

Interrelationship of Lipid Indices in Alcoholic and Non-Alcoholic Patients

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Abstract: Alcoholism is a medical and social problem worldwide. Patients with more advanced alcohol related problems may meet the criteria for alcohol dependence or abuse. Consumption of alcohol in large amounts for a long duration produces toxic effects on liver, thus impairing the lipid metabolism, and hence alteration of serum lipid profile is seen. Aim: The aim of the study is to compare the serum lipid profile and lipid indices among alcoholic patients (study group) and non-alcoholic patients (control group). Materials and methods: This is an age matched comparative study. The study population includes 50, self-reported, chronic, regular and excess alcohol drinking persons; and the control group includes 50 persons who did not consume alcohol. Fasting serum lipid profile was estimated and lipid indices were calculated. Result and observation: Mean and Standard deviation of lipid parameters and lipid indices show a significant p-value (TC/HDL ratio <0.03 and LDL/HDL ratio <0.001) when compared between alcoholic patients and non-alcoholic patients. **Conclusion:** Alcohol causes alteration in various parameters of lipid metabolism including those which predispose to atherosclerotic arterial diseases.

Keywords: VLDL-very low density lipoprotein, LPL-Lipoprotein lipase, TG's-Triglycerides, NADH-Nicotinamide Adenine Dinucleotide phosphate. CHD-Coronary heart disease

1. Introduction

Alcohol is a drug and may be classified as a sedative, Tranquillizer, Hypnotic or anesthetic depending upon the quantity consumed¹. It has diverse effects over the body and impacts directly or indirectly on almost every neurochemical system in the brain. Over the past 30 – 40 years alcohol consumption has increased in quantity and frequency. Specific criteria for diagnosing alcohol abuse have been developed by the American psychiatric association. Alcohol dependence syndrome is characterized by drink orientated behavior, tolerance to the cerebral effects of alcohol, continued drinking despite harm and withdrawal symptoms and awareness of a compulsion to drink excessively². Excess alcohol consumption may be considered as regular alcohol intake at levels at which there is a high risk of harm particularly from organ injury. Worldwide an estimated 2 – 3 million people die from alcohol related causes. A national survey found that the about 31.9% of men and 2.2% of women drink alcohol and about 9.9% of men drink alcohol everyday in India. The overall prevalence in our state is about 40% and these surveys had been taken during 2005-06³. High alcohol intake defined as 75g or more per day becomes an independent risk factor for CHD⁴. Low doses of alcohol (one or two drinks per day) may have potential beneficial effects over the high density lipoprotein and aggregation of platelets with a decrease in risk for occlusive coronary artery disease and embolic stroke⁵. Chronic heavy drinkers have a six fold increased risk for coronary heart disease partly related to increase in low density lipoprotein and cardiomyopathy due to the direct effect of alcohol over the cardiac muscle.

Factors that enhance both the synthesis of triacylglycerol and the secretion of VLDL by the liver include ingestion of ethanol⁶. Oxidation of ethanol by alcohol dehydrogenase leads to excess production of NADH. In chronic alcoholism, the fat accumulation in the liver is

caused by a combination of impaired fatty acid oxidation and increased lipogenesis, which is thought to be due to changes in the $[NADH]/[NAD^+]$ redox potential in the liver, which also interferes with the action of transcription factors regulating the expression of the enzymes involved in the pathways. Thus promoting hepatic triglycerides synthesis and VLDL secretion.

The NADH generated competes with reducing equivalents from other substrates, including fatty acids, for the respiratory chain, inhibiting their oxidation and causing increased esterification of fatty acids to form triacylglycerol, resulting in the fatty liver. This increased concentration of NADH also inhibits gluconeogenesis and lactate accumulates leading to hypoglycemia and lactic aciduria⁷.

Since the cytochrome P450 dependent microsomal ethanol oxidizing system for ethanol metabolism uses oxygen, free radicals are generated that damage the tissues in chronic alcoholism. Because the system consumes NADPH the antioxidant glutathione cannot be regenerated which exacerbates the oxidative stress, causing chronic endothelial injury with increased permeability and accumulation of lipoproteins in the intima of the vessel wall^{8, 9}. Oxidative modification of these accumulated plasma lipoproteins (LDL) associated with proteoglycans occur within the intima of the arteries, forming fatty streak¹⁰ and converting them to foam cells, thus enhancing the atherosclerotic processes^{11, 12}. Ethanol also inhibits the metabolism of some drugs, e.g., barbiturates, by competing for cytochrome P450-dependent enzymes.

