ORIGINAL ARTICLE

Investigation on Lipid Profile in Affective Disorder at a Hospital Clinic in Kolkata, West Bengal, India

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Abstract

Aim: Prior research has shown that particular types of mental states contribute to one's risk for depression, and that abnormal blood lipid levels can be associated with the manifestation of mood dysfunction. The role of lipid metabolism in the pathophysiology of depressive behavior has received particular attention recently. As depressive disorders vary in regard to etiology and diagnostic marker, the present study aimed to explore any lipid-profile disparity among the sample of depressive patient groups visiting a clinic for treatment.

Materials and methods: The study group consisted of 80 patients diagnosed with three types of depressive disorders—endogenous, reactive, and dysthymic types. Groups were tried to match according to age, gender, and education.

Results: The demographical difference between marital status and economic status revealed among patients. The present study reveals the difference among serum lipid levels among groups in regard to LDL cholesterol (lipoproteins of low-density). Further after adjusting the confounding factors such as age and BMI, the ratio of HDL (lipoproteins of high-density)/cholesterol and also the ratio of LDL/HDL were found to be significantly different among the groups.

Conclusion: The present study shows the difference in lipid profile such as LDL cholesterol, HDL/cholesterol, and HDL/LDL ratios among psychogenic, reactive, and dysthymic groups. The psychogenic group reflects lower LDL and lower LDL/cholesterol, HDL/cholesterol ratios while compared to others.

Clinical significance: This study highlights how the lipid profile can act as a biological marker in distinguishing depression subgroups and assessing associated cardiovascular risks.

Keywords: Cholesterol, Depression, High-density lipoprotein, Lipid profile, Low-density lipoproteins.

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Introduction

The role of lipid status in patients with affective disturbance as depressive disorders has been investigated for the last few years. While various genetic, environmental, and social factors are found to have influences in the pathophysiology of depression, the search for biological precursors continued.[1] Most of the essential human physiological molecules that are related to affect human mood status (such as the neurotransmitters serotonin or dopamine, vitamin D, and steroid and sex hormones, including DHEA, testosterone, and estrogen) are directly or indirectly linked to the available quantity of cholesterol molecule. Some studies indicate that suppression or availability of serotonin (a neurotransmitter that modulates brain functioning, resulting in behavior changes) is somehow being connected to a low serum-cholesterol level.[2]

Some studies indicated a significant relationship between mood disorder and serum cholesterol levels. A lower level of cholesterol has been found to be mostly related to the prevalence of depressive disorders. Other findings reflect a close relationship between lipid profile components such as triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-cholesterol), and low-density lipoprotein cholesterol (LDL-cholesterol),[3] with various psychiatric disorders such as depression, bipolar disorder, anxiety disorders, aggressive and impulse control disorder, post-traumatic stress disorder (PTSD), and even schizophrenia.[4–6] A number of findings referred to a low cholesterol level being associated with deliberate self-harming attempts and suicide.[6]

The question as to whether an agressive treatment to lower serum cholesterol level in patients with cardiac risks may develop other conditions such as depression, increased violent behavior, suicide, bipolar disorder, anxiety, and Parkinson's disease still remains unanswered. Sometimes, in general practice, lowering of blood cholesterol may be considered, keeping in mind other psychological risks.[5,6]

While functions of cholesterol in the human body have been evaluated, cholesterol remains as one of the main constituents of central nervous system participating in various functioning as being in neuronal membrane and having a role in the process of neurotransmission and in the second messenger system in the brain.[7] Additionally, some investigations have indicated that neuronal dysfunction due to changes in microviscosity of the cellular membrane or disorders in signal transduction cause vulnerability to depression.[8,10] While many studies showed the relationship between serum cholesterol level and affective state of the human mind, not all authors agreed with this observation. Low serum cholesterol levels have been observed by researchers

