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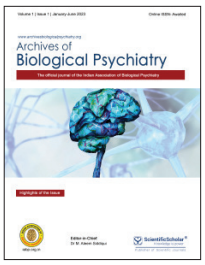

Original Article *Psychiatry*

Serum lipid level as a biomarker in depressive disorder: A cross-sectional case control study

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ABSTRACT

Objectives: This study investigates the potential of serum lipids as markers for depression, specifically focusing on symptoms such as suicidal ideation and anhedonia. In the context of advancing psychiatric biomarker research, this study aims to identify lipid-related markers and their underlying biological connections to depression, offering valuable insights for clinical practice and patient outcomes.

Material and Methods: This case-control observational study was conducted over 18 months at a tertiary care center. The study enrolled patients aged 18–60 years diagnosed with depression attending outpatient and inpatient departments, totaling 100 subjects, including 100 cases and 100 controls, with gender and body mass index (BMI)-matched controls. Inclusion criteria for cases required depression diagnosis using the International Classification of Diseases-10-Diagnostic Criteria for Research criteria, while controls comprised healthy individuals within the same age range. Exclusion criteria encompassed comorbid psychiatric illnesses, substance use disorders (except tobacco), unstable medical conditions, lipid-lowering agent use, and a BMI over 30. Clinical assessments, including the Hamilton Depression Rating Scale-17 item scale, Modified Scale for Suicidal Ideation, and Snaith-Hamilton Pleasure Scale-Clinician administered, were administered. Serum lipid parameters, including triglycerides (TG), total cholesterol (TC), and high-density lipoprotein (HDL)-cholesterol, were measured.

Results: In a cross-sectional case-control study (n = 200), we examined serum lipids as potential depression biomarkers. Cases (n = 100) matched controls in age, BMI, and gender. Cases had lower TC (153.27 mg/dL vs. 171.34 mg/dL, $P < 0.01$*). Serum TG and low-density lipoprotein also varied significantly with depression severity ($P < 0.01$*). However, HDL levels remained consistent. No significant associations were found between suicidal ideation and anhedonia, and *post hoc* analyses revealed significant differences ($P \leq 0.05$) in lipid parameters across various depression severity levels.

Conclusion: These findings suggest a complex relationship between serum lipids and depression, with potential implications for understanding the biological underpinnings of depression and its severity. However, there was no such relationship that was observed between serum lipids and anhedonia or suicidal ideation. These insights could inform clinical practices and improve patient outcomes in depression management.

Keywords: Depressive disorder, Serum lipid profiles, Suicidal behaviors, Anhedonia, Cholesterol-serotonin theory

INTRODUCTION

Depression is a widespread mental health disorder affecting a diverse range of people globally. According to estimates, it impacts roughly 350 million individuals worldwide.[1] A leading cause of disability, particularly among young adults (aged 25–49), depression ranks sixth in disability-

adjusted life years as of 2019.[2] The severity of depression varies considerably, ranging from mild to severe, and is determined by the intensity of symptoms and their impact on daily functioning.[3-5] Characterized by a combination of emotional, cognitive, and physical symptoms, depression manifests differently in each person.[3] Mounting research delves into the connections between depression and physiological factors, with a particular focus on abnormalities in lipid profiles.[6] Several studies suggest that individuals with depression might exhibit disruptions in their lipid profile levels.[7-9] For instance, Glueck *et al*. observed significantly lower levels of total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) in patients diagnosed with affective disorders encompassing depression.[10] Similarly, Olusi and Fido reported lower serum TC levels in patients with major depressive disorder (MDD) compared to a healthy control group. These findings suggest a potential association between low serum TC and depression across various age groups and genders. Anhedonia, a core symptom of depression, has also been linked to lipid profile abnormalities.[11] Moreira *et al*. reported elevated LDL levels in individuals with unipolar depression and anhedonia.[4] However, Su *et al*. found contrasting results, with depressed patients experiencing anhedonia having lower LDL levels compared to those without anhedonia. These conflicting findings highlight the intricate nature of the relationship between anhedonia, lipid profiles, and depressive symptoms, underscoring the need for further research to gain a comprehensive understanding.[12] Hopelessness, another prominent symptom of depression, has been suggested to influence lipid profile levels. A study by Fawcett *et al*. observed a potential association between hopelessness and elevated triglyceride and LDL levels.[13] Moreover, higher hopelessness scores correlated with a higher LDL to HDL ratio, indicating an unfavorable lipid profile.[14,15] These findings suggest a possible link between hopelessness and cardiovascular health, considering the established role of elevated triglycerides (TG) and LDL as risk factors for heart disease.[16] Cholesterol, a critical component of the lipid profile, plays a key role in various bodily processes. LDL cholesterol (LDL-C), often referred to as "bad cholesterol," transports cholesterol to peripheral tissues and contributes to atherosclerosis and cardiovascular diseases. Conversely, HDL cholesterol (HDL-C), known as "good cholesterol," helps eliminate excess cholesterol, thereby reducing cardiovascular risk. Imbalances in LDL-C and HDL-C levels are associated with increased cardiovascular risks among individuals with depression.[17,18]