After the secretion of VLDL by the liver into the plasma, TG's of VLDL are hydrolyzed by LPL and triglyceride depleted VLDL forms Intermediate Density Lipoprotein which is further remodeled by Hepatic Lipase to Low Density Lipoprotein¹³. The ratio of TG/HDL-C has been proposed to be an easily obtainable atherogenic

marker¹⁴. The total cholesterol /high-density lipoprotein (HDL) cholesterol ratio, known as the atherogenic or Castelli index and the LDL/HDL cholesterol ratio are two important components and indicators of vascular risk, the predictive value of which is greater than the isolated parameters¹⁵ in assessing the cardiovascular risk, insulin resistance and metabolic syndrome¹⁶.

2. Aim and Objective

Aim of the study is to estimate the fasting serum lipid profile and objective is to compare the lipid parameters and indices in alcoholic and nonalcoholic patients.

3. Materials and Methods

This is an age matched comparative study conducted after getting the approval from the ethical committee of Government Stanley Medical College. The study population includes 50, self-reported, chronic, regular and excess alcohol drinking persons; (using AUDIT; Alcohol Use Disorder Identification Test Questionnaire)¹⁷ and the control group includes 50 persons who did not consume alcohol and they were selected from the outpatient department of the Government Stanley medical college.

Inclusion criteria:

Patient's with Chronic, excess and regular intake of alcohol.

Exclusion criteria:

1. Persons with liver disease
2. Patients taking drugs like Phenytoin, Fibrates, Barbiturates, Rifampicin and.
3. Patients who were not willing to give informed consent, however, were excluded from the study.

Sample collection and Analysis:

12-14 hours fasting sample was collected from all subjects during their hospital visit and analysis of total cholesterol, triacylglycerol, Low density lipoprotein and high density lipoprotein were done. Very low density lipoprotein values and lipid indices were calculated. All analytes were analyzed by ERBA Transasiakit method using fully automated Beckman coulter auto analyzer.

Data collected during study was interpreted and analyzed statistically using biomedical software SPSS for Windows

20.0 statistical package program, and the analysis was done using Student's *t*-test and Pearson's correlation.

RESULTS AND STATISTICAL ANALYSIS:

The total number of subjects included for the study was 100. Out of this 100 -50, were self-reported, chronic, regular and excess alcohol drinking persons, (using AUDIT - Alcohol Use Disorder Identification Test Questionnaire) and the control group includes 50 persons who did not consume alcohol.

The students 't' tests were used to find out the test of significance (p value) of both cases and controls along with mean and standard deviation.

Age Distribution among the Study and Control Group:

Male patients in the age group of 30 years to 60 years were taken in the study. Both the study and control group were age matched.