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in patients with low-mood symptoms,[7–10] and a correlation among cholesterol levels in serum and with symptoms of self-harming and suicide in a group of psychiatric patients.[8]

In an attempt to investigate the components of lipid profile other than cholesterol in psychiatric patients, the role of triglyceride, LDL, and HDL cholesterols have been examined.[10] Comparing with a healthy control group, depressive patients showed a significantly lower concentration of serum cholesterol, HDL-cholesterol, and cholesterol/HDL-cholesterol ratio.[11] Some authors have found difference between groups of depression (as in patients with melancholic symptoms and atypical depression symptoms) in regard to levels of triglycerides, very-low-density lipoprotein cholesterol (VLDL-cholesterol), and HDL-cholesterol.[10] Some contradictory findings reflect no difference in levels of triglycerides in depressive patients and control group but found a significantly lower LDL-cholesterol level in depressive patients than in the control group.[12]

The depressive disorder has several subtypes (Diagnostic and Statistical Manual, DSM-5) and although a number of studies have been conducted in establishing relationships among serum cholesterol levels and low mood symptoms, very few studies investigated variation in serum cholesterol levels and types of depressive disorders. Among group-wise studies, some detected no significant differences in serum lipid levels of patients with types of depressive disorder such as melancholic and non-melancholic depression,[11,13] or in patients with psychogenic and atypical depression.[14] In contrast in another study (including psychogenic and atypical depression groups), Huang et al. indicated a significant difference in the concentrations of triglycerides, VLDL-cholesterol, and HDL-cholesterol.[10]

No confirmatory finding in case of a lipid profile of depressive patients of the eastern part of India has yet been established. While treating patients with depressive symptoms, three diagnostically different types (psychogenic, reactive, and dysthymic types) are often encountered in Kolkata hospital clinic outdoors. Thus, the present study aims to investigate whether there is any difference in regard to serum lipids (cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol) and lipid fraction ratios (cholesterol/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol) in three types of depressive disorder—namely psychogenic, reactive, and dysthymic groups.[3]

Materials and Methods

Subjects

Totally, 80 subjects (males: 32; females: 48) with detected depressive disorders who came for treatment at a hospital clinic in Kolkata, West Bengal during the period of April 2015 to March 2017 have been included in the present study. The demographics indicated that sample mean age ± SD was = 46 ± 10 years and the disease onset was (mean ± SD) was 40 ± 11 years, while disease duration (mean ± SD) was 8 ± 5 years. The detected mean body mass index (BMI) (mean ± SD) was 24.60 ± 5.49 kg/m^2. The socio-demographic features of the patients were duly summarized and presented in Table 1.

Besides the inclusion criteria for depressive disorders such as DSM-5, the exclusion remained for psychiatric addictive symptoms (substance abuse disorders—alcohol, cannabis, and other types) and other comorbid psychiatric symptoms/disease (such as bipolar affective types, psychotic manifestations, obsessive–compulsive features, and neurocognitive disorders). Additionally, medical problems such as cardiovascular diseases, hypertension, thyroid disorders, diabetes mellitus, lipoprotein metabolism disorders, organic brain syndrome, and nutrition disorders are excluded. As the patients came for treatment to the clinic, some pharmaceutical interventions had been offered. Antidepressants in SSRI groups (such as sertraline, fluoxetine, fluvoxamine, paroxetine) or in TCA group (such as clomipramine) are used for necessary remission of symptoms. Among other drugs, anxiolytics of benzodiazepine group (such as clonazepam, alprazolam, oxazepam) and diazepam are used for controlling low-mood-related symptoms. Those drugs have no detectable altering effect on serum lipid-level concentrations.[15]

Since dietary habits and physical activity may affect test results, all tests were conducted during the same treatment time and at the same time of the day as far as practically possible. The instruction was given to maintain a uniform diet and a uniform level of physical activity for 48 hours during testing in all subjects. All subjects signed their written consent for participation in the study, and the study was approved by a competent ethical committee.[3]

