

## RESEARCH ARTICLE

# A brief reflection on the role of cholesterol in psychopathology among female psychiatric patients

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**Objective:** Cholesterol is one of the cardiovascular risk factors, but also a core component of the central nervous system. Moreover, hypercholesterolemia and hypocholesterolemia are directly related to numerous mental illnesses too. This study intends to examine the association between cholesterol level and autolytic behavior among female psychiatric patients. **Methods:** The present study involves 123 female subjects, who suffered from suicidal thoughts at the moment of hospitalization. The risk of suicidal intentions was assessed by the Modified Scale for Suicide Ideation (Miller et al) and their total serum cholesterol levels were measured. We performed a case-control, analytical, randomized, observational study at the Clinical Hospital of Neurology and Psychiatry Brasov among adult female psychiatric patients admitted during 2014. **Results:** By our results we distinguished 3 categories: 38 patients with low suicide risk, 32 with moderate risk and 53 with high suicide risk. Significant difference can be noticed in the higher suicide risk patients' blood cholesterol levels: 44 patients having under 4,5mmol/L total cholesterol level (83%). Although, in other two categories, this proportion is minimal: in the moderate-risk category were 8 patients, representing just 25 %, and in the low-risk category only 1 patient had her cholesterol level under 4,5mmol/L (2,6%). **Conclusions:** According to our results, proposing cholesterol-level as a biomarker for the determination of high-risk suicide behavior can be important. The presence of other important risk factors (sociodemographic and psychiatric variables) can increase exponentially the suicide behavior. The limitations of this study are the relatively small number of cases and the lack of longitudinal subsequent follow-up. Further investigations are needed on a larger and more heterogenous sample of patients in order to clarify this suggestive correlation.

**Keywords:** cholesterol, psychopathology, suicide risk

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## Introduction

Suicide is a multifactorial phenomenon that can be approached from different perspectives: theological, philosophical, demographic, sociological, psychological, biological, evolutionary, health, biochemical, legal, preventive, global, political, and supranational [1]. In addition, although not specifically mentioned by Shneidman, the psychiatric approach is one of the strongest bases in suicidology today [2].

Suicide, as defined by the World Health Organization, is an act in which an individual ends his or her own life [3]. Because this act presupposes intent and consciousness, it is considered a human specificity.

Numerous research evidence points to the predictive nature of biological and genetic factors in the background of suicidal behavior. One of the most significant of the various neurobiological dysfunctions is the decreased serotonin turnover in the central nervous system. This has been associated with increased suicidal ideation and medically serious suicide attempts, as well as decreased levels of noradrenaline in the brainstem of people who have committed suicide [4].

Increased hypothalamic-pituitary-adrenal cortex activity (resulting in elevated cortisol levels) due to chronic stress has been associated with an increased risk of suicide

in patients with major depression [5]. Low cholesterol also increases the risk of suicide, while genetic factors are responsible for 45% of the variable of self-harming thoughts and behaviors [6].

This alarmingly high rate rightly calls for further investigation and follow-up regarding the relationship between cholesterol levels and suicidal behavior and intent.

By reviewing the currently very limited literature data, we are looking for the answer to whether total cholesterol levels can be treated as a possible bio-marker for the prediction and screening of suicidal tendencies. One of the first studies was Morgan R. E.'s 1993 observation that depressive symptoms were much more common in men over 65 years of age with low total cholesterol levels [7]. In addition, E. Olie stated in a 2011 study that low cholesterol can be linked to high-risk suicidal thoughts [8].

It is not possible to determine exactly how the bio-mechanisms of cholesterol influence depression, suicidal ideation and aggressive behavior, but its role in the human body is known to be vital. The human brain makes up only 2% of total body weight, yet it contains 25% of our body's total cholesterol [9].

