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RESEARCH ARTICLE

A STUDY TO ASSESS ANTHROPOMETRIC PARAMETERS AND SERUM LIPID VARIATIONS IN HIV PATIENTS RECEIVING HAART

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Abstract

Background:- There is evidence that ART is associated with lipodystrophy syndrome, a disturbance of lipid metabolism characterised by insulin resistance, dyslipidaemia and fat maldistribution, usually presenting as visceral abdominal obesity and cervical fat pad accumulation (buffalo hump)[1],metabolic bone disease (osteopenia and/or osteoporosis) and lactic acidosis. ART- associated dyslipidaemia is characterized by elevated serum concentrations of total cholesterol, triglycerides, low density lipoprotein 2(LDL-c), very low-density lipoprotein (VLDL), Apo lipoprotein B (apoB) and low levels of high density lipoprotein (HDL-c) constituting an atherogenic lipid profile[2].

Materials And Methods:- In this study 100 young patients who were attending the Antiretroviral Therapy Plus Centre & Medicine Wards, ACSR GMC, NELLORE were included randomly.

Anthropometric Measurement :- Body weights were measured (to the nearest 0.5 kilogram) with the subject standing on a weighing scale after it was adjusted to zero kg. Heights were measured (to the nearest 1.0 centimeter) with the subject standing in an erect position against a vertical scale of portable standiometer and a L-square placed on the head and the head positioned to a level with the inferior margin of the bony orbit. The waist measurements were taken from the middle point between the iliac crest and the last rib as recommended by the WHO. Hip circumference was measured as the maximal circumference over the buttocks. BMIs were then calculated as weight in kilograms divided by the height in meter squared.

Results:- The results of the study showed that the Anthropometric parameters on analysis showed a normal range BMI in 59% of patients. Waist-to-hip ratio which have been shown to be better reflector of body fat distribution and is significantly elevated in the HIV-infected patients on HAART. Waist-Hip ratio value analysis showed normal in 18.19% and abnormal in 81.81% of cases. The mean value in males is 0.9578 and in females is 0.9204. This showed a significant correlation to Waist/ hip ratio and the gender.

Conclusions:- Significant metabolic and morphological alterations occur in HIV infected patients especially in patients on HAART. The patients on HAART had an elevated Castelli Index I, indicating an

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increased risk for atherosclerotic cardiovascular disease in this population. Waist-to-hip ratio which are the key indices for assessing body fat distribution were significantly raised in HAART-experienced patients in this study implying that HAART could result to lipodystrophy.

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Introduction:-

Annual assessment of body fat is recommended for adults who begin combination antiretroviral therapy that includes two nucleoside analogues or a protease inhibitor, as well as for any patients who switch antiretroviral agents.

Dual-energy x-ray absorptiometry is useful for assessing fat in the limbs over time. Anthropometric measurements of truncal and limb fat, including measurement of waist, hip, and thigh circumferences may provide additional information about cardiovascular risk. No technique has been validated for the assessment of facial lipoatrophy.

Materials And Methods:-

In this study 100 young patients who were attending the ART Plus Centre & Medicine Wards, ACSR GMC, NELLORE were included randomly.

Inclusion Criteria:-

1. Patients selected in random attending ART plus centre.
2. Age group 20 – 49 years.
3. HIV infection confirmed by Triple ELISA testing according to NACO guidelines.
4. Patients on HAART treatment groups for more than 2 years.

Exclusion Criteria:-

1. Diabetic patients.
2. Nephrotic range proteinuria.
3. Overt Hypothyroidism.
4. Patients on Antihyperlipidemic drugs,Thiazides, Steroids, Beta blockers.
5. HIV patients on HAART for less than 2 years. Age group of 20-49 years were selected because by 20 years a person attains adult anthropometric proportions and remains more or less static until around 49 years after which, age related changes occur especially in the waist circumference and waist/hip ratio. The triple ELISA testing according to NACO Guidelines was used for diagnosis of HIV infection .The total number of 100 patients were included in the study.

Patients included in the study were divided into 4 regimen groups.

1. TEL (Tenofovir, Efavirenz, Lamivudine)
2. TLAR (Tenofovir, Lamivudine, Atazanavir, Ritonavir)
3. ZLE (Zidovudine, Lamivudine, Efavirenz)
4. ZLN (Zidovudine, Lamivudine,Nevirapine)

Results:-

BMI has been shown in several studies[3] not to give a good reflection of body fat distribution but fat to muscle mass ratio (obesity). Indeed waist circumference, hip circumference and waist-to-hip ratios which have been shown to be better reflectors of body fat distribution were significantly elevated in the HIV-infected patients on HAART.