Psychiatric Assessment for Diagnosis

Inclusion criteria established according to the diagnosis of depressive disorders of the Diagnostic and Statistical Manual for Mental Disorders, 5th revision (DSM-5),[16] Hamilton rating scale for depression (HAMD-17)[17] had been used for diagnostic purposes. Subtypes of depression (psychogenic, reactive, and dysthymia) was assessed using a structured clinical interview (by trained clinical psychologist/psychiatrist) and diagnostic questionnaire based on the DSM-5 criteria.[16,18] Subjects were divided into groups based on diagnostic categories and double-checked by clinicians for grouping purposes, as showing psychogenic characteristics, or reactive characteristics, or with dysthymic symptoms.

Biochemical Measures

Subjects were asked to fast for 12 hours before the venipuncture procedure was carried out by certified technicians. Venous blood samples were collected and within 30 minutes of blood collection, the samples were centrifuged at 2,000*g* for 15 minutes at 4°C after adding EDTA and sent for preservation at the laboratory. Cholesterol oxidase method was used for HDL cholesterol estimation. Triglyceride concentrations were measured using a glycerol-blanked enzymatic method. The total cholesterol, HDL cholesterol, and triglycerides laboratory coefficient of variations (CVs) were 1.6%, 2.9%, and 4.0%, respectively. The Friedewald formula is used for calculation of LDL cholesterol. The ratio of two indices (total/HDL cholesterol ratio and LDL/HDL cholesterol ratio) was also calculated for the purpose of this study.

The height and weight of each patient, who was barefoot and in light clothes, were measured in a standing position on a medical scale that measures height and weight. Body mass index (BMI) was calculated by dividing kilograms by squared height in meters.[3]

Statistical Analysis

For collection and storing of data, MS Access 2000 database has been used. For running statistics, SPSS statistical program (SPSS for Windows 16.2, SPSS, Chicago, IL, USA) was used for needed analysis. One-way analysis of variance (ANOVA) was used to test differences in the serum lipid level between three depressive groups. While for assessing differences between individual groups, a *post hoc* analysis is used; covariance analysis (ANCOVA) was applied to control the effect of age and body mass index on investigated

Table 1: Sociodemographic features of the study group patients

Variables	*N*	*%*	X^2	*p*
Gender				
Men	32	39.5	3.37	0.66
Women	48	60.5		
Qualification				
Primary school education	17	21.1	30.73	<0.001
Secondary school education	49	63.2		
University degree	14	15.8		
Marital status				
Married	54	68.4	10.32	0.001
Single	26	31.6		
Employment status				
Employed	30	36.8	0.74	0.692
Unemployed	24	28.9		
Pensioners	26	34.2		
Residence				
Village	20	27.3	13.64	<0.001
Town	60	72.7		
Economic status				
Low	25	32.4	0.11	0.947
Middle-class	30	35.1		
High	25	32.4		

Table 2: Serum lipids (mean ± SD) in patients with three types of depressive disorders

	Type of depressive disorder				
	Reactive	*Psychogenic*	*Disthymic*	*F**	*p*
Triglyceides (mmol/L)	1.90 ± 1.41	1.43 ± 0.40	1.80 ± 0.45	1.62	0.153
Cholesterol (mmol/L)	6.03 ± 0.86	5.92 ± 1.33	5.42 ± 0.61	2.87	0.086
HDL-cholesterol (mmol/L)	2.11 ± 0.43	2.04 ± 0.42	1.68 ± 0.39	0.24	0.689
LDL-cholesterol (mmol/L)	4.82 ± 0.89	5.11 ± 0.71	3.24 ± 0.51	5.13	0.014
VLDL-cholesterol (mmol/L)	0.28 ± 0.35	0.29 ± 0.20	0.38 ± 0.11	2.19	0.162
Cholesterol/HDL-cholesterol ratio	5.12 ± 1.84	4.21 ± 0.45	3.48 ± 1.12	0.89	0.481
LDL-cholesterol/HDL-cholesterol ratio	3.31 ± 0.88	3.52 ± 1.20	3.11 ± 1.10	1.73	0.341

*One-way ANOVA

parameters. Normality and stem leaf for descriptive statistics checked for the data as far practicable and to assess differences in sociodemographic data. Some nonparametric analysis for sample distribution was tested by Kolmogorov–Smirnov test. For the present analysis, a $p < 0.05$ probability level was considered statistically significant.

