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A CROSS-SECTIONAL COMPARATIVE STUDY OF LIPID PROFILE IN MAJOR ENDOGENOUS DEPRESSIVE DISORDER PATIENTS ATTENDING PSYCHIATRIC OPD WITH MATCHED NORMAL CONTROLS

Dr. M. Venkatesh[1*], Dr. R. G. Enoch[2] and Dr. R. Aravazhi[3]

[1*]Associate Professor, Department of General Medicine, Government Theni Medical College and Hospital, Theni, Tamil Nadu-625512, India.
[2]Assistant Professor, Department of Psychiatry, Government Theni Medical College and Hospital, Theni, Tamil Nadu-625512, India.
[3]Assistant Professor, Department of Cardiology, Government Theni Medical College and Hospital, Theni, Tamil Nadu-625512, India.

[*]**Corresponding author:** Dr. R.G.Enoch
*Assistant Professor, Department of Psychiatry, Government Theni Medical College and Hospital, Theni, Tamil Nadu-625512, India.

Abstract

Background: Major Depressive Disorder (MDD) is a mood disorder associated with significant alterations in lipid metabolism. Dyslipidemia may contribute to the pathogenesis of depression and is also a risk factor for cardiovascular disease. This study compares lipid profiles between MDD patients and age- and sex-matched healthy controls to explore their potential role as biomarkers.

Methods: A cross-sectional study was conducted on patients attending the Psychiatry Outpatient Department (OPD) who were diagnosed with major endogenous depressive disorder, alongside age- and sex-matched healthy controls. Following ethical clearance and informed consent, lipid profiles were assessed using fasting blood samples. Hamilton Depression Rating Scale (HAM-D) was used to quantify depressive severity.

Results: Patients with MDD had significantly higher levels of total cholesterol (198.37 ± 34.51 mg/dL vs. 162.13 ± 34.14 mg/dL; p = 0.0001), LDL (123.97 ± 27.87 mg/dL vs. 99.97 ± 32.52 mg/dL; p = 0.003), triglycerides (192.37 ± 122.84 mg/dL vs. 132.20 ± 39.41 mg/dL; p = 0.013), and VLDL (38.46 ± 24.56 mg/dL vs. 26.44 ± 7.88 mg/dL; p = 0.013). HDL levels were lower in the MDD group but not statistically significant (p = 0.159). Female patients exhibited significantly higher triglyceride and VLDL levels than males (p = 0.03). No significant correlation was found between lipid levels and HAM-D scores or depression severity.

Conclusion: MDD is associated with significant dyslipidemia, particularly elevated total cholesterol, triglycerides, LDL, and VLDL levels. These alterations may increase cardiovascular risk and suggest the potential utility of lipid screening in depressive patients. However, lipid levels do not appear to correlate with depression severity. Further studies are needed to investigate causal mechanisms and therapeutic implications.

Keywords: Major Depressive Disorder, Lipid Profile, Cholesterol, Triglycerides, LDL, HDL