Mechanisms underlying the relationship

The exact biological pathways connecting depression, anhedonia, hopelessness, and lipid profile abnormalities remain unclear.[19] Several hypotheses have emerged, including alterations within the neuroendocrine system, dysfunction of the hypothalamic-pituitary-adrenal axis (HPA axis), and epigenetic modifications influencing lipid metabolism.[20,21] Chronic stress, often found alongside depression, can lead to disruptions in cortisol levels, insulin resistance, and imbalances in lipid metabolism. Recent research sheds light on the complex interplay between epigenetic mechanisms, depression, and lipid dysregulation.[20] Epigenetic modifications, such as DNA methylation and histone acetylation, play a crucial role in shaping gene expression patterns relevant to both mood regulation and lipid metabolism.[21] Individuals with depression frequently exhibit epigenetic changes in genes associated with mood regulation and neurotransmitter function, impacting both depressive symptoms and lipid metabolism. Understanding these connections holds promise for developing comprehensive interventions targeting both psychological and physiological aspects of depression and its associated health risks.[21,22] Another proposed mechanism involves inflammation. The link between depression and chronic low-grade inflammation can have consequences for lipid metabolism. Inflammatory markers, such as C-reactive protein, influence lipid profile levels, including LDL-C and HDL-C. These inflammatory processes may disrupt the balance between cholesterol synthesis, absorption, and elimination, leading to dyslipidemia.[23,24] Dysregulation of neurotransmitters, particularly serotonin, might be a factor in the relationship between depression, anhedonia, hopelessness, and lipid profile abnormalities.[25] Serotonin's involvement in mood regulation and its altered levels in individuals with depression suggest that disturbances in serotonin signaling may affect lipid metabolism, contributing to changes in lipid profile levels.[14] Understanding the relationship between depression, anhedonia, hopelessness, and lipid profile levels holds significant clinical weight. Monitoring lipid profile levels in individuals with depression, particularly those experiencing anhedonia or hopelessness, could aid in the early identification of those at higher risk for cardiovascular diseases.[26] In addition, managing depression and its associated symptoms, such as anhedonia and hopelessness, may positively impact lipid profile levels and cardiovascular health.[27] Existing treatment modalities for depression encompass psychotherapy, antidepressant medications, and lifestyle modifications. Incorporating regular physical activity, a balanced diet, and stress reduction techniques can significantly benefit both depressive symptoms and lipid profile levels.[28-30]

This investigation uniquely concentrates on serum lipids as potential indicators for depression, spanning symptoms such as suicidal ideation and anhedonia. In the evolving field of psychiatric biomarker research, this study promises to reveal lipid-related markers and the underlying biological links to depression, offering valuable insights for clinical practice and patient outcomes.

MATERIAL AND METHODS

The primary objective of this case-control observational study is to investigate the potential of serum lipids as peripheral markers for depression. In addition, the study aims to explore the associations between serum lipids and two key aspects of depression: suicidal ideation and anhedonia. The study was conducted at a tertiary care center over 18 months. The study population consisted of patients diagnosed with depression, aged 18–60 years, attending the outpatient and inpatient departments. A sample size of 200 subjects, with 100 cases and 100 age matched controls, was selected for the study.