Results

Serum lipid concentrations in relation to the type of depression have been indicated in Table 2. Analysis of the results shows that the psychogenic depression group reflects a significantly lower LDL-cholesterol level when compared with the dysthymic group (F (2.63) = 5.14, p = 0.014, ANOVA; p = 0.010, *post hoc* test). This trend continued when adjustments for age and BMI were made (ANCOVA F (2.61) = 8.46; p = 0.011, ANCOVA). A comparison among three groups in regard to other lipid estimates indicated no significant difference using a one-way analysis of variance. Thus, the serum level of triglycerides, cholesterol, and cholesterol/HDL ratio and LDL-cholesterol/HDL-cholesterol ratio in patients with psychogenic and reactive depression and dysthymia are in the same range. The serum lipid concentration ratios in depressive groups have been summarized and presented in Table 2.

As age and BMI could be confounding factors, an analysis controlling those was worth testing. While those adjustments were done for age and BMI statistically, certain explicit variations were indicated. However, after age and BMI adjustments, a comparison among groups with reactive and dysthymia (F (5.13) = 3.94; p = 0.024, ANCOVA). In regard to cholesterol/HDL-cholesterol ratios, patients with psychogenic depression showed a lower ratio than in reactive and dysthymic patients (F (2.61) = 4.52; p = 0.014, ANCOVA). Also, in regard to LDL-cholesterol/HDL-cholesterol ratios, the psychogenic group reflected a significantly lower ratio (F (2.61) = 6.13; p = 0.004, ANCOVA) (Table 3) than the reactive depression group and dysthymia group. Serum lipids' concentration ratios after age and BMI adjustments have been summarized and presented in Table 3.

Table 3: Serum lipids (mean (95% CI) after age and BMI adjustment in patients with three types depressive disorders

	Type of depressive disorder				
	Reactive	*Disthymic*	*Psychogenic*	*F**	*p*
Triglyceides (mmol/L)	1.90 (1.61–2.14)	1.86 (1.12–1.08)	1.82 (0.24–1.08)	1.82	0.157
Cholesterol (mmol/L)	6.20 (5.59–6.89)	6.86 (5.30–6.47)	5.87 (5.21–5.96)	3.94	0.024
HDL-cholesterol (mmol/L)	1.71 (1.56–1.73)	1.62 (1.22–1.31)	1.88 (1.43–1.82)	2.11	0.312
LDL-cholesterol (mmol/L)	4.12 (3.56–3.77)	5.6 (4.02–4.33)	3.01 (3.10–3.40)	8.46	0.001
VLDL-cholesterol (mmol/L)	0.60 (0.42–0.48)	0.36 (0.20–0.46)	0.34 (0.27–0.38)	1.80	0.173
Cholesterol/HDL-cholesterol ratio	5.13 (4.12–4.58)	5.11 (3.88–4.32)	4.10 (3.27–4.12)	4.52	0.014
LDL-cholesterol/HDL-cholesterol ratio	3.51 (2.18–3.23)	3.18 (3.11–4.12)	2.30 (2.10–2.83)	6.13	0.004

*One-way ANOVA

Discussion

Recent researches highlight the lipid profile influencing the behavioral aspects of human subjects. Indication about lower values of lipid profile components in cases with impulse control disorder has somewhat been established. A series of studies indicated psychiatric patients with suicidal attempts show lower levels of cholesterol. Some authors proposed that low total cholesterol can be a marker for suicidal behavior or risk. The connections between low cholesterol and various risk-taking behaviors have been highlighted in recent research, which suggested that a low total cholesterol level can be used as a marker for various risk-taking behaviors, including suicide or harming others. The present study indicated lower cholesterol values for certain depressive groups of patients, and a possibility of impulsive acting out can be considered for future treatment purposes.