Introduction

Major Depressive Disorder (MDD) is a common psychiatric condition marked by chronic melancholy, lack of interest in activities, and a severe decrease in everyday functioning [1]. Globally, it affects about 6% of the population, with roughly 350 million people suffering from some type of depression [2, 3]. Depression affects approximately 15.9% of the population in India, which is comparable to Western countries [4]. The illness usually appears in early adulthood, with an average onset age of 24 years, and is more common in women than in males [5, 6]. Several social and personal factors, such as being unmarried, living in cities, lacking social support, having chronic medical illnesses, and being elderly, all raise the risk of getting MDD [7-9]. Depression is diagnosed mostly through clinical evaluation with standardized methods such as the ICD-10 and DSM-5, which rely on subjective symptom reporting [10, 11]. This technique may not fully address the basic roots of the condition, and approximately 30% of individuals are considered treatment-resistant. As a result, establishing trustworthy biological markers may enhance diagnosis and treatment [12, 13]. Lipids have an important role in brain function, including cell membrane construction, neurotransmitter modulation, and neuroplasticity [14, 15]. Individuals with MDD have abnormal lipid levels, including higher total cholesterol, triglycerides, and low-density lipoproteins (LDL), as well as lowered high-density lipoproteins (HDL). These disruptions may be caused by a variety of processes, including protein malfunction, chronic stress, hormone imbalance (particularly cortisol), and the use of psychiatric medicines, which can cause metabolic alterations. High triglyceride levels have also been linked to increased blood viscosity, which may limit oxygen transport to the brain, adding to depressive symptoms [16, 17]. However, the available literature yields conflicting results, with some research finding a favorable, negative, or no relationship between lipid levels and depression [18, 19]. This diversity could be attributed to changes in study design, population demographics, and eating habits [20]. Despite global interest, there is little research on South India, and existing findings are sometimes conflicting [21]. Hence, this study aims to compare the lipid profiles of patients with Major Depressive Disorder against age- and sex-matched healthy controls, with the goal of exploring lipid abnormalities as potential biomarkers for MDD. This could assist in early detection, better treatment planning, and reduce long-term morbidity and mortality associated with depression and related cardiovascular complications.

MATERIALS AND METHODS

Place of Study

This study was conducted at the Department of Psychiatry, Government Mohan Kumaramangalam Medical College Hospital, Salem.

Ethical Approval

Ethical clearance was obtained from the Institutional Ethical Committee of Government Mohan Kumaramangalam Medical College Hospital.

Study Design and Duration

A cross-sectional study was carried out over a period of one year from January 2018 to December 2018.

Study Population

The study included 30 patients diagnosed with major depressive disorder (according to ICD-10 Diagnostic Criteria for Research) and 30 age- and gender-matched healthy individuals as controls.

Inclusion Criteria

- Age between 20 and 50 years
- Diagnosis of depressive disorder based on ICD-10 criteria
- Willingness to participate and provide informed consent

Exclusion Criteria

- History of cardiovascular diseases or familial cardiac issues
- Diagnosed hypertension, diabetes, Cushing's disease, kidney disease, or hypothyroidism
- Use of steroid medications or second-generation antipsychotics
- Age below 20 or above 50 years

Operational Design

Eligible patients were selected from the Psychiatry OPD. Sociodemographic data were collected using a semi-structured proforma. After obtaining informed consent, patients were admitted and assessed using the Hamilton Rating Scale for Depression (HAM-D). A 12-hour fasting blood sample was collected to evaluate lipid profiles. Similar procedures were followed for control subjects.

Tools Used

Semi-Structured Proforma: Captured sociodemographic and clinical variables such as education, occupation, marital status, and illness history.
ICD-10 DCR: Used for the clinical diagnosis of depressive disorders.

Hamilton Depression Rating Scale (HAM-D): A 17-item clinician-administered tool used to assess the severity of depressive symptoms. Scores helped categorize depression into normal, mild, moderate, severe, and very severe.

Research Method

After recruitment and assessment, data were analyzed using appropriate statistical software. Lipid profile parameters—total cholesterol, triglycerides, HDL, LDL, and VLDL—were compared between cases and controls. Associations between depression severity and lipid levels were also examined to explore lipid profile as a potential biomarker for major depressive disorder.

Results

Participant Characteristics

A total of 60 individuals participated in the study, comprising 30 patients diagnosed with Major Depressive Disorder (MDD) and 30 healthy controls, matched for age and gender. The mean age of participants in the MDD group was 36.70 ± 7.21 years, and that of the control group was 36.47 ± 7.08 years. The difference was not statistically significant ($p = 0.929$), indicating successful age matching. Similarly, the mean BMI was 24.63 ± 3.57 in cases and 23.98 ± 2.94 in controls, with no significant difference ($p = 0.442$). Gender distribution was identical across both groups, with 36.7% males and 63.3% females in each ($p = 1.000$), confirming proper matching (Table 1).

