



A REVIEW ON THE INCONSISTENT RELATIONSHIP BETWEEN CHOLESTEROL AND SUICIDE

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ABSTRACT

Cholesterol is a key component of the central nervous system, as it is required for cell membrane stability and proper neurotransmission. Any substance shows its biological effect within normal range; exceeding the normal range or below the range shows unwanted effects, similar with the levels of body cholesterol levels. Many of the hypothesis came out to show that low levels of serum cholesterol in blood leads to suicidal and violent behaviour in mood disorders. Some of the studies have proven that low cholesterol levels lead suicidal attempt of individuals, as low cholesterol leads to improper uptake of serotonin and low membrane viscosity of brain which leads to mood depressive disorders and which further provokes to suicidal behaviour. Relationship between serum cholesterol and suicidality, on the other hand, have been questioned in recent years, based on the findings of a few recent studies that showed no link. However, the discussion over the link between cholesterol and suicide is still ongoing, and longitudinal studies including a larger sample of patients are needed to better elucidate this crucial subject. The objective of our paper is to assess the relationship between levels of serum cholesterol and individuals attempting suicide.

Keywords: Cholesterol, Suicide, Serotonin, Neurotransmission/Neuron communication, Mood disorders

INTRODUCTION

Suicide is a worldwide occurrence, accounting for 1.4% of all deaths, making it the 17th greatest cause of death [1]. Suicide and non-fatal suicidal behaviours are leading causes of death and morbidity around the world, showing that both suicide and non-fatal suicidal behaviours must be treated as a serious health concern [2].

According to a prior study by Harwood D, Hawton K, Hope T et al. 77% of people who committed suicide had a mental illness at the time of death, the most common of which was depression (63%). Some of the previous research has found that people with depression had a high risk of suicide ideation and attempt, both of which have been linked to complete suicide. However, the exact parameters linked to suicide attempts in patients with major depressive disorder (MDD) are unknown [3]. Suicide is one of the most common side effects of mental illnesses, thus finding new indicators could be useful in clinical practice [4].

Cholesterol is a chemical found in almost all body tissues that is essential for the regular function of cell membranes. It is required by the human brain to wrap around nerves in many of the brain's essential activities [3]. It has a wide range of neurobiological implications for the central nervous system which is a component of the second messenger system

and plays an important role in neuronal protection, membrane stability, lipid metabolism and proper neurotransmission.

It is also been related to norepinephrine and serotonin levels in the brain in an indirect way. It has been linked to the mechanism of action of antidepressants and mood stabilizers and could be implicated in the etiology and pathogenesis of mood disorders [5-7].

The major dietary lipid group, cholesterol was found to be significantly linked to suicidal behaviour and an increased risk of suicide in several studies. Lower cholesterol levels have been linked to higher levels of sadness, anger and impulsivity. All of these have been linked to a rise in suicidal attempts [8,9].

The link between lipid/cholesterol levels and suicide behavior/attempt in particular has gotten a lot of attention. However, the outcomes have been mixed. For example, one study identified a link between suicide and both high-density lipoprotein (HDL) and very low-density lipoprotein (VLDL) levels, while another found no link [3].

Scientists have debated the significance of lipids in the function of the serotonergic system for many years. In 1992, Engelberg proposed a link between low cholesterol levels and serotonergic system dysfunction. Low cholesterol levels, he believes, may contribute to changes in cell membrane

fluidity, which may impact receptor functioning, enzyme activity, and transmembrane transport, including serotonin reuptake in brain cells and that further provokes to suicidal behaviour [10]. Since 1990, when Muldoon et al. first revealed that treatments able to lower cholesterol levels may attenuate the excess of suicidal behaviours and injury deaths in their sample, the link between low total cholesterol and cholesterol metabolites in serum and higher suicide risk has been explored [2].

STUDIES THAT IDENTIFIED A CORRELATION BETWEEN CHOLESTEROL AND SUICIDE

MD. Gallerani et al. reported data from 331 parasuicides in a controlled population and discovered that this group had reduced cholesterol levels. In a study of 90 men and women with MD, Sullivan et al. looked at the link between total cholesterol and suicidality and discovered a substantial link between decreased cholesterol levels and greater suicidality. These findings were verified by Kunugi et al., who discovered a link between low serum cholesterol and suicide attempts, and by Papas Sotiropoulos et al., who found that increasing total cholesterol levels reduced the incidence of acute suicidality regardless of age, gender or nutritional status. Tripodianakis et al. reported decreased serum cholesterol in violent suicide attempters, as well as an

increase in noradrenaline turnover in these individuals, confirming this idea [6].