"Data analysis was performed using Statistical Package for the Social Sciences, version 28. Various statistical tests, including unpaired *t*-test, Chi-square, one-way Analysis of Variance (ANOVA), Analysis of Covariance (ANCOVA), Partial correlation analysis, and *post hoc* analysis-pairwise comparison (Bonferroni correction), were employed to analyze the data. $P < 0.05$ was considered significant for *t*-test, Chi-square, one-way ANOVA, and ANCOVA. However, the *P*-value for the *post hoc* analysis-pairwise comparison of lipids and depression - Bonferroni correction was done, and a corrected *P*-value of 0.002 was obtained. Corrected *P*-value = original alpha level (0.05)/No. of comparisons (6/lipid parameter × 4 parameters).

The sample size calculation was performed using the formula: N = (Z^2 × P × (1–P))/d^2, where Z^2 represents the table value of the alpha error from the Standard Normal Distribution table, which is 1.96 ×1.96, equaling 3.84. The desired power (P) was set at 0.05, and (1-P) was calculated as 0.95. The precision error of estimation (d) was determined as 5%, resulting in d^2 being 0.0025. Therefore, N = (3.84 × 0.05 × 0.95)/0.0025, which equals 73 (rounded off to 75). However, to increase the power of the study, a sample size of 100 patients per group was used, leading to a total sample size of 200 patients selected for the study. Cases were selected from the inpatient department and outpatient department of the psychiatry department at the medical college, while controls were recruited from attendants accompanying the patients and medical college staff who met the inclusion and exclusion criteria. Blood samples for serum lipid analysis were collected in the early morning after an overnight fast, and the blood was processed in the central laboratory of the medical college. "Outpatients were instructed to come to the hospital after an overnight fast of 8 h."

Inclusion criteria for cases required patients to be diagnosed with depression using the International Classification of Diseases-10-Diagnostic Criteria for Research, diagnostic criteria, and be between 18 and 60 years of age. (We had taken patients with a primary diagnosis of depression. We also included the patients with co-morbid anxiety as part of depressive symptoms). Controls included healthy individuals within the same age range. Exclusion criteria for both cases and controls involved participants with co-morbid psychiatric illnesses (except depression and depression with comorbid anxiety) or recent substance use disorders except tobacco use disorders, active unstable medical conditions, participants on lipid-lowering agents, and those with a body mass index (BMI) >30.

The methodology involved recruiting eligible participants who provided written informed consent. Clinical interviews were conducted, and height, weight, and BMI measurements were taken. The severity of depression was assessed using the Hamilton Depression Rating Scale-17 (HAMD-17) item scale, while suicidal ideation and anhedonia were evaluated using the Modified Scale for Suicidal Ideation (MSSI) and Snaith-Hamilton Pleasure Scale-Clinician administered (SHAP-C), respectively. Laboratory procedures were conducted to measure plasma levels of TG, TC, and HDL cholesterol.

RESULTS

The cases and controls had an average age of 38 years, and gender distribution was consistent between the two groups, comprising 44% males and 56% females in both. The mean BMI among the cases and the controls was 23.5. However, marital status did exhibit significance ($P = 0.003$ – Chi-square test), with most controls being married (72%) compared to cases (52%). Employment and education status did not significantly differ between cases and controls. We used the HAMD-17 item to quantify the severity of depression. In the case group, the mean HAMD score was 20.32, whereas it was 4.28 in the control group. Suicidal ideation in the case group was assessed using the MSSI, revealing a mean score of 14.84, with most cases (49%) reporting mild/moderate suicidal ideation. In addition, we evaluated hopelessness using the SHAPS-C in the case group, which yielded a mean score of 35.16.

Regarding the serum lipid levels, the case group demonstrated a statistically significant difference with the lower mean serum TC levels in comparison to the control group (153.27 mg/dL vs. 171.34 mg/dL, $P < 0.01$*- unpaired *t*-test). However, there were no statistically significant variances in other lipid parameters, including TG, HDL-C, and LDL-C, between the two groups.

In the case group, serum lipid parameters were analyzed using one-way ANOVA, stratified by severity levels of depression (HAMD-17 item score). Significant variations were found in TC, TG, and LDL levels across different depression severity ($P < 0.01$*). According to *post hoc* analysis, individuals with severe and very severe depression exhibited higher lipid levels compared to those with mild or moderate depression. However, no significant differences were observed in serum

HDL-C levels among these groups ($P = 0.14$), as mentioned in Table 1. *Post hoc* analysis – pairwise comparison in the case group, with a significance threshold of <0.002- corrected *P*-value (Bonferroni correction), highlighted substantial differences in lipid parameters based on depression severity. Comparison between mild to very severe depression showed high significance ($P \leq 0.002$), emphasizing the impact of mental health severity on lipid profiles as mentioned in Table 2.