The proposed mechanism possibly works by lipid microviscosity reduction in neural membranes in these subjects. Owing to a decreased neural membrane lipid micro-viscosity, serotonin receptor exposure on the membrane surface may be reduced, resulting in hypo-function of those receptors.[19] Several studies indicated that lower concentrations of 5-hydroxy in doleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF) can be linked to impulsive act outs such as suicides and suicide attempts. Thus, the proposed link between low total cholesterol and serotonergic system is being recognized as having a central role in impulse control behaviors.[19,20]

Analysis of the results of this the study points that a comparison among three selected depressive groups in regard to some components of lipid profile as serum levels of triglycerides, HDL-cholesterol, and VLDL-cholesterol did not reveal significant differences. Findings show a fairly similar profile in regard to above components among patients with reactive depression, psychogenic depression, and dysthymia. While the noteworthy finding in this study reflects that in the psychogenic depressive group, estimations of LDL-cholesterol, cholesterol, cholesterol/HDL-cholesterol ratio, and LDL-cholesterol/HDL-cholesterol ratios were significantly lower compared to reactive and dysthymia groups. Huang and Chen worked on psychogenic and melancholic depressive groups of patients to found that serum concentration of triglycerides, VLDL-cholesterol, and HDL-cholesterol might be used as biological markers for group differentiation. The distinction among those groups was revealed after doing the statistical adjustments of age of the samples.[10] Some other studies observed similar findings on lipid components, but those have not been shared by all authors.[14] Applying similar statistics and after adjustment of BMI in another study, patient groups with melancholic and psychogenic characteristics of depressive disorder indicate no difference in serum lipid concentration.[14] Considering those differences in previous studies, we applied the analysis of covariance and age and BMI adjustments to find any difference among groups. When the confounding factors of age and BMI were adjusted, the results of the present study validated the fact that lipid profile may have a role as a possible biological marker of depressive groups. In our study, levels of cholesterol, LDL-cholesterol, cholesterol/HDL-cholesterol ratio, and LDL-cholesterol/HDL-cholesterol ratio are found to be possible indicators for differentiation between certain clinical subtypes of depressive disorder and thereby predicting some risk-taking behavior as well.

The relationship between cholesterol and depression or suicide is also complex. For example, studies from France and Canada linked low cholesterol levels to an increased incidence of suicide, and research from the Netherlands and Turkey reported an association between low cholesterol levels and depression. On the other hand, data from Hawaii found the reverse: high cholesterol levels were connected with an increased risk of suicide.

Since so many lifestyles and health factors influence both the body's metabolism and the mind's function, it is not surprising that population-based observational studies have produced conflicting results.[21] Randomized clinical trials of cholesterol-lowering medications avoid many of these pitfalls, and here the results are reassuring. Placebo-controlled trials of lovastatin and simvastatin (which can cross into the brain) and of pravastatin (which does not) have not identified any adverse effects on cognitive function or psychological well-being. In fact, a long-term use of statin drugs has been associated with reduced risks of anxiety, hostility, depression, and suicide, perhaps because of the improved physical health that results from these medications. Similarly, a meta-analysis of 19 trials of cholesterol-lowering interventions found no effect on the risk of death from suicide, accidents, or violence. And men who claim that a heart-healthy diet will drive them over the edge should note that dietary interventions that lower cholesterol is as psychologically friendly as medications. Thus diet has a greater role to play in psychiatric patients.