Lower serum cholesterol levels have been linked to aggressive suicide attempts, which appears to be related to schizophrenia. Marcinko et al. discovered that schizophrenia patients who attempted suicide violently had significantly lower cholesterol and significantly greater cortisol levels than patients who attempted suicide nonviolently and control participants [6].

An exploratory cross-sectional clinical study by Ma YJ, Wang DF, Yuan M et al. found a high frequency of recent suicide attempts (20.14%) among depressed inpatients, which was comparable with prior findings in the Chinese population of 18.5–23.5% suicide attempt rate in patients with major depressive illness. Patients who attempted suicide had a longer duration of illness, more psychotic symptoms, lower LDL (Low Density Lipoprotein) cholesterol, and lower total cholesterol than non-attempters [3].

A cross sectional study by Capuzzi E, Caldiroli A, Capellazzi M et al. comprised 163 people who had recently attempted suicide and were admitted to the hospital. In the 72 hours leading up to admission, about a third of the participants had attempted suicide violently. In total, 17 people had schizophrenia, 19 had bipolar illness, 37 had major depressive disorder, and 90 had a personality disorder. In

patients with mental illnesses, low cholesterol, LDL, and VLDL were linked to a violent method of suicide attempt [4]. Early psychosis is associated with a high likelihood of suicide, according to some studies. A cross-sectional, naturalistic cohort study at a tertiary general psychiatric center by Shrivastava A, Johnston M, Campbell R found that 26 early psychosis patients (43.3%) shown high suicidality scores on the SIS-MAP (Scale for Impact of Suicidality – Management, Assessment and Planning of Care) scale. When compared to the high suicidality group, the patients with higher suicidality had lower serum cholesterol levels. Their findings suggest that cholesterol may play a key role in distinguishing suicidal from nonsuicidal patients, a finding that, if verified in a larger number of patients and future research, might have major clinical implications [5].

Ainiyet B, Rybakowski JK conducted a clinical assessment study among 148 (69 male, 79 females.) schizophrenia patients with the mean age of 32 ± 10 years; all individuals were admitted recently for suffering with mental illness. Suicide mortality in people with schizophrenia is about 4 to 5% of the time, which is greater than the overall population. The result of their study shown that suicidal thoughts and attempts were found to be linked to low total cholesterol, LDL cholesterol,

triglycerides and total lipids in both male and female patients [11].

Even after accounting for age, gender, Body Mass Index (BMI) and comorbid substance abuse, Jokinen et al. discovered a significant positive correlation between serum total cholesterol and CSF 5-HIAA (5-hydroxyindoleacetic acid in cerebrospinal fluid) levels in suicide attempters, which remained significant after correction for age, gender, BMI, and comorbid substance abuse. Hibbeln et al., who investigated total cholesterol and CSF 5-HIAA in 42 drug-naive suicide attempters (with blood samples collected and lumbar punctures performed in a standardized manner in a controlled study setting) discovered a substantial positive connection between serum total cholesterol and CSF 5-HIAA level [6].

When compared to the general population, the rate of suicide among people with first-episode psychosis is three times greater and suicide rates are known to be high throughout the duration of schizophrenia. Suicide rates in people with psychosis were 8.6% before their initial hospital visit and 5.3% throughout the first year of therapy, according to a ten-year follow-up study by Shrivastava A, Shah N, Johnston M, et al. According to a Canadian study by Jow GM, Yang TT, Chen CL published 35 years ago, low serum total cholesterol was connected

to 27 suicides in a sample of 11,554. According to epidemiological findings by Marcinko D, Martinac M, Karlovic D, et al. violent suicidal attempts had significantly lower cholesterol levels and higher cortisol levels, which can be ascribed to probable depressed symptoms and malnutrition [5].

Violent suicides were shown to have lower gray-matter cholesterol content than nonviolent suicides, particularly in the frontal cortex, according to postmortem brain research by Lalovic A, Levy E, Luheshi G, et al. [12].