Tables 3 and 4 collectively indicate that following rigorous statistical analyses—ANCOVA for suicidal ideation and Partial Correlation for anhedonia — no significant relationships were observed between various lipid parameters and both suicidal ideation and anhedonia.

Table 1 shows the analysis of serum lipid parameters in the case group (using one-way ANOVA) and stratified by the various severity levels of depression as measured by the HAMD-17 item score, revealing significant variations. Statistically significant differences were observed in serum TC, serum TG, and serum LDL levels among individuals with different severity levels of depression.

Table 2 shows the *post hoc* analysis of different depression severity levels in relation to serum cholesterol levels. The most significant variations were observed when comparing the following pairs: mild to very severe depression, moderate to severe depression, moderate to very severe depression, and severe to very severe depression. In all these cases, except for HDL, all lipid parameters exhibited high statistical significance ($P \leq 0.05$).

DISCUSSION

Our analysis of serum lipid profiles revealed significant distinctions between the case and control groups. Individuals diagnosed with depression exhibited notably lower TC levels compared to the control group. This finding aligns with the previous research by Terao *et al.*[31] and Khalid *et al.*,[32] suggesting a potential link between low TC and depression. However, it contrasts with the observations

Table 1: Serum Lipid parameters based on HAMD (17 item scale) score rating in case group.

Serum lipid parameters based on severity of depression in the case group					
	Mild depression (8–13)	**Moderate depression (14–18)**	**Severe depression (19–22)**	**Very severe depression (≥23)**	***P*-value**
Mean serum TC (mg/dL)	147.28+28.09	149.89+26.45	155.73+39.9	155.8+28.32	<0.01*
Mean serum TG (mg/dL)	102.57+24.19	109.17+22.06	120.7+21.81	111.8+24.18	<0.01*
Mean serum HDL-C (mg/dL)	51.21+7.53	49.51+8.05	52.42+7.15	50.39+7.44	0.14
Mean serum LDL-C (mg/dL)	77.57+21.52	82+19.03	86.52+26.2	86.15+26.67	<0.01*

HAMD: Hamilton Depression Rating Scale, TC: Total cholesterol, TG: Triglyceride, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, *: *P* value less than 0.05 (statistically significant).

Table 2: The *post hoc* analysis, which involves pairwise comparisons of depression severity with serum TG, serum LDL-C, and serum TC after detecting statistical significance in a one-way ANOVA.

Comparison of various severity of depression	***P*-value for TC level**	***P*-value of TG level**	***P*-value of LDL-C level**
Mild depression versus Moderate depression	0.15	0.16	0.08
Mild depression versus Severe depression	0.14	0.15	0.05
Mild depression versus Very severe depression	<0.001	<0.001	<0.01
Moderate depression versus Severe depression	0.04	0.03	<0.001
Moderate depression versus Very severe depression	<0.001	<0.001	<0.001
Severe depression versus Very severe depression	<0.001	<0.001	<0.001

ANOVA: Analysis of Variance, TC: Total cholesterol, TG: Triglyceride, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol

Table 3: Relationship of serum lipid parameters and suicidal ideation severity score after controlling the influence of depression severity on lipid parameters in case group: (P<0.05 considered significant by ANCOVA test).

	***P*-values for serum cholesterol levels**	***P*-values for serum TG levels**	***P*-values for serum HDL levels**	***P*-values for serum LDL levels**
Suicidality ideation severity	0.40	0.53	0.72	0.77

ANCOVA: Analysis of Covariance, TG: Triglyceride, HDL: High-density lipoprotein. LDL: Low-density lipoprotein.

Table 4: Partial correlation coefficient of anhedonia (assessed by SHAP-C) and lipid parameters by partial correlation analysis, $P<0.05$ considered significant, to control the effect of depression on lipid parameters.

	Partial Correlation coefficient (r)	*P*-value
Serum TC (mg/dL)	0.17	0.09
Serum TG (mg/dL)	0.18	0.08
Serum HDL-C (mg/dL)	0.02	0.84
Serum LDL-C (mg/dL)	0.15	0.14

TC: Total cholesterol, TG: Triglyceride, LDL-C: Low-density lipoprotein cholesterol, SHAP-C: Snaith-Hamilton Pleasure Scale-Clinician, HDL-C: High-density lipoprotein cholesterol.

of Olusi and Fido,[11] where no such correlation was identified.

