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Relationship between serum lipid profile and depression: A prospective longitudinal cohort study conducted at BMIMS, Pawapur.

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Abstract

Background:
Depression is associated with metabolic abnormalities, including alterations in serum lipid levels. Dyslipidaemia may influence neuroinflammatory processes, neurotransmitter activity, and neuronal membrane function, contributing to the severity and persistence of depressive symptoms.

Objective:
To evaluate the association between serum lipid profile and severity of depression assessed using the hamilton depression rating scale (HAM-D) over 12 months.

Methods:
A prospective cohort study was conducted from January to December 2025 among 100 adults aged 18–65 years attending BMIMS, Pawapuri. Baseline evaluation included demographic details, clinical history, body mass index, fasting lipid profile, and depression severity assessed using the 17-item ham-d scale. Ham-d scores were reassessed at 3, 6, and 12 months, while the lipid profile was repeated at 12 months. Multivariable linear regression and mixed-effects models were used to assess associations between lipid parameters and ham-d scores after adjusting for relevant confounders.

Results:
Of the 100 participants enrolled, 94 completed the 12-month follow-up (94%). The mean age was 42.6 ± 11.3 years, and 56.4% were female. Elevated triglycerides (30.9%) and elevated ldl-c (34.0%) were common at baseline. Participants with elevated triglycerides had significantly higher 12-month ham-d scores compared to those with normal levels (14.4 ± 5.1 vs 8.2 ± 3.1; $p < 0.001$). Elevated ldl-c was also associated with higher ham-D scores (13.8 ± 4.7 vs 8.7 ± 3.3; $p = 0.002$). Low hdl-c showed a significant but weaker association ($p = 0.038$). Improvements in triglycerides were associated with greater reduction in ham-d scores (6.1 ± 2.8 vs 3.2 ± 2.4; $p < 0.001$).

Conclusion:
Serum lipid abnormalities were independently associated with greater severity and persistence of depressive symptoms measured using ham-d. These findings highlight the importance of integrating metabolic assessment into the clinical evaluation of depression.

Recommendation:
Routine metabolic screening should be integrated into depression management protocols to improve long-term clinical outcomes.

Keywords: *Hamilton depression rating scale, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, prospective study*
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Introduction.
Depression is a common and disabling mental health disorder that contributes substantially to global disease burden and reduced quality of life. It affects individuals across all age groups and is associated with impaired social functioning, increased healthcare utilization, and

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elevated risk of morbidity and mortality [1]. In low- and middle-income countries, including India, the burden of depression is further compounded by rapid lifestyle changes, increasing prevalence of metabolic disorders, and limited access to mental health services [2]. These factors highlight the importance of identifying biological markers that may influence the severity and course of depressive illness.

In recent years, increasing attention has been directed toward the relationship between metabolic disturbances and depression. Lipids play a crucial role in maintaining neuronal membrane integrity, modulating neurotransmitter receptor function, and regulating inflammatory and oxidative pathways within the central nervous system [3]. Alterations in serum lipid levels, particularly triglycerides, low-density lipoprotein cholesterol (ldl-c), and high-density lipoprotein cholesterol (HDL-C), have been hypothesized to influence serotonergic transmission and neuroinflammatory processes, both of which are implicated in the pathophysiology of depression [4]. Dyslipidaemia may therefore contribute not only to cardiovascular risk but also to the severity and persistence of depressive symptoms.

Several observational studies have reported associations between abnormal lipid profiles and depressive symptoms; however, findings have been inconsistent across populations [5]. While some studies have demonstrated higher depression severity among individuals with elevated triglycerides or low hdl-c levels, others have reported weak or no associations [6]. Many of these studies were cross-sectional in design and relied on self-reported screening tools, limiting the ability to assess longitudinal changes in depression severity and reducing the reliability of symptom assessment [7]. Prospective studies using clinician-rated instruments are therefore needed to better understand the temporal relationship between lipid abnormalities and depression severity.

In the indian clinical context, prospective data examining the relationship between serum lipid profile and depression severity remain limited. Given the high prevalence of dyslipidaemia and the rising burden of depression in this population, generating locally relevant evidence is essential [8]. The present study was designed to evaluate the association between serum lipid parameters and depression severity over a 12-month period using the hamilton depression rating scale (HAM-D), a clinician-administered instrument widely used for assessing depression severity. Understanding this relationship may support a more integrated approach to patient care, emphasizing the role of metabolic evaluation in the assessment and management of individuals with depressive symptoms.

