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To determine the effect of hyperglycemia and lipid profile in human immune-deficiency virus infected individuals: A cross-sectional analysis

T. Nageswara Rao[1], Abhay John[2]
Ph.D Scholar, Malwanchal University, Indore, Madhyapradesh
Professor, Amaltas Hospital and Medical College, Dewas, Madhyapradesh
Corresponding Author: T. Nageswara Rao Email id: sandeshtokaloct12@gmail.com

Abstract:
Background: *There has been little study on HIV affected individuals in the initial period of the disease and during the course of disease on insulin resistance, glucose, and lipids levels as a damaging factor have not been considered in existing studies in this part of India.* ***Aim:*** *Therefore, we hypothesize that insulin resistance, glucose, and lipids levels have no effect on glucose and lipid levels in HIV-infected individuals.*
Methodology: *The human ethics committee approved the study protocol. Since there is no computerized data, collecting it manually is cumbersome, so the sample size is 100 HIV-infected people. The control group has 100 healthy people. Plasma glucose (FBS), insulin resistance, total cholesterol, triacylglycerols (TAG), High Density Lipoprotein-cholesterol (HDLc), andLow Density Lipoprotein (LDL) were estimated.*
Results: *The study observed significant difference in the values of serum total cholesterol on comparison between the two groups of the study. Though the LDL mean level of HIV-infected group subjects was on the higher side but when compared between the two groups, we observed approximately 30 percent high in HIV-infected subjects than the non-HIV infected healthy control. On the contrary, the present study observed lower levels of HDL in HIV-infected subjects and showed significant lower levels than non-HIV healthy control subjects.FBS (t=11.24; df=198; P<0.001) showed a significant difference (Table 3) when compared between the two groups of study. The mean level of serum insulin and HOMA-IR levels were not statistical difference when compared between the HIV-infected and non-HIV healthy control group subjects.****Conclusion:*** *We conclude that if this line of research is supported, studies both in vitro and in vivo will help in the discovery of mechanistic insights that can help clinicians better control hyperglycemia and prevent the onset and progression of its HIV complications. These findings could also benefit the general public.*

Keywords: Human Immuno-deficiency Virus; Total cholesterol; High density lipoprotein; Insulin resistance; Hyperglycemia

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I. Introduction:

The CDC classifies Human Immunodeficiency Virus (HIV) infection into 3 categories based on certain infections or diseases [1,2]. These may be HIV-exacerbated or opportunistic infections. Category A is asymptomatic HIV-infection without AIDS-defining conditions. Category B is HIV-infection with HIV-related symptoms (or a defect in T-cell-mediated immunity) or HIV-related complications. Pathophysiology defines Category C as HIV with AIDS-defining opportunistic infections. CD4+ T-cell count subdivides these 3 categories. CD4+ T-cell counts above 500/L define A1, B1, and C1. A2, B2, and C2 have 200-400 CD4+ T-cells/L. HIV infections with CD4+ T-cell counts below 200/L are A3, B3, or C3 [3,4].

A study by Shulman et al., 2014, shows that contributing factors affect biomolecule breakdown. When there's glucose in the blood, pancreatic beta cells release insulin [5,6]. Insulin-dependent tissues like skeletal muscle, adipose tissue, and liver take up glucose for further metabolism [5-7]. Hyperglycemia prevents muscles and fat from using glucose when insulin is present [8]. This is glucose toxicity. When glucose isn't properly absorbed, it activates HMG-Co-A reductase and slows Triacylglycerols (TAG) oxidation outside the liver [9]. This causes hyperglycemia and dyslipidemia.

High Density Lipoprotein-cholesterol (HDLc) takes fats and cholesterol from cells outside the liver and brings them back to the liver to be discarded or reused [10]. Lower HDL cholesterol levels are linked to a higher risk of hyperglycemia, insulin resistance, and cardiovascular disease, while higher levels are linked to better cardiovascular health. Animal studies have shown that HDLc improves insulin secretion and controls glucose levels. Experimental evidence [11,12]. These studies suggest HDLc levels may cause insulin resistance.

There has been little study on HIV affected individuals in the initial period of the disease and during the course of disease on insulin resistance, glucose, and lipids levels as a damaging factor have not been considered in existing studies in this part of India, therefore, we hypothesize that insulin resistance, glucose, and lipids levels have no effect on glucose and lipid levels in HIV-infected individuals.