Several explanations can be explored to understand the observed association between low serum cholesterol and depression. Cholesterol plays a critical role in cell membrane structure and influences cellular signaling processes. Alterations in cholesterol levels may modulate serotonin, a neurotransmitter implicated in mood regulation and depression. Reduced cell membrane cholesterol could lead to decreased exposure to serotonin receptors, resulting in poorer serotonin uptake and its reduced availability in the brain.[33,34] Dysregulation of the lecithin-cholesterol acyltransferase enzyme, involved in cholesterol metabolism, may also contribute to altered peripheral serum cholesterol levels. Dysfunction in serotonin release and abnormalities in lipid metabolism may be interconnected with depression, potentially leading to changes in serum lipid profiles.[35] The association between low serum lipid levels and depression might also be attributed to alterations in the HPA axis, known to be dysregulated in depression.[20] Dysfunctional HPA axis activity can lead to changes in lipid metabolism and potentially contribute to the severity of depressive symptoms. Conversely, increased stress-induced secretion of cholesterol in the liver, derived from the release of free fatty acids in adipose tissues, may contribute to higher serum cholesterol levels in some individuals with depression.[36] Dysfunctionality of sterol carrier protein 2, involved in cholesterol metabolism, could also play a role.[37]

Depression severity and lipid profile variations

Within the case group, individuals with mild depression exhibited lower levels of LDL-C, TG, and TC compared to those with moderate, severe, or very severe depression. This aligns with prior studies by Wagner *et al.*[37] and Rabe-Jabłońska and Poprawska.[38] Notably, the observed decrease in physical activity in individuals with severe depression may contribute to the lipid level differences.[39]

The cortisol theory posits that severe depression is associated with elevated cortisol levels stemming from HPA axis dysregulation. This heightened cortisol release in severe depression could induce chronic inflammation, potentially leading to increased cholesterol breakdown on cell membranes and subsequently elevating lipid levels in the circulation in severe depressive cases as compared to mild depression.[4] Our study did not identify a statistically significant relationship between serum lipid levels and anhedonia. Previous studies have also shown conflicting results regarding this association.[12]

More research is needed to understand the association between serum lipid levels and depression fully. The observed lower levels of serum cholesterol in individuals with depression suggest that lipid profiles may serve as potential biomarkers for depressive disorders. By elucidating the relationship between depression and lipid metabolism, we can advance our understanding of the pathophysiology of depression and develop more targeted interventions for its management.

Limitations

The study was conducted at a single tertiary care center, and the exclusion of other comorbid disorders might limit the generalizability of findings to other populations or settings. The study design limits the ability to establish a causal relationship between serum lipid levels and depression. Longitudinal studies would be beneficial to better understand the temporal nature of these associations. The study did not consider other variables that could influence serum lipid levels and depression, such as dietary habits, physical activity, and medication use. Controlling these factors in future studies would enhance the validity of the findings. The study only assessed serum lipid levels and depressive symptoms at a single time point. Following the participants over a longer duration would provide insights into the stability and fluctuations of these markers.

CONCLUSION

The present study indicates a potential association between low serum lipid levels, specifically TC and LDL-C, and depressive symptoms. The findings contribute to the growing body of literature on the relationship between lipid metabolism and depression, supporting the notion that disturbances in cholesterol metabolism may play a role in the pathophysiology of depression. However, the lack of a significant correlation between serum lipid levels and anhedonia suggests that different biological mechanisms may underlie this specific symptom of depression.

Future directions

The longitudinal studies would provide a better understanding of the temporal relationship between serum lipid levels and depression, as well as the potential predictive

value of lipid markers in the development and progression of depressive symptoms. This approach would provide valuable insights into whether fluctuations in serum lipid levels precede or coincide with the onset of depression. To gain a more comprehensive perspective on the relationship between serum lipid levels and depression, it is crucial to consider additional factors in multivariate analyses. These factors may include lifestyle elements such as diet and exercise, genetic predispositions, and medication usage. By accounting for these variables, researchers can discern the independent contribution of serum lipids to depression. This holistic approach will enhance the accuracy of the findings and help in better understanding the complex interplay between lipid metabolism and depressive symptoms. This knowledge will not only deepen our understanding of the biochemical basis of depression but also identify potential targets for intervention and treatment strategies. Moreover, they can help establish causality and guide clinicians and policymakers in developing effective treatment approaches that consider lipid metabolism as a modifiable factor in depression management.