A retrospective case control study conducted by Vivera et.al. found that patients who attempted suicide violently had considerably shown lower cholesterol levels than patients who attempted suicide nonviolently and control participants. Hence the study shows that low cholesterol levels are linked to an increased proclivity for impulsive conduct and violence, as well as a more violent pattern of suicide behaviour [13].

Recent research by Ludwig B, Dwivedi Y looked into the effect of cholesterol levels in violent vs. non-violent suicide attempts, and found that the former was connected with 30% lower cholesterol blood levels than the latter [14].

Wu S, Ding Y, Wu F et al. published a massive meta-analysis of 65 epidemiological studies with 510,392 participants, looking into the link between

serum lipid levels and “suicide” subjects, defined as people who had suicidal ideation, attempted suicide, threatened suicide, or died by suicide. According to their findings, Total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-c) levels were lower in suicidal patients than non-suicidal patients and healthy controls, high density lipoprotein cholesterol (HDL-c) levels were lower in suicidal patients than healthy controls, and triglycerides (TG) levels were lower in suicidal patients than healthy controls. When the three groups were combined, decreased serum TC was found to be linked to a 112% increased risk of suicidal conduct [15].

A one-year cross sectional survey by Reddy A, Lokesh KK was conducted among the 98 parasuicide subjects. Subjects with other Psychiatric disorders was excluded. The study results shown that a strong association between decreasing cholesterol levels there is an increased levels of ideas supporting aggressiveness, suicide, attitude toward violence and views regarding aggression. With increased cholesterol levels shows an increased Non-violent activity [8].

The findings of the study by Messaoud A, Mensi R, Mrad A et al. aimed to study that any alterations in lipid profile results leads to an increased risk of major depressive disorder and suicide attempt. They found

that suicidal conduct was linked to a low total cholesterol level in the blood. As a result, they believe that plasma cholesterol can be used as a biological status marker to estimate the risk of suicide in patients suffering from a major depressive episode [16].

STUDIES THAT IDENTIFIED NO CORRELATION BETWEEN CHOLESTEROL AND SUICIDE

A cross-sectional study by Capuzzi E, Bartoli F, Crocama CA, et al.^[17] concluded that correlation between lipid profile and suicide attempts in subjects with mental disorders is not fully supported and a systematic review and meta-analysis by Wu S, Ding Y, Wu F et al. mentioned an inverse relationship between suicidality and serum cholesterol and triglyceride levels. Despite the fact that subgroup analysis suggested a possible link between lower blood total cholesterol and violent suicide attempts, several investigations found the contrary. Overall, studies looking at a possible link between lipid serum profile and suicidal behaviour in people with mental illnesses yielded mixed results, probably due to methodological differences [4].

Another meta-analysis concentrating on bipolar illness patients by Bartoli F, Di Brita C, Crocama C, et al. found no change in lipid profile between suicide attempters and non-attempters [18].

A retrospective analysis of 213 psychiatric inpatients (including 61 patients with affective disorders) by Haung TL found no significant differences in serum cholesterol levels between patients who attempted suicide and those who did not. Despite a significant reduction in depression and suicidality scores in a prospective study of 92 inpatients with an MD (Major Depression) episode at admission, analyses of serum lipid concentrations after 1 and 4 weeks of antidepressant treatment revealed no significant differences in lipid levels between patients with and without a history of attempted suicide, even in patients who used a violent suicide method. Huang TL also provided more evidence for the lack-of-association hypothesis, evaluating serum lipid profiles in 168 subjects over a 2-year period and finding that, even if serum lipid profile changes in patients with MD were observed during the acute phase, there were no significant differences in serum lipid profiles between MD patients and healthy controls [6].

De Leon et al. studied 193 current suicide attempters and discovered that low cholesterol levels were not linked to an increased risk of suicide in women, but were linked to a lower risk in men. Persons et al. considerably corroborated the lack-of-association theory. More recently, D Ambrosio et al. found no link between

serum lipid levels and suicide in bipolar disorder patients [6].

Several studies have looked into the relationship between triglycerides, HDL cholesterol, LDL cholesterol, depression and suicidal behaviour in addition to total cholesterol. Cantarelli et al., on the other hand, found no change in HDL or LDL cholesterol between depressive patients with and without suicidal behaviour [19].