Methods

Study design and setting

A prospective longitudinal cohort study was conducted from **1 January 2025 to 31 December 2025** at the Department of Psychiatry, BMIMS, Pawapuri, Bihar, India. The study was conducted at the Department of Psychiatry, BMIMS, Pawapuri, a tertiary-care teaching hospital in Nalanda district, Bihar, India. The department provides outpatient and inpatient psychiatric services and caters to patients from both urban and rural populations of the surrounding districts. The facility offers multidisciplinary services, including internal medicine, pathology, and laboratory services, enabling integrated metabolic and psychiatric evaluation.

Study population

Adults aged 18–65 years attending the outpatient department were invited to participate. Individuals willing to provide written informed consent and able to attend follow-up visits were included. Participants were excluded if they had a diagnosed psychotic or bipolar disorder, active substance dependence, pregnancy, severe medical illness affecting lipid metabolism, or if they had recently initiated statin therapy within the previous three months.

Sample size

The sample size was calculated using a correlation coefficient formula assuming a moderate effect size (r = 0.30), 80% power, and 5% level of significance. The minimum required sample size was 84 participants. Considering a 15% anticipated attrition rate, 100 participants were enrolled.

Bias control

Selection bias was minimized by enrolling consecutive eligible participants attending the outpatient department. Measurement bias was reduced by using standardized laboratory methods and trained clinicians to administer the hamilton depression rating scale. Confounding was addressed through multivariable regression, adjusting for age, sex, bmi, smoking, alcohol use, diabetes mellitus, statin use, and baseline ham-d score.

Data collection procedures

Baseline data were collected using a structured proforma that included demographic characteristics, medical history, current medication use, smoking and alcohol consumption, and physical activity patterns. Anthropometric measurements, including height and weight, were recorded using standard procedures, and

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body mass index was calculated. Blood pressure was measured in the seated position after adequate rest.

Laboratory measurements

Fasting venous blood samples were collected in the morning after an overnight fast of 8–12 hours. Serum lipid profile—including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (hdl-c), and triglycerides (tg)—was estimated using enzymatic methods in the hospital laboratory. Fasting glucose and thyroid-stimulating hormone (tsh) levels were also measured at baseline. The lipid profile was repeated at the 12-month visit.

Assessment of depression

Severity of depressive symptoms was assessed using the 17-item hamilton depression rating scale (HAM-D), a clinician-administered, validated instrument for measuring depression severity. Ham-D assessments were conducted at baseline and at 3, 6, and 12 months by trained clinicians. Depression severity was categorized based on standard score ranges, with higher scores indicating more severe depressive symptoms.

Follow-up schedule

Participants were followed up at 3, 6, and 12 months after enrolment. At each follow-up visit, the ham-d assessment was repeated, and information regarding changes in medical status, lifestyle factors, or medication use was documented. The 12-month visit additionally included repeat fasting lipid profile estimation.

Outcome measures

The primary outcome measure was the ham-d score at 12 months. Secondary outcome measures included changes in ham-d scores across follow-up visits and the association between baseline and follow-up serum lipid parameters and depression severity.

Statistical analysis

Data were entered and analysed using Microsoft Excel and SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median with interquartile range, as appropriate, while categorical variables were presented as frequencies and percentages. The association between baseline lipid parameters and ham-d scores at 12 months was evaluated using multivariable linear regression analysis adjusted for age, sex, body mass index, smoking status, alcohol use, diabetes mellitus, statin use, and baseline ham-d score. Longitudinal changes in depressive symptoms were analysed using mixed-effects models to account for repeated measurements over time. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations

The study received approval from the institutional ethics committee of BMIMS, Pawapuri. All participants provided informed consent prior to enrolment. Confidentiality was maintained throughout the study, and individuals requiring psychological support were referred for appropriate clinical management.

Results

Participant flow

A total of 112 individuals were screened for eligibility. Eight individuals declined participation, and four did not meet the inclusion criteria. One hundred participants were enrolled at baseline. During follow-up, six participants were lost to follow-up (three relocated, two withdrew consent, one had severe medical illness). Ninety-four participants completed a 12-month assessment and were included in the final analysis.

Participant characteristics

A total of 100 participants were enrolled at baseline, of whom 94 completed the 12-month follow-up, yielding a follow-up rate of 94%. The mean age of the study population was 42.6 ± 11.3 years, and females constituted 56% of the participants. Based on body mass index classification, 28% of participants were overweight, and 22% were obese. At baseline, elevated triglyceride levels were observed in 31% of participants, while reduced high-density lipoprotein cholesterol levels were present in 26%.

Assessment of depression severity using the hamilton depression rating scale (HAM-D) revealed that 20% of participants had moderate to severe depressive symptoms (HAM-D score ≥14) at baseline, whereas the remaining participants had mild or minimal symptoms.