Ethical approval

The research/study approved by the Institutional Review Board at H.B.T. Medical College and Dr. R.N Municipal General Hospital, Mumbai, Number 012/2019, dated 21/6/2019.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. World Health Organization. The world health report 2001-mental health: New understanding, new hope. Geneva: World Health Organization; 2013.
2. World Health Organization. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020;396:1204-22.
3. World Health Organization. The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
4. Moreira FP, Jansen K, Cardoso TA, Mondin TC, Vieira IS, Magalhães PV, *et al*. Metabolic syndrome, depression and anhedonia among young adults. Psychiatry Res 2019;271:306-10.
5. Regier DA, Kuhl EA, Kupfer DJ. The DSM-5: Classification and criteria changes. World Psychiatry 2013;12:92-8.
6. Huang TL, Wu SC, Chiang YS, Chen JF. Correlation between serum lipid, lipoprotein concentrations, and anxious state, depressive state, or major depressive disorder. Psychiatry Res 2003;118:147-53.
7. Maes M, Smith R, Christophe A, Vandoolaeghe E, Van Gastel A, Neels H, *et al*. Lower serum high-density lipoprotein cholesterol (HDL-C) in major depression and in depressed men with serious suicidal attempts: Relationship with immune-inflammatory markers. Acta Psychiatr Scand 1997;95:212-21.
8. Partonen T, Haukka J, Virtamo J, Taylor PR, Lönnqvist J. Association of low serum total cholesterol with major depression and suicide. Br J Psychiatry 1999;175:259-62.
9. Apter A, Laufer N, Bar-Sever M, Har-Even D, Ofek H, Weizman A. Serum cholesterol, suicidal tendencies, impulsivity, aggression, and depression in adolescent psychiatric inpatients. Biol Psychiatry 1999;46:532-41.
10. Glueck CJ, Kunkel R, Tieger M. Pathophysiologic relationships and linkage among triglycerides, hypocholesterolemia, and depression. In: Lipids, health, and behavior. United States: American Psychological Association; 2004. p. 99-112. Available from: https://www.record/1997-97127-005 [Last accessed on 2020 Jun 27].
11. Olusi SO, Fido AA. Serum lipid concentrations in patients with major depressive disorder. Biol Psychiatry 1996;40:1128-31.
12. Su M, Li E, Tang C, Zhao Y, Liu R, Gao K. Comparison of blood lipid profile/thyroid function markers between unipolar and bipolar depressed patients and in depressed patients with anhedonia or suicidal thoughts. Mol Med 2019;25:51.
13. Fawcett J, Busch KA, Jacobs D, Kravitz HM, Fogg L. Suicide: A four-pathway clinical-biochemical model. Ann N Y Acad Sci 1997;836:288-301.
14. Papakostas GI, Öngür D, Iosifescu DV, Mischoulon D, Fava M. Cholesterol in mood and anxiety disorders: Review of the literature and new hypotheses. Eur Neuropsychopharmacol 2004;14:135-42.
15. Penttinen J. Hypothesis: Low serum cholesterol, suicide, and lnterleukin-2. Am J Epidemiol 1995;141:716-8.
16. Rujescu D, Thalmeier A, Möller HJ, Bronisch T, Giegling I. Molecular genetic findings in suicidal behavior: What is beyond the serotonergic system? Arch Suicide Res 2007;11:17-40.
17. Dietschy JM, Turley SD. Cholesterol metabolism in the central nervous system during early development and in the mature animal. J Lipid Res 2004;45:1375-97.
18. Gupta A, Jadhav AA, Petkar SB, Dubey V. Study of lipid

