection that requires life-long treatment. But this is associated with various complications such as lipodystrophy, dyslipidemia, hyperglycemia and & hypertention which are also components of metabolic syndrome and increase the prevalence of MeTS in HIV infected patients & cariovacular risk.

The present syududy included 100 HIV patients and 100 age sex matched HIV negative controls.

In our study males outnumbered females in both cases and controls and the males to female ratio was 1.78:1.

Age Distribution:
Majority of patients were between age group 31-50 years (83%) in both HIV cases and HIV negative controls.(Fig-2)

Age Distribution of Metabolic Syndrome:
The metabolic syndrome was more frequent at the age group of 31-50 years in HIV patients.
The metabolic syndrome was more frequent at the group of 31-55 years in HIV negative controls.(Tab-4)

SEX Distribution of Metabolic Syndrome: (Tab-5)
The prevalence of metabolic syndrome in HIV patients was more in females than In
males (44.4% vs 37.5%) similar to study of Alvarez c et al[32]. But in our stydy the association was statistically not significant.
The prevalene of metabolic syndrome in HIV ngative controls was more in females than in males (33.33% vs 20,31%) But in our study the association wasstatistically not significant.

Prevalence of Metabolic syndrome(Tab-3)
In the present study ,prevalence of metabolic syndrome in HIV patients was higher than in controls (40.0% vs 25%) correlating with Gazzaruso et al[30] (33.1% vs 2.4%), Estrda et al[31] (15.8% vs 3.2%)) & Bruno et al[32] (39.8% vs 6%) and the association between HIV and metabolic syndrome is statistically significant.

Among 100 HIV patients, 50 patients, are taking First line Highly Active Anti Retroviral Therpy and pther 50 patients are taking Second line Highly Active Anti Retroviral Therpy.
The prevalence of metabolic syndrome was higher in HIV patients on second line HAART (65%vs 35%) correlating with the studies of jacobson et al[33] & katherine samaras et al[34] .

Prevalence of various parameters of metabolic syndrome: (Tables: 6 to 10) & (Fig-3)
Prevalence of abnormal fasting blood sugars was more in HIV patients than controls (45% vs 33%) correlating with Gazzaruso et al & Bonfanti P et al, but the association was not quite statistically significant in our study.
HDL cholesterol levels are low in HIV patients than in controls(69%vs 32%) and association was extremly statistically significant. The findings are similar to Caramine Gazzaruso et al [36].and Bonfanti et al[35].
Serum triglyceride levels are higher in HIV patients than in controls (60% vs 32%) similar to Bonfanti et al.[35] The association is extremly statistically significant.
Abnormal blood pressure was more in HIV patients than in controls (52% vs 27%) similar to Gazzaruso et al [30]. association is extremly statistically significant.
Centtal obesity was more in HIV patients than in controls (33% vs 27%). Similar to Gazzaruso et al[36], but the association was statistically not significant in our study.

THERAPY FOR METABOLIC SYNDROME IN HIV:

Cessation of smoking is the single most important and the easiest therapy MeTS in HIV patients without any side effects. Management of dyslipidemia should include non-drug measures like dietary modification to attain ideal body weight and incresed physical activity of the patient. Patients on Protease inhibitors based regime with complications of MeTS can be switch over to NNRTI based regimes if no contraindication exists. [9].

IV. Conclusion:

As HIV patients live longer ,health care workers are more likely to treat patients with components of metabolic syndrome. However, the presentation of MeTS in HIV patients may not be the same as genaral population . With better understanding about pathophysiology of chronic inflammation and endothelial dysfunction in HIV infection, it may become possible to initiate measures that can target the inflammatory pathways active in HIV infection.