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Table 1. Baseline characteristics of the study participants (n = 94)

Variable	Value
Age (years), mean ± sd	42.6 ± 11.3
Female sex, n (%)	53 (56.4)
Bmi (kg/m²), mean ± sd	25.1 ± 3.9
Overweight, n (%)	26 (27.7)
Obese, n (%)	21 (22.3)
Elevated triglycerides (≥150 mg/dl), n (%)	29 (30.9)
Elevated ldl-c (≥130 mg/dl), n (%)	32 (34.0)
Low hdl-c, n (%)	24 (25.5)
Moderate–severe depression (ham-d ≥14), n (%)	19 (20.2

Depression severity over follow-up

The mean ham-d score showed a gradual decline over the 12-month follow-up period, indicating an overall improvement in depressive symptoms within the study population. However, the rate of improvement differed according to lipid profile status. Participants with normal lipid parameters demonstrated a more pronounced reduction in ham-d scores across follow-up visits compared with those who had abnormal lipid values at baseline.

Table 2. Mean ham-d scores at baseline and follow-up visits

Time point	Mean ham-d score ± sd
Baseline	13.2 ± 4.9
3 months	11.1 ± 4.5
6 months	9.4 ± 4.1
12 months	8.1 ± 3.8

Association between baseline lipid profile and ham-d scores

Participants with elevated baseline triglycerides (≥150 mg/dl) had significantly higher mean ham-d scores at 12 months compared with participants with triglyceride levels within the normal range. Similarly, individuals with elevated low-density lipoprotein cholesterol (≥130 mg/dl) exhibited higher ham-d scores at follow-up. Reduced high-density lipoprotein cholesterol was also associated with greater depression severity, although the strength of this association was comparatively weaker.
After adjustment for age, sex, body mass index, smoking status, alcohol use, diabetes mellitus, statin use, and baseline ham-d score, elevated triglycerides and low-density lipoprotein cholesterol remained independent predictors of higher ham-d scores at 12 months.

Table 3. Association between baseline lipid parameters and ham-d score at 12 months

Lipid parameter	Normal range (mean ham-d ± sd)	Abnormal range (mean ham-d ± sd)	Adjusted p-value
Ldl-c	8.7 ± 3.3	13.8 ± 4.7	0.002
Hdl-c	9.0 ± 3.6	12.3 ± 4.0	0.038
Triglycerides	8.2 ± 3.1	14.4 ± 5.1	<0.001
Total cholesterol	9.1 ± 3.7	11.7 ± 4.3	0.061

Longitudinal analysis of depression severity

Mixed-effects longitudinal analysis demonstrated that participants with dyslipidaemia experienced a slower reduction in ham-d scores over time compared with those with normal lipid profiles. The interaction between time and lipid status was statistically significant, indicating that lipid abnormalities influenced the trajectory of depressive symptom improvement during follow-up.

Relationship between changes in lipid parameters and ham-d scores

Participants who demonstrated improvement in serum lipid parameters over the 12-month period, particularly reductions in triglyceride levels and increases in high-density lipoprotein cholesterol, showed greater reductions in ham-d scores. Although the study was not designed to establish causality, the parallel improvement observed in lipid levels and depression severity suggests a dynamic association between metabolic status and depressive symptoms.

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Table 4. Relationship between changes in lipid parameters and reduction in ham-d scores

Lipid change over 12 months	Mean reduction in ham-d score ± sd	P-value
Improved triglycerides	6.1 ± 2.8	<0.001
No change in triglycerides	3.2 ± 2.4	
Increased hdl-c	5.7 ± 2.6	0.004
No increase in hdl-c	3.5 ± 2.3	

Discussion

The present prospective study demonstrates a significant association between serum lipid abnormalities and the severity of depressive symptoms assessed using the hamilton depression rating scale (HAM-D) over a 12-month follow-up period. Participants with elevated triglycerides and low-density lipoprotein cholesterol, as well as those with reduced high-density lipoprotein cholesterol, exhibited higher ham-d scores at follow-up and showed a slower improvement in depression severity over time. These findings suggest that dyslipidemia may influence not only the presence but also the persistence and clinical course of depressive symptoms.

Several previous studies have reported a relationship between lipid parameters and depressive disorders, supporting the biological plausibility of the present findings. Elevated triglyceride levels have been associated with increased inflammatory activity and oxidative stress, both of which are implicated in the neurobiology of depression [9]. Chronic low-grade inflammation may alter neurotransmitter metabolism and hypothalamic–pituitary–adrenal axis regulation, contributing to sustained depressive symptomatology. Similarly, elevated ldl cholesterol has been linked to endothelial dysfunction and impaired cerebral microcirculation, which may negatively affect brain regions involved in mood regulation [10].