Table 1: Comparison of Sociodemographic and Anthropometric Characteristics between MDD Patients and Controls

Variable	MDD Patients (n = 30)	Controls (n = 30)	p-value
Age (mean ± SD)	36.70 ± 7.21	36.47 ± 7.08	0.929
BMI (mean ± SD)	24.63 ± 3.57	23.98 ± 2.94	0.442
Marital Status (Married %)	76.70%	70.00%	0.56
Education Level	Primary–Secondary	Primary–Secondary	NS
Occupation	Semiskilled/Housewives	Skilled workers	NS
Socioeconomic Status (Low %)	43.30%	16.70%	0.08

NS = Not Significant

Sociodemographic Variables

There were no statistically significant differences between cases and controls in terms of education level, occupation, marital status, or socioeconomic status. Most participants in both groups had completed either primary or secondary education. A higher proportion of MDD patients were semiskilled workers (36.7%) and housewives (36.7%), whereas a notable percentage of controls (20%) were skilled workers. Regarding marital status, the majority in both groups were married (76.7% in MDD group vs. 70.0% in controls; p = 0.56). Although not statistically significant (p = 0.08), a higher percentage of MDD patients belonged to the lower socioeconomic strata (43.3%) compared to controls (16.7%) (Table 2).

Table 2: Socio-demographic Details – Gender

Variable	Cases (N=30)	%	Controls (N=30)	%	Total (N=60)	%	P value
Male	11	36.7	11	36.7	22	36.7	1
Female	19	63.3	19	63.3	38	63.3	

Depression Severity and Duration

The severity of depression was assessed using the 17-item Hamilton Depression Rating Scale (HAM-D). The mean HAM-D score in the MDD group was 21.0 ± 4.49. Of the 30 cases, 6.7% had mild depression, 26.7% had moderate depression, 40.0% had severe depression, and 26.7% had very severe depression (Table 3). These scores reflect the clinical heterogeneity in depression severity among the study population.

Table 3: Severity of Depression among MDD Patients (Based on HAM-D Scores)

Severity Level	Number of Patients (n=30)	Percentage (%)
Mild	2	0.067
Moderate	8	0.267
Severe	12	0.4
Very Severe	8	0.267
Mean HAM-D Score	–	21.0 ± 4.49

Lipid Profile Comparison

A significant difference was observed between the MDD group and healthy controls in multiple lipid parameters. MDD patients had significantly higher levels of total cholesterol (198.37 ± 34.51 mg/dL vs. 162.13 ± 34.14 mg/dL; p = 0.0001), LDL cholesterol (123.97 ± 27.87 mg/dL vs. 99.97 ± 32.52 mg/dL; p = 0.003), triglycerides (192.37 ± 122.84 mg/dL vs. 132.20 ± 39.41 mg/dL; p = 0.013), and VLDL (38.46 ± 24.56 mg/dL vs. 26.44 ± 7.88 mg/dL; p = 0.013). However, there was no statistically significant difference in HDL levels (37.23 ± 3.98 mg/dL in cases vs. 35.83 ± 2.61 mg/dL in controls; p = 0.159) (Table 4). These findings suggest a clear association between depression and dyslipidemia, with atherogenic lipid fractions being markedly elevated in the MDD group.

Lipid Profile and Sociodemographic Correlation in MDD Patients

Further analysis was conducted within the MDD group to assess the influence of sociodemographic factors on lipid profile. Gender was found to be significantly associated with lipid abnormalities: female patients had higher levels of triglycerides (p = 0.03) and VLDL (p = 0.03) than male patients. Other variables—age, education level, occupation, and socioeconomic status—did not show statistically significant associations with lipid parameters, although triglycerides and VLDL tended to be elevated in patients from lower socioeconomic backgrounds (p = 0.07), suggesting a possible trend worth exploring in larger studies (Table 5).