II. Materials & Methods:

The Human ethics committee at the institution approved the research protocol. The HIV patients who participated in this research had detectable levels of the virus in their blood (the presence of HIV was confirmed by an ELISA that utilized two distinct antigens), but they were not receiving any form of antiretroviral therapy. Because our organization does not have the necessary resources, the HIV RNA load experiment could not be carried out. Individuals who tested positive for HIV were subjected to screening in accordance with the standards set forth by the National AIDS Control Organization and were recruited from an antiretroviral facility or ICTC that was situated within the college. Diabetes mellitus type 1 or type 2, HIV infection, pathological sequelae, and therapy with HAART were all considered to be ineligible for participation. One hundred individuals who appeared to be in good health and showed no signs of HIV infection made up the control group. In order to qualify as healthy controls for the non-HIV group, participants must not have diabetes, not take any dietary supplements, be free of any other health concerns, not smoke, and not drink alcohol. Participants with HIV are not allowed to be taking HAART. After receiving informed written consent from every individual in the study group, 5 milliliters of venous blood were collected and placed in plane vials (red top). In order to separate the serum, the blood will be centrifuged for 20 minutes at a speed of 3000 rpm. The serum was then refrigerated until it tested.

Plasma glucose was estimated by Glucose Oxidase and Peroxidase (DPEC – GOD/POD) method purchased from Avantor laboratories. Serum Insulin was estimated by using ELISA kit obtained from Invitrogen Laboratories. The HOMA-IR was calculated, as proposed by Muniyappa et al [13]. Serum total cholesterol was estimated by using the method Glycerol Phosphate Oxidase and Peroxidase (Liquid stable) and serum TAGs was estimated by using the method of Cholesterol Oxidase and Peroxidase (CHOD/POD) purchased from Avantor Performance Materials India Limited, Dehradun, Uttarakhand, India. Serum TC was estimated by using the method polyethylene glycol (PEG) and phenol and 4-aminoantipyrine (PAP). LDL-c was calculated by using Friedwald and Fredrickson's formula. Serum melatonin was estimated by using the Elisa Assay method purchased from Eagle Biosciences laboratories. Serum metallothionein were estimated with ELISA kit obtained from LSBiotech Research laboratories.

Statistical Analysis:

The most recent version of IBM SPSS would be utilized in order to carry out statistical analysis. Use the Unpaired t-test whenever you want to compare the means of the variables that are associated with two different groups. When comparing the medians of two or more groups, the authors conduct a one-way analysis of variance on their data (ANOVA). To determine the nature of the connection between two variables, we will use the Pearson correlation. The significance level of 0.05 is statistically significant.

III. Results:

Demographic details of the present study population (Table 1):

The study estimated age, BMI, systolic and diastolic pressure of the study population. Age, systolic and diastolic pressure showed no significant difference in the results when compared between the two groups, whereas BMI showed significant difference when compared between the two groups of the study.

Lipid profile details of the present study population (Figure 1):

The mean values of total cholesterol, TAG, HDL, and LDL in HIV-infected subjects and in non-HIV healthy control subjects have been estimated. The study observed significant difference in the values of serum total cholesterol on comparison between the two groups of the study. Though the LDL mean level of HIV-infected group subjects was on the higher side but when compared between the two groups, we observed approximately 30 percent high in HIV-infected subjects than the non-HIV infected healthy control. On the contrary, the present study observed lower levels of HDL in HIV-infected subjects and showed significant lower levels than non-HIV healthy control subjects.

Glycemic details of the present study population (Figure 2):

FBS ($t=11.24$; $df=198$; $P<0.001$) showed a significant difference (Table 3) when compared between the two groups of study. The mean level of serum insulin and HOMA-IR levels were not statistical difference when compared between the HIV-infected and non-HIV healthy control group subjects.

Discussion:

Factors that affect blood lipids are age, obesity, sex, weight, diet, alcohol, and hormone levels in an individual. In the present study, age and sex of HIV and control subjects were analyzed and there was no significant

difference observed. None of the study subjects used alcohol and cigarette as these were excluded. In studies, it was reported that HIV can affect anyone irrespective of age, but it is most likely to contract at any years of age [14-16]. These reports also reported that HIV disease affects both the genders.