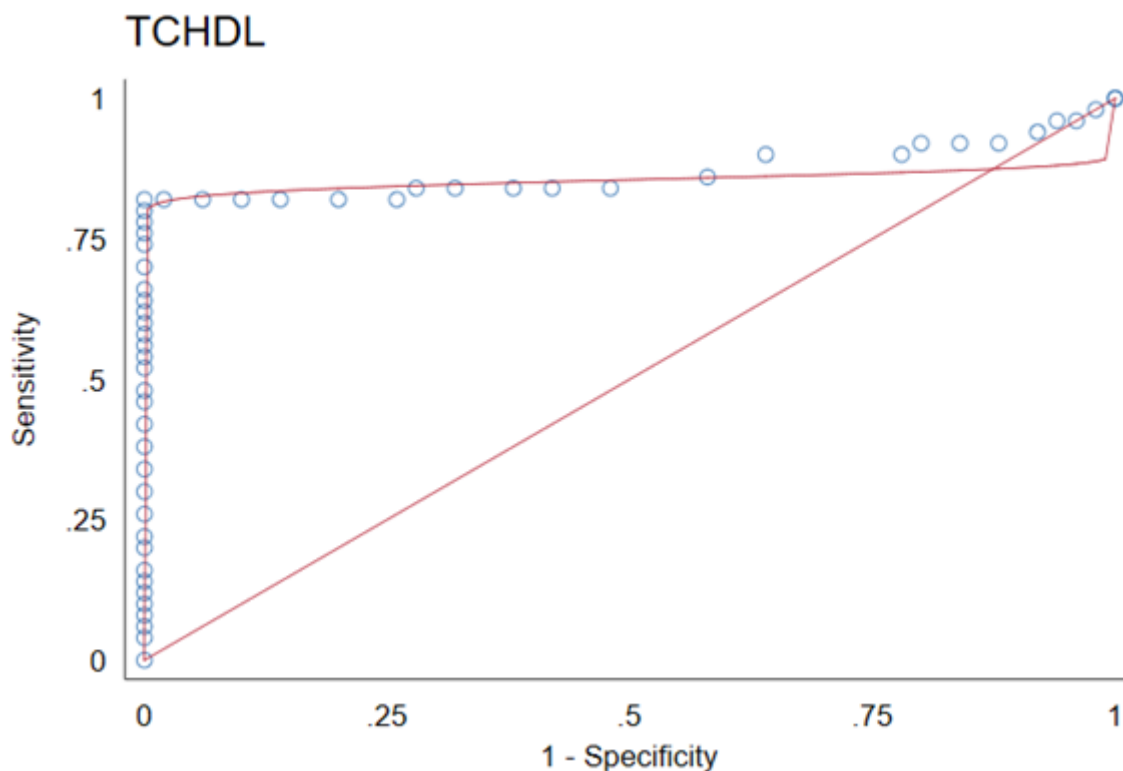
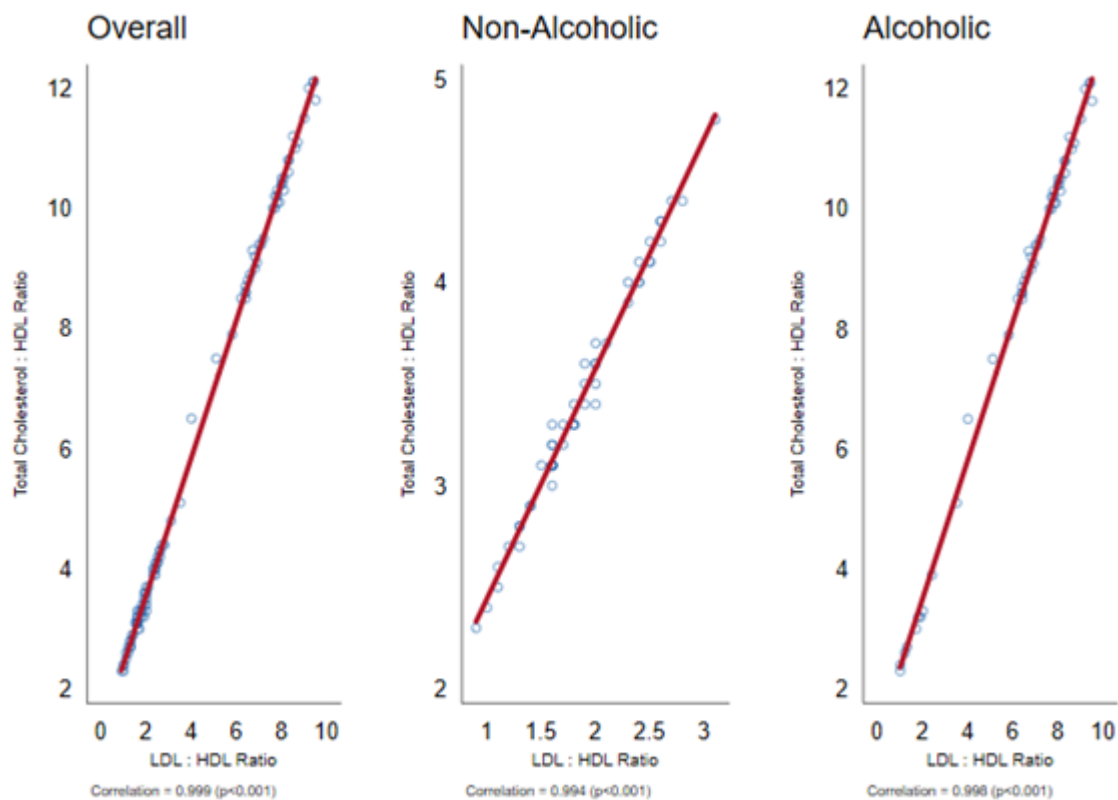
The mean age of the control group is 47.52 and the mean age of the study group is 47.58

| Group | N | Minimum age | Maximum age | Mean | Standard Deviation | Student independent 't' test |
|---------|----|-------------|-------------|-------|--------------------|------------------------------|
| Control | 50 | 34 | 59 | 47.52 | 6.7 | P=0.95 |
| Study | 50 | 33 | 59 | 47.58 | 7.4 | Not Significant |

Table: Comparison between Alcoholic and non-alcoholic

| Factors | Non-Alcoholic Mean/SD | Alcoholic Mean/SD | p-value |
|----------------|-----------------------|-------------------|---------|
| Age | 47.52 (6.7) | 47.58 (7.4) | >0.95 |
| Cholesterol | 160.7 (15.7) | 236.9 (39.2) | <0.06 |
| TGL | 130.9 (8.4) | 164.2 (29.1) | <0.02 |
| HDL | 47.7 (6.5) | 31.9 (13.0) | <0.03 |
| VLDL | 26.2 (1.7) | 32.8 (5.8) | <0.01 |
| LDL | 86.8 (16.3) | 172.1 (45.3) | <0.04 |
| TC : HDL | 3.4 (0.6) | 8.5 (3.0) | <0.03 |
| LDL : HDL | 1.9 (0.5) | 6.4 (2.6) | <0.001 |
| Log (TG : HDL) | 0.5 (0.1) | 0.7 (0.2) | <0.01 |

