Journal of Anxiety & Depression

Yumed Text
OPEN ACCESS JOURNALS

Editorial | Vol 5 Iss 1
ISSN: 2582-3264
https://dx.doi.org/10.46527/2582-3264.e101

Dyslipidemia as a Risk Factor for Suicidal Behavior

Yury Evgeny Razvodovsky*

Institute Biochemistry of Biologically Active Substances, Academy of Science of Belarus, Grodno, Belarus

***Corresponding author:** Razvodovsky YE, Institute Biochemistry of Biologically Active Substances, Academy of Science of Belarus, Grodno, Belarus, Tel: +375 17 284-18-01; E-mail: yury_razvodovsky@mail.ru

Received: June 27, 2022; **Accepted:** June 28, 2022; **Published:** June 30, 2022

Keywords: ***Dyslipidemia; Cholesterol; Suicidal behavior***

The present paper aims at a systematic review of the current knowledge on the relationship between dyslipidemia and the risk of suicidal behavior. Studies examining the relationship between lipid profile and risk of parasuicide/suicide show conflicting results. Most of the data suggest that dyslipidemia, especially low cholesterol, is a risk factor for suicidal behavior. Further investigation is needed into the possibility of using dyslipidemia as a marker of suicidal behavior.

Currently, there is a lot of data indicating the existence of an association between dyslipidemia and suicidal behavior [1-9,10-29]. For the first time, a possible link between plasma lipid profile and suicidal behavior was noticed after reports of an increase in suicide rates among people taking cholesterol-lowering drugs [30]. Even after the publication of the results of a meta-analysis, which showed that statin use does not increase the risk of violent death (suicide, murder, fatal injuries) [31,32], researchers have not lost interest in this problem.

The results of most studies suggest that dyslipidemia, in particular low cholesterol, is a risk factor for suicidal behavior [25,26,33-39,40-46]. A meta-analysis of works devoted to this problem showed that in patients suffering from depression and who made a suicide attempt, the level of triglycerides (TG), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) in blood plasma is lower than in depressed patients, who did not commit parasuicide [43].

Lester found lower plasma cholesterol levels in parasuicidal individuals compared to those who did not attempt suicide, and also showed that low cholesterol levels are a risk factor for completed suicide [19]. Papapolou et al. found that suicidal risk decreases as cholesterol levels rise, regardless of gender and age [29]. Olie et al. showed that low cholesterol increased the risk

of suicide by 7.3 times in men and 15.6 times in women [26]. Wu et al calculated that low cholesterol increased the risk of parasuicide by 123% and the risk of completed suicide by 85% [43].

There is also evidence that low cholesterol is associated with increased impulsivity and is a predictor of the likelihood of using highly lethal methods of parasuicide [32]. It has been established that the level of cholesterol in those who have made a suicide attempt by a highly lethal method is significantly lower than in those who have committed parasuicide in a non-violent way [3].

Currently, the most recognized is the serotonin hypothesis, which explains the high risk of suicidal behavior in hypocholesterolemia, proposed in 1992 by Engelberg [11]. As is known, insufficient activity of the central serotonergic system is associated with increased impulsivity, aggressiveness, and suicidal behavior [28]. A number of studies have shown a low level of the end product of serotonin degradation, 5-hydroxyindoleacetic acid, in the cerebrospinal fluid of parasuicidal and suicide patients [4,28]. Cholesterol is an important structural component of the neuronal membrane, which determines its fluidity, which affects the functioning of membrane-bound proteins, ion channels, and synaptic signal transmission [28]. The affinity of 5-HT1A receptors for serotonin is also regulated by the degree of neuronal membrane fluidity [7]. Hypocholesterolemia increases membrane fluidity, which leads to a decrease in the binding of serotonin and G-protein to 5-HT1A receptors [33,34,41]. The serotonin hypothesis is supported by data indicating a positive relationship between cholesterol levels and the concentration of 5-hydroxyindoleacetic acid in the cerebrospinal fluid of parasuicides, which remained statistically significant after adjusting for sex, age, and other variables [4].