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Clinical mesures	WHO(1998)	EGIR(1999)	ATPIII(2001)	AACE(2003)
Insulin resistance	IGT,IFG,T2DM, or lowered insulin sensitivity plus any 2 of the following	Plasma insulin >75th percentile plus any 2 of the following	None,but any 3 of the following 5 features	IGT or IFG plus any of the following based on the clinical judgement
Body weight	Men; waist-to-hip ratio >0.90; women; waist-to-hip ratio > 0.85 and/or BMI > 30KG/M^2	WC ≥ 94cm in men or ≥ 80cm in women	WC ≥ 102cm in men or ≥88cm in women	BMI ≥ 25kg/m^2
Lipids	TG ≥ 150/dL and /or HDL-C < 35mg/dL in men or < 39 mg/dL in women	TGs≥150mg/dL and/ or HDL-C < 39mg/dL in men or women	TGs≥150mg/dL HDL-C < 40mg/dL in men or < 50 mg/dL in women	TGs≥150mg/dL HDL-C < 40mg/dL in men or < 50 mg/dL in women
Blood Pressure	≥ 140/90mmHg	≥ 140/90mmHg or on hypertensionRx	≥ 130/85mm Hg	≥ 130/85mm Hg
Glucose	IGT,IFG, or T2DM	IGT or IFG (but not diabetes)	>110mg/dL (includes diabetes)	IGT or IFG (but not diabetes)

Table 1 : Diagnostic criteria for the clinical diognosis of the MetS (2-8)

SEX	NUMBER	PERCENTAGE
MALE	64	64%
FEMALE	36	36%

TABLE:2: SEX DISTRIBUTION IN HIV - METABOLIC SYNDROME

Among the 100 HIV patients, 64 were mles and 36 were females with M:F of 1.78: 1.

Metabolic syndrome	No of cases	No of controls	total
present	40	25	65(32.5%)
Absent	60	75	135(67.5%)
Total	100	100	200(100%)

Table: 3 : Prevalence of Metabolic Syndrome

Chi-square equals 5.128 with I degree of freedom. The two tailed p value equals to 0.024 association is stastically significant.

1	
Age in years	Number(%)
25-30	1(2.5%)
31-35	7(17.5%)
36-40	16(40.0%)
41-45	7(19.5%)
46-50	4(10.0%)
51-55	2(5.0%)
56-60	1(2.5%)
61-65	2(5.0%)
Total	40(100.0%)

Table:4a: Age Distribution Among HIV Patients with Metabolic syndrome (CASES)

Majority of patients with metabolic syndrom were between the age groups of 31-50

2	
Age in years	Number(%)
25-30	1(4.00%)
31-35	5(20.00%)
36-40	8(32.00%)
41-45	5(20.00%)
46-50	3(12.00%)
51-55	2(8.00%)
56-60	1(4.00%)
61-65	0(0.00%)
Total	25(100%)

TABLE: 4b -Age Distribution among controls (HIV -ve patients) with metabolic syndrome (CONTROLS)

Majority of controls with metabolic syndrome are between age group of 31-55

1			
Metabolic syndrome	Females No(%)	Males No(%)	Total No(%)
present	16(44.44%)	24(37.5%)	40(40.0%)
Absent	20(55.56%)	40(66.67%)	60(60%)
Total	36(100.0%)	64(100.0%)	100(100.0%)

Table- 5a : Sex Distribution of metabolic syndrome in CASES

Chi-square equals 0.219 with 1 degree of freedom. The two tailed p value to 0.6399 Association is not statistically significant.

2			
Metabolic syndrome	Females No(%)	Males No(%)	Total No(%)
present	12(33.33 %)	13(20.31 %)	25(25.0%)
Absent	24(66.67 %)	51(79.63 %)	75(75.0%)
Total	36(100.00 %)	64(100.00 %)	100(100.0 %)

Table-5b :Sex distribution of metabolic syndrome in CONTROLS

Chi-square equals 2.083 to with 1 degree of freedom. The two tailed p value equals to 0.1489.Association is not statistically significant

	Cases	Controls	Total
Normal	48(48.0%)	73(73.0%)	121(60.5%)
Abnormal	52(52.0%)	27(27.0%)	79(39.5%)
Total	100(100.0%)	100(100.0%)	200(100.0%)

Table:6 : Hypertention in HIV metabolic syndrome (≥ 130/85mm of Hg)

Chi-square equls 13.077 with I degree of freedom. The two tailed p value is less than 0.0001 Association is highly significant

	cases	Controls	Total
Normal	55(55.0%)	68(68.0%)	123(61.5%)
Abnormal	45(45.0%)	32(32.0%)	77(38.5%)
Total	100(100.0%)	100(100.0%)	200(100. 0%)

Table: 7: FASTING GLUCOSE LEVELS≥100mg/dL

chi-square equals 3.041 with 1 degree of freedom. The two tailed p value equals to 0.0812. Association is not statistically significant.