The role of cholesterol is also extremely important in various brain functions and in neurotransmission, as it serves as a molecule for many neuroactive steroid precursors. These steroids strongly affect the function of gamma-aminobutyric acid (GABA), N-methyl-d-aspartate (NMDA), and serotonin receptors, all of which play a

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role in various psychiatric disorders [10]. They are also involved in mood regulation and cognitive functions, and have a modulating role in synaptic plasticity and apoptosis in a neuroprotective manner [10]. Keeping neuroactive steroids at a constant normal level is essential for normal brain function because low levels can lead to depression, epilepsy, multiple sclerosis, psychosis, and inflammation of the nervous system. In contrary, high levels of neuroactive steroids can produce stress, ADHD-like attention deficit / hyperactivity symptoms. Vital molecules in neuropsychiatric activity, such as pregnane, androstane, and sulfated neurosteroids, are all synthesized from cholesterol and are essential for neuropsychiatric activity [11].

Overall, cholesterol is a multipurpose molecule; it is a critical component of the cell membrane, regulating intercellular viscosity, a precursor of liposoluble vitamins (vitamins A, D, E, and K) and of several signaling molecules. All of these mechanisms of action provide insight into how cholesterol levels affect different brain functions [12].

For both extreme cholesterol levels, early mortality is very high. Hypercholesterolemia can lead to death from early cardiovascular disease, but low cholesterol increases the tendency to mood disorders, suicide, aggression [13]. Even in the absence of statin treatment, individuals with naturally low cholesterol levels have significantly higher rates of unnatural mortality [14].

According to a study conducted at the University of Minnesota, there is a strong correlation between low total cholesterol and suicide risk, describing that individuals with total cholesterol levels below 160mg/dl were much more likely to commit suicide than those with higher [15].

Another study in Zagreb found that total cholesterol levels were lower in bipolar patients with a history of suicide, in contrast to bipolar patients who did not have this factor [16].

Cholesterol remains a high cardiovascular risk factor. However, lower- or higher cholesterol levels are directly related to numerous mental illnesses too.

The aim of the present study is to support the following hypothesis that there is a relationship between low total cholesterol and psychiatric patients with severe suicidal ideation.

## Methods

We performed a case-control, analytical, randomized, observational study at the Clinical Hospital of Neurology and Psychiatry Brasov among adult psychiatric patients admitted during 2014. Our current study involves 123 female psychiatric patients, who struggled with expressed suicidal ideation when seeking emergency care. The risk of suicidal intentions was measured with the Modified Scale for Suicide Ideation – Miller et al.

During the study we followed the recommendations of the Declaration of Helsinki, the study protocol was approved by the ethics committee of the institute. All patients signed a consent form prior to enrollment in the study.

It was an exclusion criterion if the patient had expressed his intention of not to participate in the study, if she was under 18 years of age, or if she was taking a medication that had a proven effect on cholesterol levels. None of these women included followed oral contraceptive treatment.

The data of the involved patients were reviewed using the hospital electronic database and then recorded anonymously in the standardized table used in our study.

The following patient data were processed: demographics (age, residence), psychosocial data (social background, education, family background), somatic comorbidities, psychiatric background: pre-existing psychiatric illnesses, previous suicide attempts and their characteristics, and total cholesterol levels. The biochemical tests (lipid profile) were performed in each case in the hospital's own laboratory from freshly collected samples. The values obtained were measured in mmol/L. The association between the severity of the suicide risk and low serum cholesterol level was measured by Chi<sup>2</sup>-test, keeping the 95% confidence interval.

The risk of suicide is quantified by using the Modified Scale for Suicide Ideation – Miller et al. questionnaire. This psychological diagnostic tool was developed in 1979 by Aaron Beck, Maria Kovacs and Arlene Weissman (Scale for Suicide Ideation). It aims to quantify the intensity of suicidal ideation. It can be categorized into three parts: the conscious intention to die, methods of accomplishment, the passive desire for death. It contains 19 items that can be rated from 0 to 2, with the total score ranging from 0 to 38 [17]. This is further developed by Miller et al as “The Modified Scale for Suicide Ideation” (MSSI), using 13 elements from the original “Scale for Suicide Ideation” test and introducing 5 new elements. This change increased the credibility and validity of the test [19]. Using a semi-structured interview with patients, they were divided into 3 categories based on their scores: 1. category (0-8 points) those with mild suicidal ideation, 2. category (9-20 points) those with moderate suicide ideation and 3. category (21 points and above) patients with severe, verbal intent to die.