An additional mechanism may be steroid modulation of the activity of the central serotonergic system. It is known that such cholesterol derivatives as testosterone and corticosteroids reduce the sensitivity of 5-HT1A receptors, thus increasing aggressiveness, impulsivity, and, accordingly, the risk of suicide [28]. In addition, low cholesterol levels can reduce the activity of the central serotonergic system, causing inflammation in the brain [21]. The mechanism of the pro-inflammatory effect of hypocholesterolemia is a decrease in the ratio between omega-6-polyunsaturated fatty acids, which have pro-inflammatory properties, and omega-3-polyunsaturated fatty acids, which have anti-inflammatory properties [23].

In some studies, published recently, the involvement of cholesterol in the etiology of suicidal behavior is questioned [31]. A retrospective study of 213 patients with affective disorders showed no difference in cholesterol levels between parasuicidal and non-parasuicidal patients [1]. Another study demonstrated the absence of differences in the lipid profile of depressed patients who made and did not make a suicide attempt [10].

Moreover, a number of studies have shown that the risk of committing a suicide attempt increases with an increase in the level of cholesterol in the blood plasma. A study of 193 American men who attempted suicide and 1091 men who did not commit parasuicide found that high total cholesterol increased the risk of parasuicide [37]. A positive association between high cholesterol and the risk of suicide was found in a study of 7.309 Japanese American men [20]. In a large sample of the general population, it has been shown that the relative risk of committing violent suicide in the group with the highest level of total cholesterol is twice as high as in the group with the lowest level of total cholesterol [40]. Kim et al. found that both hypercholesterolemia and hypocholesterolemia provoke suicidal thoughts in the elderly [16].

There are several possible mechanisms for the association between hypercholesterolemia and the risk of suicidal behavior. It is assumed that people with high cholesterol levels are prone to maladaptive eating behavior (overeating), which may be one of the symptoms of depression, which is a risk factor for suicide [18]. Perhaps this relationship is explained by the fact that an atherogenic lipid profile increases the likelihood of stroke, which increases the risk of suicidal behavior [42]. An abnormal lipid profile may be a sign of other metabolic disorders associated with a high risk of suicidal behavior. One of the mediators of the association between lipids and suicidal activity may be omega-3 polyunsaturated fatty acids, low levels of which are associated with depression and suicidal behavior [23]. Because there is an inverse relationship between omega-3 polyunsaturated fatty acids and total cholesterol/HDL ratio, subjects with high cholesterol, low HDL and omega-3 polyunsaturated fatty acids are at high risk of suicide [23]. It has also been established that hypercholesterolemia increases the activity of monoamine oxidase (MAO) types A and B, thus increasing the risk of depression [28].

Proatherogenic (TC, triglycerides, LDL, HDL) and antiatherogenic lipids (HDL) may play different roles in the etiology of suicidal behavior. Studies investigating the relationship between lipid levels and the risk of parasuicide/suicide show conflicting results. Segoviano-Mendoza et al. found high TG levels in depressed patients who attempted suicide [37], which contrasts with the results of another study in which the risk of parasuicide was associated with low TG levels [47]. The higher VLDL found in depressed patients compared to healthy controls found in one study [44] is inconsistent with another study showing that the risk of depression increases with low VLDL [45]. A meta-analysis of 36 studies confirmed the association between low LDL levels and the risk of depression [32]. Other work has shown that both low and high LDL levels are associated with a high risk of parasuicide in depressed patients [22]. Data on the relationship between HDL levels and the risk of suicidal behavior are also controversial. One study found no difference in HDL levels between suicidal and non-committed depressed patients [32], while in another study low HDL levels were associated with the risk of suicidal attempts in women [46].

In conclusion, studies examining the relationship between lipid profile and risk of parasuicide/suicide show conflicting results. Therefore, the exact nature of the association between lipid profile and risk of suicidal behavior remains unclear. Accumulating evidence suggests that changes in cholesterol levels in both directions increase the risk of suicidal behavior. The gender aspect of the relationship between dyslipidemia and suicidal behavior remains underdeveloped, since most of the studies on this problem have been performed with the participation of men. Further investigation is needed into the possibility of using dyslipidemia as a marker of suicidal behavior.