	Cases	Controls	Total
Normal	31(31.0%)	68(68.0%)	99(49.5%)
Abnormal	69(69.0%)	32(32.0%)	101(500.5%)
Total	100(100.0%)	100(100.0%)	200(100.0%)

Table: 8 : LOW HDL LEVELS(Males≤40mg/dl, Female≤50mg/dl)

Chi-square equals 25.923 with I degree of freedom. The two tailed p value equals to less than 0.0001. Association is highly significant

	Cases	Controls	Total
Normal	40(40.0%)	68(68.0%)	108(54.0%)
Abnormal	60(60.0%)	32(32.0%)	92(46.0%)
Total	100(100.0%)	100(100.0%)	200(100.0%)

Table: 9 : Hyper triglyceride levels (≥150mg/dl)

Chi-squre test equals 14.674 with 1 degree of freedom. The two tailed p value equals to 0.0001. Association is highly significant.

	Cases	Controls	Total
Normal	67(67.0%)	73(73.0%)	140(70.0%)
Abnormal	33(33.0%)	27(27.0%)	60(30.0%)
Total	100(100.0%)	100(100.0%)	200(100.0%)

Table: 10 CENTRAL OBESITY. :- WAIST CIRCUMFERENCE (≥ 102cm in Male, ≥ 88cm in Female)

Chi-square equals 0.857 with 1 degree of freedom. The two tailed p value equals to 0.44. Association is not statistically significant.

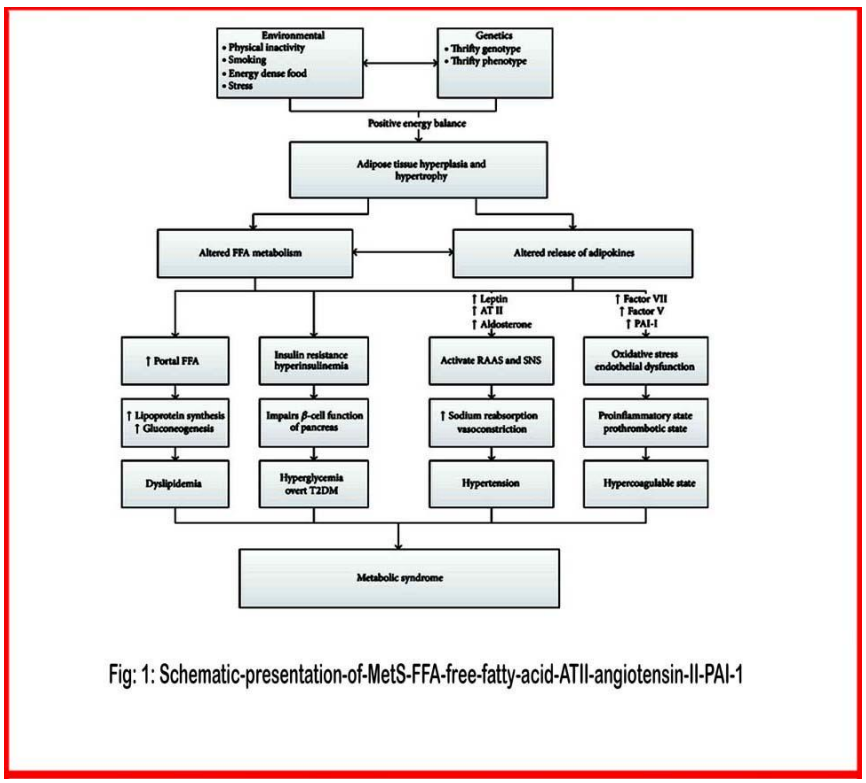

Fig: 1: Schematic-presentation-of-MetS-FFA-free-fatty-acid-ATII-angiotensin-II-PAI-1