Another clinical significance of the present study is the prediction of atherosclerosis, which may in the long term indicate coronary heart disease. It has been speculated that values of total estimates of cholesterol, HDL-cholesterol, and LDL-cholesterol concentrations have lesser predictive value in assessing atherosclerosis or coronary risk. More prognostic value for risk factors for the onset of coronary heart disease have been entitled to ratios such as cholesterol/HDL-cholesterol ratio and LDL-cholesterol/HDL-cholesterol ratio.[15] As the present study disclosed a statistically significant variation

in regard to serum levels of triglycerides, HDL-cholesterol and VLDL-cholesterol and significantly lower values of LDL-cholesterol, cholesterol, cholesterol/HDL-cholesterol ratio, and LDL-cholesterol/HDL-cholesterol ratio in certain patient groups, consideration of a future cardiac risk related to the progression of atherosclerosis in those groups of depressive disorder can be anticipated.

Various mechanisms may be responsible for depressive symptoms as well as serum cholesterol concentrations. Recent investigations undoubtedly established the neurotransmitter serotonin dysfunction as one major cause of the mood disorder. That serotonin dysfunction can be somewhat related to a decline in the serum cholesterol level may lead directly to a reduction in cerebral 5-HT activity by various mechanisms such as changes in concentrations of 5-hydroxy tryptamine (5-HT) of the 5-HT receptor, and in 5-HT transporter activity. Other mechanism possibilities can be free-disturbed cholesterol esterification in impulsive patients causing self-harming. A possible explanation of subjects having a comparatively higher level of serum cholesterol and having depressive symptoms can be that an elevated cholesterol level may cause a decrease in 5-HT receptor sensitivity or in 5-HT transporter activity by direct binding to membrane receptors or transporter molecules. Cholesterol can also be responsible indirectly by altering fluidity of the neuronal membrane and thus causing an imbalance of neurotransmitters. Thus more evidence points to the fact that serum cholesterol profile plays a prominent role in controlling the balance of brain neurotransmitters, which in turn have been responsible for the precipitation of some psychiatric symptoms. A study found an increased risk of suicide in patients with a low cholesterol level (<4.0 mmol/L) and in contrast, the presence of comorbid anxiety disorder and treatment resistance in patients with an elevated cholesterol level (>5.6 mmol/L).[22] As we have noted in our clinic, clinicians have to be aware of the confounders, such as diet and medication, affecting the lipid profile status in depressive patients coming for treatment. Ghaemi et al.[9] have reported that medication is not the only contributor to changes in the lipid profile. No significant difference had been found in lipid concentrations based on the types of antidepressants used for treatment purposes.

Conclusion

Finding biological correlates in psychiatric disorders always pose a challenge and the present study has thrown some light in using physiological markers as lipid profile components, namely serum cholesterol- and LDL-cholesterol concentrations as well as cholesterol/HDL-cholesterol- and LDL-cholesterol/HDL-cholesterol ratios to differentiate between clinical subtypes of the depressive disorder. Furthermore, assessing cardiovascular risks in those groups can be possible besides psychiatric diagnosis, as indicated in our findings. Since depressive groups may sometimes present with similar symptoms, using above markers can help in diagnosis and preventive health risk can also be ascertained.

The study has limitations of a comparatively smaller sample size of patients in assigned groups. It could be better if all treatment interventions could be done earlier keeping the difference minimum between groups, but that could not be maintained uniformly between the groups. Inclusion of a healthy control group could supplement the findings, which we plan to do in our next study. The whole picture of the pathophysiology of depressive disorders can be clearer with the investigations on biological markers such as cholesterol. The modern trend of a frequent use of lipid-lowering agents to cut down cardiovascular risks can be questioned in the context of the present study. A further study aiming to link the lipid profile status with impulse control disorder and a risky behavior in depressive subgroups comprising a bigger sample size should be proposed. Furthermore, the role of low serum cholesterol in the course of recovery from depressive disorder needs further investigation.

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