RELATIONSHIP BETWEEN CHOLESTEROL AND SUICIDE: A NEUROBIOLOGICAL MECHANISM

A proposed mechanism by Emily D is as follows: Cholesterol is a component of a "lipid raft," which floats in cell membranes and is critical for neuron-to-neuron communication. Lower cholesterol, in particular, appears to affect the activity of the 5HT-1A (serotonin 1A) receptor, which is the most prevalent serotonin receptor in the brain. Activators of this receptor have been shown to reduce anxiety, as well as having downstream effects on a variety of other neurotransmitters that affect depression and neuron healing and repair. The central nervous system's low serotonin activity has long been linked to violence and suicide. This suggests that low levels of cholesterol in the brain may cause impaired serotonin transmission and as a result, an increased risk of suicidal behaviour [20].

According to Reuter C, Caldwell B, Basehore H; lowering cholesterol may

modify the micro viscosity of the brain cell membrane, which refers to the friction of a particle moving apart, and so diminish serotonin receptor exposure on the membrane's surface [21].

A study by Mann JJ reported that suicide and violent behaviour have been linked to hypocholesterolemia and low 5-hydroxyindolacetic acid (5-HIAA - the primary breakdown product/metabolite of serotonin) levels in the cerebrospinal fluid (CSF) [22].

A review by Troisi A explained that serotonin receptor exposure on the membrane surface may be reduced as a result of decreased lipid micro viscosity in brain membranes, resulting in receptor hypofunction. Lower quantities of 5-hydroxyindolacetic acid (5-HIAA) in the cerebrospinal fluid (CSF) in suicides and suicide attempters have been identified in various research, indicating that the serotonergic system is associated to suicidality, impulsive, and aggressive behaviour [23].

De Berardis D, Serroni N, Marini S, et al. investigated the clinical and laboratory variables which were associated with suicidal ideation in alexithymic individuals with Obsessive-Compulsive Disorder (OCD) and reported that, individuals with OCD who are alexithymic may have a dysregulation of cholesterol balance [high-density lipoprotein cholesterol (HDL-C),

low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), triglyceride (TG), and very-low-density lipoprotein cholesterol (VLDL-C)], which may be linked to suicide ideation and this association's mechanism is unknown [24].

Maes et al. studied the phenotype of haptoglobin linked to chromosome 16, which contains the gene for lecithin-cholesterol acetyltransferase (LCAT), an enzyme that catalyzes cholesterol esterification in the blood. The scientists speculated that a decrease in esterified cholesterol concentration could be linked to a chromosome 16 abnormality, which could enhance depression susceptibility by altering the viscosity of the cellular membrane, raising the risk of aggressive and auto aggressive behaviour [25].

Post-partum women show depression (PPD)? Did the serum cholesterol have any significance on postpartum depression?

Postpartum depression symptoms are known to occur at varying rates in and across nations, ranging from 10% to 42%, with greater prevalence in underdeveloped countries [26].

A cross-sectional study was carried out at a tertiary care hospital in South India by Ramachandran Pillai R, Wilson AB, Premkumar NR, et al. [24] PPD was assessed in women who came for a postpartum check-up at the 6th week after

delivery (September 2014-October 2015). A total of 186 cases and 250 controls were matched for age and BMI in this study. Low levels of blood HDL-c have been linked to the development of severe depression symptoms in postpartum women, according to their findings and a study by Paris R, Bolton RE, Weinberg MK [27] examined the prevalence of suicidality in women with PPD and found that one group of women (47%) had a few provisional thoughts of wanting to harm themselves or thinking that their babies would be better off without them (low suicidality group), whereas another group (53%) strongly endorsed thoughts of wishing they could leave this earth, wanting to harm themselves, being better off dead or feeling that death was the only way out (high suicidality group).

CONCLUSION

Even though additional investigations are needed to elucidate a probable pathophysiological mechanism for cholesterol and suicide, the majority of the studies in this paper revealed an interesting association between cholesterol levels and suicidality. Overall, research on a probable link between low cholesterol/triglyceride levels and suicidality in people with mental illnesses has yielded mixed results, probably due to methodological variability. As a result, according to some of the studies, they believe that plasma cholesterol

can be used as a biological status marker to estimate the risk of suicide in patients suffering from a major depressive episode. Although it has been difficult to get a definite conclusion on this issue to date, we urge that further investigation is required whether adding a cholesterol supplement to the diet will minimize the risk of suicide in depressed people and longitudinal studies on a larger sample of patients are needed to further clarify this important issue.

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