Table 4: Comparison of Lipid Profile between MDD Patients and Controls

Lipid Parameter	MDD Patients (mean ± SD)	Controls (mean ± SD)	p-value

Total Cholesterol (mg/dL)	198.37 ± 34.51	162.13 ± 34.14	0.0001
LDL (mg/dL)	123.97 ± 27.87	99.97 ± 32.52	0.003
HDL (mg/dL)	37.23 ± 3.98	35.83 ± 2.61	0.159
Triglycerides (mg/dL)	192.37 ± 122.84	132.20 ± 39.41	0.013
VLDL (mg/dL)	38.46 ± 24.56	26.44 ± 7.88	0.013

Table 5: Association between Gender and Lipid Profile among MDD Patients

Lipid Parameter	Male (mean ± SD)	Female (mean ± SD)	p-value
Total Cholesterol	NS	NS	> 0.05
LDL	NS	NS	> 0.05
HDL	NS	NS	> 0.05
Triglycerides	Lower	Higher	0.03
VLDL	Lower	Higher	0.03

Association between Depression Severity and Lipid Levels

To explore whether lipid abnormalities correlate with the severity of depression, the MDD group was stratified based on HAM-D scores into mild, moderate, severe, and very severe categories. A Kruskal-Wallis test revealed no statistically significant association between the severity of depression and levels of total cholesterol ($p = 0.617$), LDL ($p = 0.898$), HDL ($p = 0.393$), triglycerides ($p = 0.391$), or VLDL ($p = 0.391$) (Table 6). These results suggest that while lipid abnormalities are more prevalent in patients with MDD, they do not correlate linearly with the clinical severity of depressive symptoms.

Table 6: Association between Depression Severity (HAM-D Category) and Lipid Profile in MDD Patients

Lipid Parameter	p-value (Kruskal-Wallis Test)
Total Cholesterol	0.617
LDL	0.898
HDL	0.393
Triglycerides	0.391
VLDL	0.391

Correlation between HAM-D Scores and Lipid Profile

Pearson correlation analysis was used to examine the relationship between HAM-D scores and individual lipid parameters within the MDD group. No statistically significant correlations were found: total cholesterol ($r = 0.07$; $p = 0.71$), LDL ($r = 0.01$; $p = 0.92$), HDL ($r = 0.21$; $p = 0.26$), triglycerides, and VLDL showed weak, non-significant correlations (Table 7). These findings reinforce the conclusion that while MDD is associated with dyslipidemia, the lipid profile does not directly reflect the severity of depressive symptoms.

Table7: Correlation Between HAM-D Scores and Lipid Profile in MDD Patients

Lipid Parameter	Pearson Correlation (r)	p-value
Total Cholesterol	0.07	0.71
LDL	0.01	0.92
HDL	0.21	0.26
Triglycerides	Weak, NS	> 0.05
VLDL	Weak, NS	> 0.05