Cholesterol in the body is transported with the help of lipoproteins. One of the lipoproteins that is high density lipoprotein which is in short form called as HDL plays a vital role. HDL carries the extra-hepatic cholesterol to the liver and mutual exchanges the cholesterol between other lipoproteins through cholesterol esterase transfer protein [16]. In diseases where the causative factor is immunity including diabetes mellitus, and HIV are bound to exhibit higher levels of serum cholesterol in body. Studies[17,18] on HIV subjects has shown increased cholesterol levels when compared to control. Another study reported an increase in the total lipids ofpsoriatic serum [19]. In another study [20]it has been shown that dyslipidemia existed in HIV subjects, but these altered levels were significantly prominent in HDL levels when compared to control. Feinglod et al., 1993 [21], demonstrated serum LDL levels of control subjects were significantly lower than the HIV patients. This present study findings also showed a significantly higher cholesterol and lower HDL levels in HIV subjects when compared to healthy control subjects of the study. However, a study [22] could find no significantdifferences in serum cholesterol levels betweenHIV-infected and normal individuals. Another study [23] likewise found no evidence for adisturbance of lipid metabolism accompanyingHIV.

Varied theories have been proposed for the higher cholesterol levels in HIV. Parra et al [24], observed altering levels of paraoxanase as the contributing causes for the increases cholesterol levels in subjects affected with HIV. Emokpae et al 2018 [25], demonstrated statistically significant increase in lipase levels which were attributed to the increased cholesterol levels in HIV patients. Grunfeld et al., 1993 [18], reported that over-expression of interferon-alpha and C-reactive protein were the cause for altered cholesterol levels in HIV individuals. Some studies [26-28] highlighted the influence of cytokines produced by the host immune system during disease release large concentrations of TNF and IL-1β responsible for chronic inflammation which is thought to be responsible for increased cholesterol levels.

But, we infer from the available data from the present study that improper transport of cholesterol to the liver from extra-hepatic tissues led to the significant increase in the levels in the subjects of HIV in the present study. Lately, studies [29,30]have demonstrated altered functioning of HDL lipoprotein in the chronic inflammatory disorders including HIV and atherosclerosis.

The physiological functions of cholesterol are it is a precursor of steroid hormones and bile acids, and also providing structure to cell membranes [16]. The total cholesterol metabolism in the body is maintained by a highly coordinated balancing cycle between ingestion, synthesis, absorption, and excretion and this balancing is maintained by certain hormones in the body [16] [Vasudevan., 2010]. Any disruption in this dynamic cycle due to age[31,32], disease [33], hormonal disorders [16, 34], and by oxidative stress would lead to the derangement in the levels of cholesterol [35]. We observed positive relation between age and cholesterol in control subjects. Similar positive relationship was observed between age and cholesterol in HIV subjects' group. At first it seems contradictory but possible explanation could be that the increase in cholesterol levels is compensatory to the increase in age [16, 31-35]. More importantly the literature reports ageing is a degenerative process in any mortal beings and ageing hastens the oxidative stress and vice versa. Therefore, the relationship observed in HIV and control subjects can be attributed to the factors reported in the studies.

IV. Conclusion:

We conclude that if this line of research is supported, studies both in vitro and in vivo will help in the discovery of mechanistic insights that can help clinicians better control hyperglycemia and prevent the onset and progression of its complications. These findings could also benefit the general public. It is possible that for HIV-infected patients, any natural compensation mechanism could become inadequate to meet the patho-physiological alterations; however, this has not been thoroughly investigated.

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Table 1: The mean values of physical parameters of HIV-infected and non-HIV control subjects of the study

Variable	HIV-infected Subjects (n=100)	N0n-HIV Controls (n=100)	P Value
Age (Years)	54.4±4.3	56.6±8.1	>0.05
BMI (kg/mt^2)	31.4±2.7	27.4±2.8	**<0.05**
Systolic Pressure (mm of Hg)	148±4.1	151.1±7.2	>0.05
Diastolic Pressure (mm of Hg)	89.2±2.9	91.9±4.2	>0.05

