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Original Research Article

A Case Control Study on the Evaluation of Lipid Profiles as Markers of Depressive Disorders

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ABSTRACT

Objective: To evaluate the lipid profiles as markers of depression.
Methods: A total of 65 depressive patients and 65 healthy control subjects were recruited from the department of Psychiatry of a tertiary care hospital. We measured serum total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein cholesterol and triglyceride levels of both patient and control group.
Results: The serum TC, TG, LDL and VLDL cholesterol levels were found to be significantly lower in case group than that of control group. However, HDL was found to be significantly higher in cases than controls. HDL had high sensitivity as a marker of depression.
Conclusion: The results of this study suggest that the lipid levels could serve as biological markers to distinguish between clinical depressive disorders, however, studies on larger sample size are required for robust conclusion.

Key words: Lipid levels, Depression, Markers.

INTRODUCTION

Major depressive disorder (MDD) is a prevalent, heterogeneous illness characterized by depressed mood, anhedonia, and altered cognitive function. The lifetime prevalence of MDD is approximately 17% of the population and results in tremendous secondary costs to society. [1] Diagnosis and treatment of MDD is based on relatively subjective assessments of diverse symptoms representing multiple end phenotypes. To date, the biological bases for the heterogeneity of MDD remain poorly defined. Toward this goal, identification of biological markers could improve the diagnosis and classification of MDD subtypes, as well as stratify patients into more homogeneous, clinically distinct subpopulations. [2] Despite decades of searching, a non-invasive, quantitative clinical test to aid in the diagnosis and treatment of MDD remains elusive. [3]

Cholesterol is a core component of the central nervous system (CNS), essential for the cell membrane stability and the correct functioning of the neurotransmission. [4] It is known that cholesterol affects the fluidity of cell membranes, membrane permeability, exchange processes, and may influence serotonergic function, therefore, if there is cholesterol depletion, it may impair function of 5-HT1A and 5-HT7 receptors and serotonin receptor activity. Over time, lower cholesterol levels may further decrease expression of serotonin receptors and cause

a reduction serotonergic activity. [5] Many psychiatric diseases can occur due to such reductions and alterations

Certain psychiatric symptoms have been shown to be associated with low cholesterol; these include anxiety, depression, euphoria, irritability, aggression, and suicidal ideation. Shrivastava et al showed a link between cholesterol and mood disorders. [5] However, in the recent years, involvement of serum cholesterol in pathogenesis of psychiatric disorders has been doubted by few authors on the basis of their studies that have not found any correlation between serum cholesterol and psychiatric disorders (John et al, 2014). [4]

Therefore, the present study was planned to evaluate the lipid profiles as markers of depression.

MATERIAL AND METHODS

This was a case-control study conducted in the Department of Psychiatric and Biochemistry, MLB Medical College, Jhansi, UP. The study was approved by the Ethical Committee of the College. The consent from each participant was taken before including in the study. The study consisted of 65 patients with depressive disorders and 65 healthy controls without being any medical or psychiatric diagnosis.

Patients attending the out-patient department of hospital were randomly contacted personally. All the subjects and controls underwent estimation of their serum cholesterol, LDL and HDL cholesterol, serum TG levels. A fasting blood sample was taken in plain tube without anticoagulant for measurement of TC, HDL and TG by standard enzymatic method. The samples were stored at −70°C until analysis. Serum cholesterol was estimated by cholesterol oxidase method, TG by enzymatic hydrolysis and HDL cholesterol by phosphotungstate-magnesium chloride precipitation method. LDL cholesterol was calculated using Friedwald formula, i.e., LDL cholesterol = Serum TC − (TG/5 − HDL cholesterol). Depression was assessed through HRSD. It was originally published in 1960 by Max Hamilton and is presently one of the most commonly used scales for rating depression in medical research. It is a 21-question multiple choice questionnaire rated on 0-4 Likert scale used to rate the severity of depression (Hamilton, 1960). [6]

RESULTS

Demographic parameters

The mean age in case group was 49.65±7.03 years while it was 49.28±9.09 years for the control group. Males constituted 66.2% of the sample cases and 58.5% in control group. There was no difference in age and sex distribution between study group and control group. The mean BMI of cases was 29.32±3.23 kg/m^2, while it was 25.57±5.87 kg/m^2 in control group. The difference in BMI between two groups was significant (P = 0.0001) (Table-1).

Table-1: Demographic profile of cases and controls

	Cases (n=65)	Controls (n=65)	p-value
Age in years, mean±SD	49.65±7.03	49.28±9.09	0.79[a]
Gender, no. (%)			
Male	43 (66.2)	38 (58.5)	0.36 [b]
Female	22 (33.8)	27 (41.5)	
BMI, mean±SD	29.32±3.23	25.57±5.87	0.0001* [a]

[a]Unpaired t-test, [b]Chi-square test, *Significant

Lipid profile

The mean cholesterol of case group was 159.57±50.53 mg/dl while it was 180.56±35.36 mg/dl for control group. The mean triglyceride case group was 167.48±77.89 mg/dl while it was 198.83±58.07 mg/dl for control group. The HDL was observed to be significantly (p=0.002) higher in cases (49.32±14.15) compared to controls (42.48±10.49). The LDL (p=0.01) and VLDL (p=0.005) were found to be significantly lower in cases than controls (Table-2).