Discussion

Major depressive disorder (MDD) is a significant contributor to the global disease burden, often exacerbated by increasing psychosocial stress. Emerging evidence has highlighted a complex relationship between depression and lipid metabolism, particularly dyslipidemia. This study aimed to evaluate serum lipid profiles—including total cholesterol, triacylglycerol, LDL, HDL, and VLDL—in patients diagnosed with MDD compared to healthy controls. In our sample, the mean age of depressive patients was approximately 36.7 years, consistent with prior research where patient ages ranged broadly but frequently clustered between the late 20s and early 40s. Variations in age observed across studies likely reflect demographic and methodological differences, including geographic and ethnic factors (Sadeghi et al., [22] Moreira et al., [23] Ravi Gupta et al.,[24]). The average BMI of 24.63 aligns closely with previous reports, supporting that depressive patients often maintain normal to slightly elevated body mass indices. Our findings demonstrated significantly elevated total cholesterol levels in patients with MDD compared to controls ($p=0.0001$). This corroborates multiple prior studies that link elevated total cholesterol with depressive symptoms (Saroj Sharma et al., Yajun Liang et al., Ahn EJ et al.,) [25-27]. However, some research has shown conflicting results, reporting an inverse relationship between cholesterol and depression, particularly in elderly populations or specific subgroups (Morgan et al.,[28], Segers MJ et al.,[29]). These discrepancies may be explained by differences in study design, sample heterogeneity, dietary habits, or comorbid conditions. Similarly, triacylglycerol levels were significantly higher in the depressive group ($p=0.013$), consistent with several other reports highlighting hypertriglyceridemia as a feature of depression (Saroj Sharma et al., [25], Ravi Gupta et al., [24], Van Reedt Dortland et al., [30]). Elevated LDL cholesterol was also observed ($p=0.003$), echoing findings from studies that emphasize the atherogenic lipid profile associated with depression (Sadeghi et al. [22], Yajun Liang et al., [26]). Conversely, HDL cholesterol was lower in depressive patients, although this difference did not reach statistical significance in our sample. This trend aligns with studies identifying reduced HDL as a potential marker of depression severity (Enko et al., [31], Van Reedt Dortland et al., [30]). Elevated VLDL levels in depressed patients further reflect a disturbed lipid metabolism that may contribute to increased cardiovascular risk in this population. Our analysis also revealed a gender difference in triacylglycerol levels, with females exhibiting higher levels than males, consistent with literature indicating sex-specific variations in lipid profiles in depression (Oxenkrug et al., [32], Liang et al., [26]). Age and socioeconomic status showed limited influence on lipid profiles in our cohort, although other studies have suggested that lipid disturbances may be more pronounced in certain age groups or socioeconomic strata. While some studies have reported correlations between depression severity and lipid abnormalities, our study did not find significant associations between lipid levels and HAM-D scores. Similarly, duration of depression and lipid profiles showed no significant relationship. These findings suggest that while lipid dysregulation is prevalent in depression, it may not directly reflect clinical severity or chronicity, underscoring the multifactorial nature of lipid alterations in depressive disorders. An important consideration is the potential influence of early life stress (ELS) on lipid metabolism in depression. Prior research has identified ELS as a strong predictor of dyslipidemia in MDD, characterized by elevated TG, LDL, and TC alongside reduced HDL. Although this study did not assess ELS, the lipid profile observed supports the hypothesis that early environmental factors could contribute to metabolic disturbances in depressive patients. Medication effects represent another limitation, as antidepressants and antipsychotics can induce weight gain and alter lipid metabolism. Our exclusion of patients on second-generation antipsychotics mitigates some confounding, but future studies should comprehensively evaluate pharmacological impacts on lipid profiles. The pathophysiological mechanisms linking cholesterol and depression may involve alterations in membrane fluidity, neurotransmitter function, and inflammatory pathways. The elevated atherogenic indices observed in depressed patients highlight their increased risk for cardiovascular diseases, which are common comorbidities and contributors to morbidity and mortality in MDD. Therapeutically, cholesterol modulation may offer new avenues for adjunctive treatment in depression. Emerging evidence supports the use of statins alongside conventional antidepressants to improve depressive symptoms, possibly by reducing inflammation and correcting lipid abnormalities.

However, the role of HDL supplementation remains unexplored and warrants further investigation. Beyond traditional lipids, other lipid species and peptide biomarkers involved in lipid metabolism, such as neuropeptide Y and leptin, may provide additional insights into depression pathogenesis and offer novel targets for intervention.

Conclusion

This study highlights a significant relationship between major depressive disorder (MDD) and altered serum lipid profiles. Patients with MDD demonstrated significantly higher levels of total cholesterol, triacylglycerol, LDL, and VLDL compared to healthy controls, while HDL cholesterol levels tended to be lower, though not statistically significant. These findings align with multiple previous studies suggesting that dyslipidemia is common in depressive patients and may contribute to the increased cardiovascular risk seen in this population. The results underscore the importance of routine lipid screening in patients with depression to identify and manage cardiovascular risk factors early. Although no significant correlation was found between lipid levels and depression severity or duration in this study, the role of lipid metabolism in depression pathophysiology warrants further exploration. Future research should focus on clarifying the mechanisms linking lipid abnormalities and depression and investigating whether lipid-modifying interventions could improve depressive symptoms and reduce cardiovascular morbidity in these patients.

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Author's contributions

All the authors have contributed equally.

Conflict of interest

The authors report no conflicts of interest in this work.

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