Abnormalities in body composition have been reported in 40 to 50 percent of ambulatory HIV-infected patients according to Lichtenstein KA,Ward DJ et al[4]. The proportion is greater in those receiving combination antiretroviral therapy[5]. The physical appearance of lipodystrophy is more apparent usually by 2 years of HAART therapy[6]. Lipodystrophy is more apparent with the increase of life expectancy in HIV patients treated with HAART on reaching up to 49.5 years when treatment is started at the age of 20 years. Prevalence rates of lipodystrophy vary widely from 11 to 83 percent in cross-sectional studies. Anthropometric parameters are important tools for

measurement of lipodystrophy including weight, BMI, Waist / Hip ratio and skin fold thickness .Many of the studies failed to show good correlation with lipoatrophy and anthropometry. Jean-Guy Baril, Patrice Junod, Roger LeBlanc et al.[7] in their study found a weak correlation with lipodystrophy and Waist / Hip ratio in HIV patients on indinavir and stavudine.

In this study 22% of the cases were underweight and 59% had a normal BMI. 17% are overweight and 2% were obese. Lichtenstein KA,Ward DJ et al.[4] in their study concluded that a decreasing BMI rather than

increasing BMI, increased triglycerides, older age and female sex are more prone for lipodystrophy[8].

Waist-Hip ratio value analysis showed normal in 18.19% of the cases and abnormal in 81.81% of the cases. The mean value in males is 0.9578 and in females is 0.9204 which is above the guideline values for men (> 0.90) as well as women (>0.80), t-value is significant <0.05, reject null hypothesis and the difference between the W.C/H.C is statistically significant with respect to the gender. This shows Waist-Hip ratio has significant relation to long standing illness and abdominal obesity. Considering the anthropometric measurements observed in this study, Waist -Hip ratio is a better parameter for assessing the visceral adiposity. Low BMI reflects the weight loss with progression of disease and an increasing Waist-Hip ratio denoting the visceral adiposity.

Similar results of our study were also seen in a study done by RA Ngala and K Fianko,et al[9] on Dyslipidaemia in HIV-infected patients on highly active anti-retroviral therapy in Kumasi Metropolis in PMC in 2010 stating that waist circumference, hip circumference and waist-to-hip ratio are the key indices for assessing body fat distribution and were significantly raised in HAART-experienced patients in Kumasi, implying that HAART could result to lipodystrophy.

Table1:- BMI among the cases.

BMI	No.of cases	Percentage
Under weight	22	22
Normal	59	59
Over weight	17	17
Obesity	2	2
Total	100	100

22% of patients were of underweight, 59% were of normal weight, 17% were of overweight and 2% were of obesity.

Table2:- Waist hip circumference ratio.

WC-HC RATIO	NO.CASES	FREQUENCY
NORMAL	18	18
ABNORMAL	82	82
TOTAL	100	100

Waist-Hip ratio value analysis showed normal in 18% of the cases and abnormal in 82% of the cases.

Table3:- Waist hip ratio with gender group.

	Gender group	N	Mean	SD	SD Mean	t-sig value	Result
W.C/ H.C	Male	63	.9578	.07604	.00801	0.05	significant
	female	37	.9204	.07385	.01014		

Mean value for waist /hip ratio in males is 0.9578 and for females is 0.9204. The **P** value is significant.

Discussion:-

The changes in the lipid profile in this study were similar in the male and female cases suggesting that the fat distribution were not exclusively due to gender effect. In several studies in Ghana[10], women have been shown to have higher waist circumference, hip circumference and hip-to-waist ratios as opposed to what is typically reported in the Western World. Similar results were observed in our study. It therefore implies that HAART is the main cause of lipid redistribution in this study since these anthropometric parameters were raised in both male and female alike.

Lipodystrophy characterized by peripheral loss of fat tissue and abnormal fat distribution including the enlargement of dorsocervical fat pad, lipomatosis, breast hypertrophy, and visceral abdominal fat accumulation have recently been reported in HIV-1 patients receiving HAART. Dyslipidaemia in the HIV-infected is mostly attributed to HAART treatment. The prolonged surge of pro inflammatory cytokines such as TNF-alpha, IL-1,IL-6 and IFN-alpha observed following the chronic state of HIV infection have been shown to contribute to lipid dysregulation. Cytokines such as TNFalpha, IL-1, IL-6 and IFN-alpha have also been reported to increase lipogenesis, decrease clearance of circulating LDL and inhibit hepatic lipase activity[11]. This probably partly account for the observed slightly increase in serum LDL levels in this study.