REFERENCES

1. Ahmadpanah M, Haghighi M, Jahangard L, et al. No evidence for metabolic syndrome and lipid profile differences in patients suffering from bipolar I disorder with and without suicide attempts. Int J Psychiatry Clin Pract. 2015;19(3):168-73.
2. Almeida-Montes LG, Valles-Sanchez V, Moreno-Aguilar J, et al. Relation of serum cholesterol, lipid, serotonin and tryptophan levels to severity of depression and to suicide attempts. J Psychiatry Neurosci. 2000;25(4):371-7.
3. Alvarez JC, Cremniter D, Lesieur P, et al. Low blood cholesterol and low platelet serotonin levels in violent suicide attempters. Biol Psychiatry. 1999;45(8):1066-9.
4. Asberg M, Träskman L, Thorén P. 5-HIAA in the cerebrospinal fluid. A biochemical suicide predictor? Arch Gen Psychiatry. 1976;33(10):1193-7.

5. Baek JH, Kang ES, Fava M, et al. Serum lipids, recent suicide attempt and recent suicide status in patients with major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2014;51:113-8.
6. Bartoli F, Crocamo C, Dakanalis A, et al. Association between total serum cholesterol and suicide attempts in subjects with major depressive disorder: Exploring the role of clinical and biochemical confounding factors. Clin Biochem. 2016;50(6):274-8.
7. Cantarelli MG, Tramontina AC, Leite MC, et al. Potential neurochemical links between cholesterol and suicidal behavior. Psychiatry Res. 2014;220(3):745-51.
8. Chen Y, Hong W. The relationship between the suicidal behavior of depressed patient and the level decline of serum, LDL and HDL cholesterols. Sichuan Mental Health. 2003;16:76-8.
9. De LJ, Mallory P, Maw L, et al. Lack of replication of the association of low serum cholesterol and attempted suicide in another country raises more questions. Ann Clin Psychiatry. 2011;23(3):163-70.
10. Deisenhammer EA, Kramer-Reinstadler K, Liensberger D, et al. No evidence for an association between serum cholesterol and the course of depression and suicidality. Psychiatry Res. 2004;121(3):253-61.
11. Engelberg H. Low serum cholesterol and suicide. Lancet. 1992;339(8795):727-9.
12. Golier JA, Marzuk PM, Leon AC, et al. Low serum cholesterol level and attempted suicide. Am J Psychiatry. 1995;152(3):419-23.
13. Guo X, Xu M, Shi T, et al. Serum levels of cholesterol, lipoproteins and apolipoproteins in patients with depressive disorder and their significance. Chin J of Behavioral Med Sci. 2006;15:137.
14. Heron DS, Shinitzky M, Hershkowitz M, et al. Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. Proc Natl Acad Sci USA. 1980;77(12):7463-7.
15. Huang TL. Serum lipid profiles in major depression with clinical subtypes, suicide attempts and episodes. J Affect Disord. 2005;86(1):75-9.
16. Kim Y. Clinical application of low serum cholesterol as an indicator for suicide risk in major depression. J Affective Disord. 2004;81(2):161-6.
17. Lee BH, Kim YK. Potential peripheral biological predictors of suicidal behavior in major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2011;35(4):842-7.
18. Lee HJ, Kim YK. Serum lipid levels and suicide attempts. Acta Psychiatr Scand. 2003;108(3):215-21.
19. Lester D. Serum cholesterol levels and suicide: a meta-analysis. Suicide Life Threat Behav. 2002;32(3):333-46.
20. Li H, Zhang X, Sun Q, et al. Association between serum lipid concentrations and attempted suicide in patients with major depressive disorder: A meta-analysis. PLoS ONE. 2020;15(12):e0243847.
21. Luo T, He Y, He H, et al. Research of serum lipid, CK and LDH levels in patients with depressive disorder. J Sichuan Univ (Med Sci EDI). 2015;46:788-90.
22. Ma YJ, Zhou YJ, Wang DF, et al. Association of Lipid Profile and Suicide Attempts in a Large Sample of First Episode Drug-Naive Patients with Major Depressive Disorder. Front Psychiatry. 2020;11:543632.
23. Maes M, Christophe A, Delanghe J, et al. Lowered omega3 polyunsaturated fatty acids in serum phospholipids and cholesteryl esters of depressed patients. Psychiatry Res. 1999;85(3):275-91.
24. Maes M, Smith R, Christophe A, 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 Psychiatrica Scandinavica. 1997;95(3):212-21.