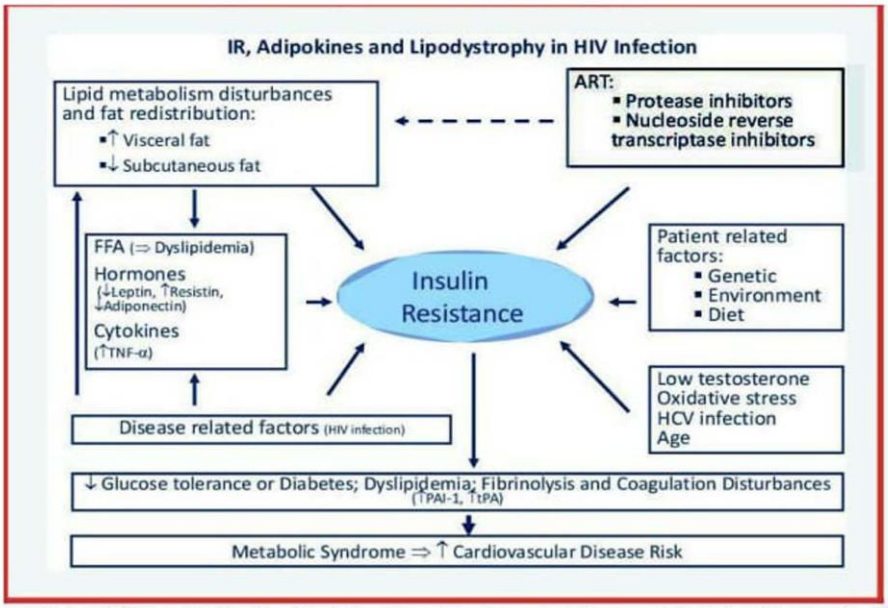

Fig-2: Paula Freitas,Davide Carvalho,Selma Souto:Lipodystrophy:The metabolic link of hiv infection with Insulin -Resistence Syndrome:April 2013: in book:CurrentPerspective in hiv infection, Edition,Chapter:12,Publisher:INTECH,Editors:Shailendra K Saxena,pp.261-300

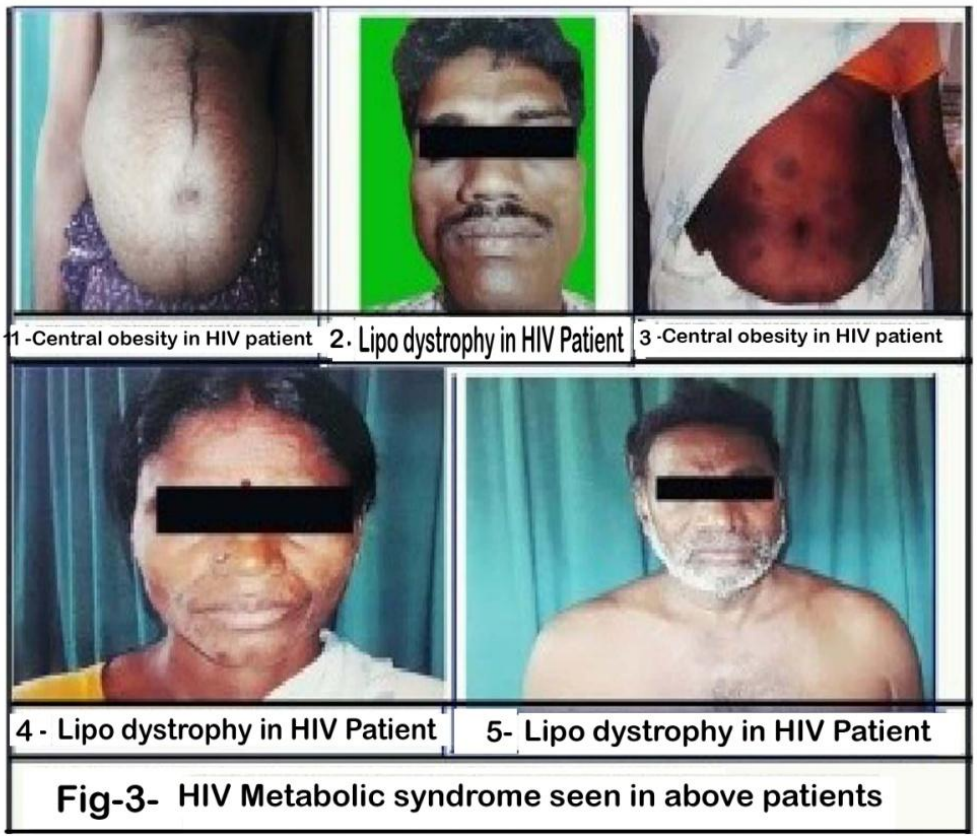

Fig-3- HIV Metabolic syndrome seen in above patients

Dr.J.Balachandrudu "Study of Metabolic Syndrome in HIV Individuals."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 6, 2018, pp 69-77.