Low levels of high-density lipoprotein cholesterol were also associated with greater depression severity in the current study. Hdl cholesterol plays an important role in antioxidant defense and anti-inflammatory processes. Reduced hdl levels may therefore enhance vulnerability to neuroinflammation and neuronal damage, which have been increasingly recognized as contributors to depressive disorders [11]. Previous clinical studies have reported similar associations between low hdl cholesterol and increased depressive symptoms, particularly in individuals with coexisting metabolic risk factors [12].

An important strength of this study is the use of ham-d, a clinician-rated scale, which provides a more objective assessment of depression severity compared to self-reported questionnaires. This approach reduces reporting bias and allows for more reliable longitudinal evaluation of symptom changes. The observed slower decline in ham-d scores among participants with dyslipidaemia suggests that metabolic abnormalities may adversely affect treatment response or natural recovery from depressive symptoms [13]. Such findings emphasize the need to consider metabolic health when monitoring depression outcomes.

The longitudinal nature of this study also allowed examination of changes in lipid parameters alongside changes in depression severity. Participants who showed improvement in triglyceride or hdl levels over time experienced greater reductions in ham-d scores. Although causality cannot be established, this parallel improvement supports the hypothesis of a dynamic interaction between metabolic status and mood regulation [14]. It raises the possibility that interventions targeting lipid abnormalities, such as lifestyle modification or pharmacological therapy, may have beneficial effects on depressive symptom trajectories.

Despite its strengths, the study has several limitations. The single-centre design may limit generalizability to other populations. Although ham-d is widely accepted for assessing depression severity, it does not establish a formal psychiatric diagnosis. Additionally, inflammatory markers, dietary intake, physical activity intensity, and psychosocial stressors were not measured, which may have influenced both lipid levels and depression severity [15]. Future studies incorporating these variables and involving larger, multicentric cohorts would help clarify the underlying mechanisms linking dyslipidaemia and depression.

Overall, the findings of this study support the growing body of evidence suggesting a meaningful association between metabolic disturbances and depression severity. Integrating metabolic evaluation into routine mental health assessment may help identify individuals at risk of persistent or severe depressive symptoms. Conversely, screening for depressive symptoms in patients with dyslipidaemia may facilitate early intervention and more comprehensive patient care.

Conclusion

This prospective study demonstrates that abnormalities in serum lipid profile are significantly associated with greater severity and persistence of depressive symptoms

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assessed using the hamilton depression rating scale over a 12-month follow-up period. Elevated triglycerides and low-density lipoprotein cholesterol, along with reduced high-density lipoprotein cholesterol, were linked to higher depression severity and a slower improvement in symptoms over time. Participants who showed improvement in lipid parameters during follow-up also experienced greater reductions in depression severity, suggesting a dynamic relationship between metabolic status and mood.

Although causal inferences cannot be drawn, these findings highlight the potential clinical relevance of metabolic evaluation in individuals presenting with depressive symptoms. Incorporating routine lipid profile assessment into mental health care may help identify patients at risk for persistent or severe depression, while screening for depressive symptoms in individuals with dyslipidaemia could facilitate earlier intervention. Further large-scale, multicentric studies incorporating additional biological and psychosocial markers are warranted to clarify underlying mechanisms and to determine whether targeted metabolic interventions can improve depressive outcomes.

Generalizability

The findings of this study may be generalizable to similar tertiary-care psychiatric settings in India, where metabolic disorders are increasingly prevalent. However, extrapolation to community populations or different ethnic groups should be undertaken cautiously due to the single-centre design.

Limitations

This study was conducted at a single tertiary-care centre, which may limit generalizability. The sample size was modest. Inflammatory markers and dietary factors were not assessed. Although ham-d is a validated severity scale, it does not independently confirm a psychiatric diagnosis. Residual confounding cannot be completely excluded.

Recommendations

Routine lipid profile screening should be considered in patients presenting with depressive symptoms. Integrated metabolic and psychiatric management strategies may improve long-term outcomes. Future multicentric studies incorporating inflammatory biomarkers are recommended.

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List of abbreviations

Ham-d – hamilton depression rating scale
LDL-C – low-density lipoprotein cholesterol
hdl-c – high-density lipoprotein cholesterol
TG – triglycerides
bmi – body mass index

Source of funding

The study received no external funding.

Conflict of interest

The authors declare no conflict of interest.

Availability of data

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Author contributions

Amardeep Kumar – conceptualization, data collection, manuscript drafting
Supriya Kumari – data analysis, manuscript revision
Amardeep Kumar (professor) – supervision, critical revision
Anant Kumar Verma – methodology guidance, final approval

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academic interests include mood disorders, psychopharmacology, and clinical research methodology.

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