25. Messaoud A, Mensi R, Mrad A, et al. Is low total cholesterol levels associated with suicide attempt in depressive patients? Ann Gen Psychiatry. 2017;16:20.
26. Olie E, Picot MC, Guillaume S, et al. Measurement of total serum cholesterol in the evaluation of suicidal risk. J Affect Disord. 2011;133(1-2):234-8.
27. Paila YD, Murty MR, Vairamani M, et al. Signaling by the human serotonin1A receptor is impaired in cellular model of Smith-Lemli-Optiz Syndrome. Biochim Biophys Acta. 2008;1778(6):1508-16.
28. Pandey GN. Biological basis of suicide and suicidal behavior. Bipolar Disord. 2013;15(5):524-41.
29. Papadopoulou A, Markianos M, Christodoulou C, et al. Plasma total cholesterol in psychiatric patients after a suicide attempt and in follow-up. J Affect Disord. 2013;148(2-3):440-3.
30. Papakostas GI, Ongur D, Iosifescu DV, et al. Cholesterol in mood and anxiety disorders: review of the literature and new hypotheses. Eur Neuropsychopharmacol. 2004 Mar;14(2):135-42.
31. Park S, Yi KK, Na R, et al. No association between serum cholesterol and death by suicide in patients with schizophrenia, bipolar affective disorder, or major depressive disorder. Behav Brain Funct. 2013;9:45.
32. Persons JE, Fiedorowicz JG. Depression and serum low-density lipoprotein: A systematic review and meta-analysis. J Affect Disord. 2016;206:55-67.
33. Pucadyil TJ, Chattopadhyay A. Cholesterol depletion induces dynamic confinement of the G-protein coupled serotonin1A receptor in the plasma membrane of living cells. Biochim Biophys Acta. 2007;1768(3):655-68.
34. Pucadyil TJ, Chattopadhyay A. Cholesterol modulates the ligand binding and G-protein coupling to serotonin1A receptors from bovine hippocampus. Biochim Biophys Acta. 2004;1663(1-2):188-200.
35. Rabejabłońska 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(3):539-47.
36. Sarchiapone M, Roy A, Camardese G, et al. Further evidence for low serum cholesterol and suicidal behaviour. J Affective Disorders. 2000;61(1-2):69-71.
37. Segoviano-Mendoza M, Cruz CDL, Salas-Pacheco J, et al. Hypocholesterolemia is an independent risk factor for depression disorder and suicide attempt in Northern Mexican population. BMC Psychiatry. 2018;18(1):7.
38. Shrivastava S, Pucadyil TJ, Paila YD, et al. Chronic cholesterol depletion using statin impairs the function and dynamics of human serotonin1A receptors. Biochemistry. 2010;49(26):5426-35.
39. Sullivan PF, Joyce PR, Bulik CM, et al. Total cholesterol and suicidality in depression. Biological Psychiatry. 1994;36(7):472-7.
40. Svensson T, Inoue M, Sawada N, et al. High serum total cholesterol is associated with suicide mortality in Japanese women. Acta Psychiatr Scand. 2017;136(3):259-68.
41. Tripodianakis J, Markianos M, Sarantidis D, et al. Biogenic amine turnover and serum cholesterol in suicide attempt. Eur Arch Psychiatry Clin Neurosci. 2002;252(1):38-43.
42. Tzavellas E, Karaiskos D, Paparrigopoulos T. Triglycerides, Depression, and Risk of Ischemic Stroke. Jama. 2009;3011338-1339.
43. Wu S, Ding Y, Wu F, et al. Serum lipid levels and suicidality: a meta-analysis of 65 epidemiological studies. J Psychiatry Neurosci. 2016;41:56-69.
44. Yu C, Ji D, Liu Y, et al. Research of serum total cholesterol concentration in depressive patients with attempted suicide. J Clin Psychiatry. 2008;18:339-40.

45. Zhang J, McKeown RE, Hussey JR, et al. Low HDL cholesterol is associated with suicide attempt among young healthy women: the Third National Health and Nutrition Examination Survey. J Affect Disord. 2005;89(1-3):25-33.
46. Zhao H, Cui S, Duan Y, et al. Low serum cholesterol and depression with suicidal behavior in women. Chin J Nerv Ment Dis. 2000;26:78-80.