A study done by RA Ngala et al[9]. suggested that the combined use of NNRTI and NRTI resulted in 24% of the subjects experiencing facial fat depletion. However, participants on zidovudine, lamivudine and efavirenz combination therapy had no changes in appearance in terms of fat depletion on the limbs as well as fat accumulation in the breast and buttocks. About 29% had truncal obesity after using the various combinations of NRTI and NNRTI. The association between visceral obesity and NRTI therapy has been reported in several studies[12].

The DAD Study Group (Data Collection on Adverse Events of Anti-HIV Drugs) by Jens Lundgren and et al.[13] in Copenhagen have done extensive studies in the growing metabolic complications in HIV from cardiovascular risk. It is an International collaboration study including investigators from all parts of the world in an HIV patient cohort of 24,437. During the first phase of study they demonstrated increased dyslipidemias and cardiovascular risk in HIV patients especially with PIs and NNRTI based HAART on a 4 year follow up.

In addition to its benefit antiretroviral drugs have been associated with an abnormal fat redistribution syndrome that might raise cholesterol and triglycerides levels. Compared to each other, the independent effect of the use of NVP and EFV based combinations on serum lipid profile level was not seen among our study participants. On the contrary, a 48 week follow up study in Australia found that the increase of HDL-C was significantly larger for patients receiving NVP than for patients receiving EFV, while the increase in TC was lower. The increase of non-HDL-C was smaller for patients receiving NVP than for patients receiving EFV, as were the increases of TG and LDL-C. In addition, a study in our country found that TC level >200 mg/dl was more common among patients who received EFV than among those who received NVP. Moreover, a study in USA and Europe found that EFV was associated with higher levels of TC and TG than with NVP. In the DAD study group[14], values of mean total cholesterol and LDL were less compared to this study but showed similar elevation. This may be attributed to the difference in the study population as DAD study was conducted in European and North American population while this study is in Asian population who are inherently prone for Metabolic syndrome & dyslipidaemias.

In our study, the lipid parameters abnormalities were more in the ZLE regimen and least in ZLN regimen compared to Margaret May, Jonathan A C Sterne, Martin Shipley, Eric Brunne et al[5]. in their study of 13300 HIV infected men who are aged 40-70 were divided into two groups parametric model based on the Gompertz distribution generalized best. Analysis of the data in this study showed that all the lipid parameters abnormalities were more pronounced in the group which had nevirapine and stavudine compared to efavirenz and zidovudine based regimens.The mean total cholesterol was 195.41 mg%, 172.15mg%, 201.64mg% and 162.10 mg% in the TEL, TLAR, ZLE and ZLN regimen groups respectively. The p value is significant. Similarly there was statistically significant increase in LDL and TC/HDL ratio.

Limitations of the study:-

This is a cross-sectional study with no follow up of patients to see the effects of HAART at individual level and inference about causal relationship is not possible. In addition, this does not include all potential confounders of dyslipidaemia such as physical exercise. Comprehensive cardiovascular risk stratifications were not assessed in this study. However, the increased risk of cardiovascular diseases associated with described lipid derangements is well known and long term use of first-line HAART may have an impact on cardiovascular system. Subsequent studies could address the issue of the small number of participants and the lack of HIV untreated and HIV-negative controls that our study could not handle.

Conclusion:-

1. Significant metabolic and morphological alterations occur in HIV infected patients especially in patients on HAART.

2. There is a statistically significant increase in the total cholesterol and LDL cholesterol. There is statistically insignificant increase in total triglycerides, VLDL and decrease in HDL cholesterol in HIV patients on HAART.
3. The patients on HAART had an elevated Castelli Index I, indicating an increased risk for atherosclerotic cardiovascular disease in this population.
4. Waist-to-hip ratio which are the key indices for assessing body fat distribution were significantly raised in HAART-experienced patients in this study implying that HAART could result to lipodystrophy.
5. Dyslipidemia is more in the efavirenz based regimens compared to nevirapine, tenofovir, lamivudine, zidovudine and atazanavir containing regimens.
6. There is need to assess lipid profiles at baseline before initiation of HAART treatment and lipid profile monitoring during therapy to monitor any rising trends.
7. New medications with more lipid friendly profiles within existing drugs such as darunavir (PI), etravirine (NNRTI), new classes of drugs such as integrase inhibitors (raltegravir) and CCR5 inhibitors (maraviroc) can be used to avoid dyslipidaemia.
8. The results also recommend implementation of well-controlled cohort studies for the evaluation of long-term effects of HAART treatment on lipid profiles.

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