derangement in pyschiatric disorder. Ind Med Gaz 2013;147:253-6.
19. Maes M. The cytokine hypothesis of depression: Inflammation, oxidative and nitrosative stress (IO&NS), and leaky gut as new targets for adjunctive treatments in depression. Neuro Endocrinol Lett 2008;29:287-91.
20. Cassano WJ Jr., D'Mello AP. Acute stress-induced facilitation of the hypothalamic-pituitary-adrenal axis: Evidence for the roles of stressor duration and serotonin. Neuroendocrinology 2001;74:167-77.
21. Pandey A, Rizwan M. Epigenetic mechanisms of depression and lipid dysregulation. Curr Opin Lipid 2021;32:545-53.
22. Li Y, Wang Y, Wang Y, Dong Y. Epigenetics of depression and lipid metabolism: A systematic review of the literature. Front Psychiatry 2022;13:803260.
23. Steegmans PH, Hoes AW, Bak AA, Van Der Does E, Grobbee DE. Higher prevalence of depressive symptoms in middle-aged men with low serum cholesterol levels. Psychosom Med 2000;62:205-11.
24. Brunner J, Parhofer KG, Schwandt P, Bronisch T. Cholesterol, essential fatty acids, and suicide. Pharmacopsychiatry 2002;35:1-5.
25. Stewart JC, Rand KL, Muldoon MF, Kamarck TW. A prospective evaluation of the directionality of the depression-inflammation relationship. Brain Behav Immun 2009;23:936-44.
26. Hu P, Seeman TE, Harris TB, Reuben DB. Does inflammation or undernutrition explain the low cholesterol-mortality association in high-functioning older persons? MacArthur Studies of Successful Aging. J Am Geriatr Soc 2003;51:80-4.
27. Nakao M, Ando K, Nomura S, Kuboki T, Uehara Y, Toyooka T, *et al*. Depressive mood accompanies hypercholesterolemia in young Japanese adults. Jpn Heart J 2001;42:739-48.
28. Ghanizadeh A, Hedayati A. Augmentation of fluoxetine with lovastatin for treating the major depressive disorder, a randomized, double-blind placebo controlled-clinical trial. Depress Anxiety 2013;30:1084-8.
29. Haghighi M, Khodakarami S, Jahangard L, Ahmadpanah M, Bajoghli H, Holsboer-Trachsler E, *et al*. In a randomized, double-blind clinical trial, adjuvant atorvastatin improved symptoms of depression and blood lipid values in patients suffering from severe major depressive disorder. J Psychiatr Res 2014;58:109-14.
30. Parsaik AK, Singh B, Murad MH, Singh K, Mascarenhas SS, Williams MD, *et al*. Statins use and risk of depression: A systematic review and meta-analysis. J Affect Disord 2014;160:62-7.
31. Terao T, Yoshimura R, Ohmori O, Takano T, Takahashi N, Iwata N, *et al*. Effect of serum cholesterol levels on meta-chlorophenyl piperazine-evoked neuroendocrine responses in healthy subjects. Biol Psychiatry 1997;41:974-8.
32. Khalid A, Lal N, Trivedi JK, Dalal PK, Asthana OP, Srivastava JS, *et al*. Serum lipids as new biological markers in depression? Ind J Psychiatry 1998;40:217-23.
33. Scanlon SM, Williams DC, Schloss P. Membrane cholesterol modulates serotonin transporter activity. Biochemistry 2001;40:10507-13.
34. Steinmetz A, Hocke G, Saïle R, Puchois P, Fruchart JC. Influence of serum amyloid A on cholesterol esterification in human plasma. Biochim Biophys Acta 1989;1006:173-8.
35. McCann BS, Magee MS, Broyles FC, Vaughan M, Albers JJ, Knopp RH. Acute psychological stress and epinephrine infusion in normolipidemic and hyperlipidemic men: Effects on plasma lipid and apoprotein concentrations. Psychosom Med 1995;57:165-76.
36. Papakostas GI, Petersen T, Mischoulon D, Hughes ME, Alpert JE, Nierenberg AA, *et al*. Serum cholesterol and serotonergic function in major depressive disorder. Psychiatry Res 2003;118:137-45.
37. Wagner CJ, Musenbichler C, Böhm L, Färber K, Fischer AI, von Nippold F, *et al*. LDL cholesterol relates to depression, its severity, and the prospective course. Prog Neuropsychopharmacol Biol Psychiatry 2019;92:405-11.
38. Rabe-Jabłońska J, Poprawska I. Levels of serum total cholesterol and LDL-cholesterol in patients with major depression in acute period and remission. Med Sci Monit 2000;6:539-47.
39. Cantarelli MG, Tramontina AC, Leite MC, Gonçalves CA. Potential neurochemical links between cholesterol and suicidal behavior. Psychiatry Res 2014;220:745-51.

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