Values are given as mean (sd); Independent t test was used at 5% level of significance



Receiver operating characteristic curve

| Factors | Cut Off | Sensitivity | Specificity | AUC |
|----------------|-----------------|-------------|-------------|-----------------------|
| TC : HDL | 5.0 (4.1 - 5.8) | 83.0 | 100.0 | 0.868 (0.783 - 0.953) |
| LDL : HDL | 3.3 (2.6 - 4.0) | 82.0 | 99.0 | 0.885 (0.807 - 0.962) |
| Log (TG : HDL) | 0.7 (0.7 - 0.8) | 82.0 | 100.0 | 0.815 (0.709 - 0.921) |

4. Discussion

The present study establishes the characterization of the various lipid parameters and the calculated lipid indices in alcoholic and nonalcoholic patients.

The AUDIT focuses on social and behavioral aspect of alcohol problem and provides greater accuracy than do frequency questions, lab test or clinical detection. More than 8 point: Positive for an alcohol use-disorder for both men and women¹⁷.

The mean and standard deviation of total cholesterol in control and study group are 160.7 and 15.7, 236.9 and 39.2 respectively with a p-value of 0.06 which is not significant. But the mean and standard deviation of VLDL (26.2, 1.7 & 328, 5.8) and Triglycerides (130.9, 8.4 & 164.2, 29.1) shows a significant p-value of 0.01 and 0.02 which is consistent with the study of Mithileshwer Raut, et al¹⁸.

In alcoholics fatty acids are reesterified with glycerol to form triglycerides and these triglycerides are offloaded by the liver by producing lipoprotein complexes and exported as VLDL into circulation leading to the increase in concentration of TGL and VLDL¹⁹.

The Mean and standard deviation of LDL cholesterol in study and control groups are 172.1, 45.3 and 86.8, 16.3 respectively. Hydrolysis of VLDL by lipoprotein lipase (LPL) in circulation, leads to the formation of VLDL remnants. These remnants are taken by the liver through E receptors and hepatic lipase hydrolysis removes the remaining TGs and converts it into smaller IDL particles and then to LDL. Thus each LDL is derived from a single precursor VLDL particle²⁰.

It is proposed that LDL particles are taken up into the intima where they become chemically oxidized to act as toxic pro-inflammatory, pro-atherogenic and chemotactic factors. This is supported by the fact that anti-oxidant drugs can inhibit atherogenesis²¹. The development of atherosclerosis is strongly associated with the concentration of circulating LDL particle²². The Mean and standard deviation of HDL cholesterol in study and control groups are 31.9, 13.0 and 47.7, 6.5 respectively. Alcohol consumption reduces the concentration and activity of cholesterol ester transfer protein which is responsible for the transfer of VLDL triglycerides with the HDL cholesterol esters resulting in an obligatory increase in HDL in moderate alcohol consumption²³ but chronic heavy alcohol consumption results in decreased levels of HDL increasing the likelihood of Coronary Heart Diseases²⁴.

The mean and standard deviation of TC:HDL and LDL:HDL in the study group are 8.5, 3.0 and 6.4, 2.6 over the control group and gives a significant P-value of 0.03 and 0.001 and a sensitivity of 83.0 and 82.0 respectively which is in close association with the study of Ichiro Wakabayashi.²⁵ The mean and standard deviation of log TG:HDL in the study group is 0.7 and 0.2 which shows a significant P-value of 0.01 and sensitivity of 82.0

becomes a good predictor of cardiovascular diseases.²⁵ These ratios also help to identify insulin resistance and all atherosclerotic complications especially the atherogenic index of plasma (log TG: HDL) which reflects the true relationship between protective and atherogenic lipoprotein and is associated with the size of pre- and anti- atherogenic lipoprotein particle²⁶.

5. Conclusion

In conclusion, this study has demonstrated definitive lipid profile changes in patients of chronic alcoholism. Alcohol screening is recommended as a component of routine preventive care for several reasons. The combined prevalence of at-risk drinking, alcohol abuse and alcohol dependence approaches 20% in any practice setting. Early identification and management of such drinking can avert more serious and irreversible health and social consequences. According to the epidemiological transition of disease, life style change, performing regular exercise and healthy diet modification is recommended.

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