Clinical parameters of patients

The duration of illness in cases ranged from 15 days to 3 years with a mean of 6.34±2.24 months. The minimum HRSD score was 11 and the maximum score was 26 with a mean of 21.56±4.15. In the case group, there were 20 cases of mild

depression, 34 of moderate and 11 patients of severe depression (Table not shown).

Table-2: Lipid levels in cases and controls

	Cases (n=65)	Controls (n=65)	p-value[1]
Total cholesterol (mg/dl)	159.57±50.53	180.56±35.36	0.007*
Triglyceride (mg/dl)	167.48±77.89	198.83±58.07	0.01*
HDL (mg/dl)	49.32±14.15	42.48±10.49	0.002*
LDL (mg/dl)	76.75±46.73	98.30±39.07	0.005*
VLDL (mg/dl)	33.49±15.57	39.76±11.61	0.01*

[1]Unpaired t-test, values are in mean±SD, *Significant

Table-3: Sensitivity and specificity of lipid profile in the diagnosis of depression

	Cut off value	Sensitivity	Specificity	AUC (95%CI)	p-value
Total cholesterol (mg/dl)	<150.50	36.9	24.1	0.34 (0.25-0.44)	0.002*
Triglyceride (mg/dl)	<161.00	55.4	66.0	0.28 (0.19-0.37)	0.001*
HDL (mg/dl)	<45.50	80.0	5.0	0.64 (0.54-0.73)	0.006*
LDL (mg/dl)	<70.50	55.4	25.0	0.33 (0.24-0.42)	0.001*
VLDL (mg/dl)	<30.20	41.5	16.0	0.28 (0.19-0.37)	0.001*

AUC-Area under the curve, CI-Confidence interval, *Significant

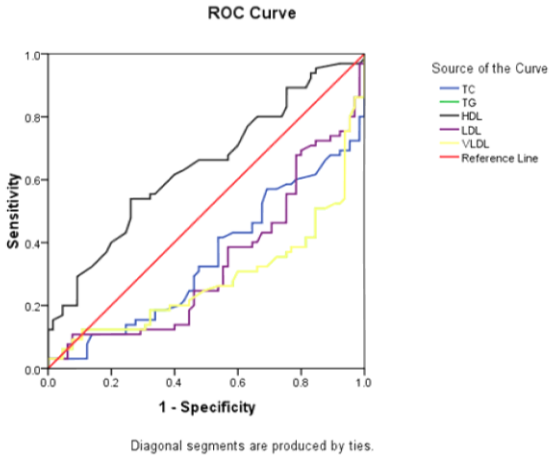

Fig.1: Receiving operating curve (ROC) showing sensitivity and specificity of lipid profile in diagnosing depression

Sensitivity and specificity of lipid profile

The ROC analysis revealed that only HDL had high sensitivity but low specificity in diagnosing the depression. The AUC was found to be significant ($p<0.01$) for all the lipid levels (Table-3 & Fig.1).

DISCUSSION

The cholesterol-serotonin hypothesis was initially proposed to explain the link between low cholesterol levels and depression. This hypothesis states that reduction of serum TC may decrease brain cell membrane cholesterol and thereby lowering micro viscosity of the cell membrane and subsequently decreasing the exposure of protein serotonin receptor on the membrane surface resulting in poorer uptake of serotonin from blood and less serotonin into brain cells leading to depression. Maes *et al* did not find any significant differences in total or free cholesterol concentrations between depressive patients, their relatives and normal controls. [7] However, Papakostas *et al* have proposed that both elevated and low cholesterol levels may be associated with serotonergic dysfunction. [8]

Phospholipids are important in myelin sheath formation, activity of neuronal membrane. Steegmans et al showed that cholesterol depletion correlates with decrease in serotonergic neural activity in CNS. [9] Few studies suggest low cholesterol level, for prevention of myocardial infarction is associated with increased mortality from suicide, accidents and violence. [10] In the present study, patients with depressive disorder had significantly lower serum cholesterol, triglyceride, and LDL and VLDL levels compared to normal controls. This is consistent with Hamidreza et al study, where they found significantly lower mean cholesterol in MDD patients compared to control subjects. [11] The results of Mehmet et al (2004) were similar to with this study, where serum cholesterol and TG levels were significantly lower in patients of co-morbid panic disorder and MDP. [12] We found that HDL cholesterol was significantly high and this finding is inconsistent with Myriam et al. [13]

Lehto *et al* showed that major depressive disorder (MDD) subjects with a long symptom duration (≥3 years) had lower levels of HDL-C compared with healthy

controls or MDD subjects with a symptom duration <3 years. [14] A study by Zhang *et al* had found a lower HDL cholesterol level to be significantly correlated with suicidal attempts. [15] One study showed that the dissimilarities in HDL cholesterol level between current MDD versus remitted MDD and controls lost statistical significance when adjusted for possible confounding factors especially BMI. [16]

Lehto *et al* found that the study population had a long history of 7-year of depressive symptoms, which is much more than that of the present study, which had only a brief duration of depressive illness (mean =5.34 months). [14] In this study, the minimum HRSD score was 11 and the maximum score was 26 with a mean of 21.56±4.15.

One of the drawbacks of this study is small sample size. Also, we did not consider differences in dietary and smoking habits and alcohol consumption of patients. It will be necessary to include larger subject samples in the further studies.

CONCLUSION

The results of this study suggest that the lipid levels could serve as biological markers to distinguish between clinical depressive disorders, however, studies on larger sample size are required for robust conclusion.

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