Figure 1: Mean Lipids values in study population

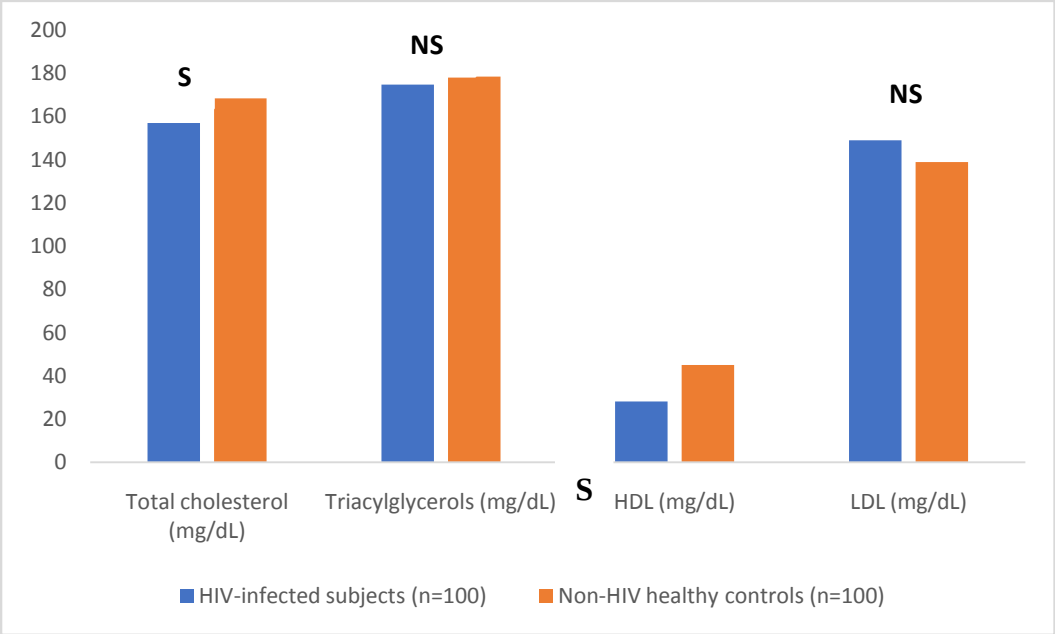
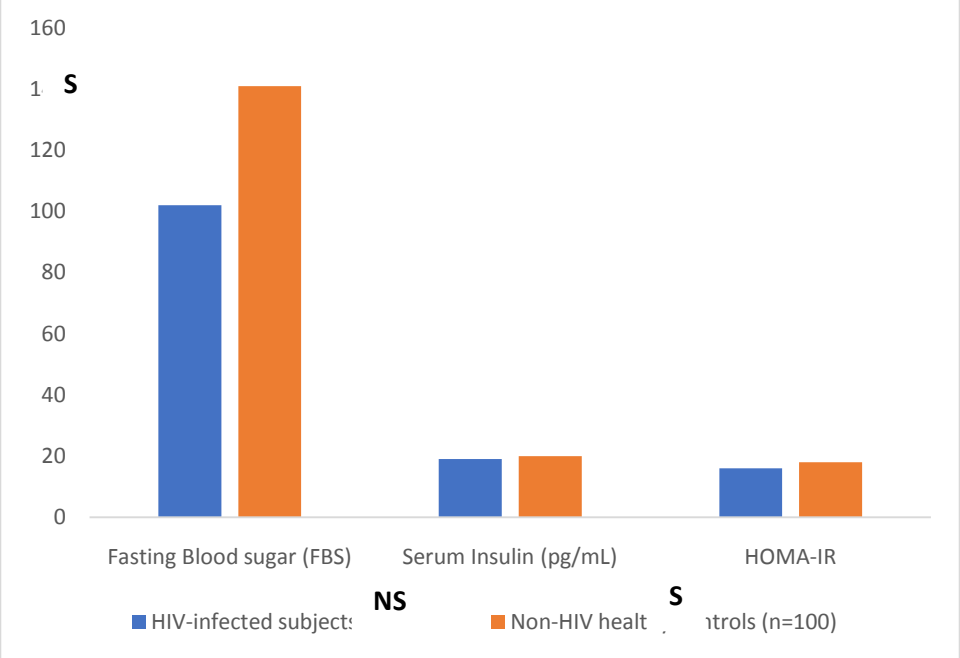


Figure 2: Mean FBS, insulin, and HOMA-IR values in study population



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