## Results

By our results we could distinguish 3 categories: 38 patients with low suicide risk, 32 with moderate risk and 53 with high suicide risk. Significant difference can be noticed in the higher suicide risk patients' blood cholesterol levels: 44 patients having under 4,5mmol/L the total cholesterol serum level (84%). Although, in other two categories, this proportion is minimal: in low-risk category only 1 patient (2,6%) and in the moderate-risk were 8 patients, representing just 25 %.

Demographic, psychosocial, and clinical characteristics are summarized in Table 1.

The following demographic data were analyzed: age, highest level of education, employment status, social living conditions, marital status, and the quality of the resulting social support network. Certain demographic indicators can be associated with increased suicidal behavior.

Table 1. The sample's sociodemographic and paraclinical variables based on 3 subcategories by the achieved MSSSI score

Parameter	Sample (n=123)	1. category	2. category	3. category
Number of cases by the achieved MSSSI scores (n, %)	n.a.	38 (31%)	32 (26%)	53 (43%)
Total serum cholesterol levels (median $\pm$ IQR, min.-max. Values in mmol/L)	4,8 $\pm$ 1,37 (3,12 – 8,22)	5,48 $\pm$ 1,2 (4,47 – 8,22)	5,02 $\pm$ 1,1 (3,64 – 6,77)	4,08 $\pm$ 0,63 (3,12 – 6,23)
Age (age, median $\pm$ IQR, min-max)	50 $\pm$ 17 (20 – 81)	54 $\pm$ 12 (27 – 72)	55 $\pm$ 17 (26 – 79)	43 $\pm$ 23,5 (20 – 81)
Residence				
rural (n, %)	34 (27,6%)	9 (23,68%)	9 (28,12%)	16 (30,18%)
urban (n, %)	89 (72,4%)	29 (76,32%)	23 (71,88%)	37 (69,82%)
Education				
primary (n, %)	11 (9%)	1 (2,63%)	5 (15,62%)	5 (9,43%)
vocational (n, %)	24 (19,5%)	7 (18,42%)	10 (31,25%)	7 (13,2%)
lower-secondary (n, %)	25 (20,3%)	9 (23,68%)	4 (12,5%)	12 (22,64%)
secondary (n, %)	45 (36,58%)	16 (42,1%)	11 (34,37%)	18 (33,96%)
tertiary/university (n, %)	18 (14,63%)	5 (13,15%)	2 (6,25%)	11 (20,75%)
Living conditions				
unemployed (n, %)	39 (31,7%)	5 (13,15%)	9 (28,12%)	25 (47,16%)
employed (n, %)	23 (18,69%)	11 (28,94%)	2 (6,25%)	10 (18,86%)
retired (n, %)	22 (18,88%)	8 (21,05%)	6 (18,75%)	8 (15,09%)
ill health pension (n, %)	34 (27,64%)	14 (36,84%)	11 (34,37%)	9 (16,98%)
disability pension (n, %)	2 (1,62%)	0 (0%)	1 (3,12%)	1 (1,88%)
social aid (n, %)	3 (2,43%)	0 (0%)	3 (9,37%)	0 (0%)
Marital status				
single (n, %)	19 (15,44%)	1 (2,63%)	4 (12,5%)	14 (26,41%)
married (n, %)	62 (50,4%)	28 (73,68%)	16 (50%)	18 (33,96%)
divorced (n, %)	23 (18,69%)	5 (13,15%)	4 (12,5%)	14 (26,41%)
widow (n, %)	19 (15,44%)	4 (10,53%)	8 (25%)	7 (13,2%)
Social support network				
inadequate (n, %)	74 (60,16%)	14 (36,84%)	19 (59,37%)	41 (77,35%)
adequate (n, %)	49 (39,38%)	24 (63,15%)	13 (40,62%)	12 (22,64%)
Somatic comorbidity (n, %)	64 (52,03%)	24 (19,51%)	18 (14,63%)	22 (17,88%)

The mean age is significantly lower in the 3. category cases (median = 43 years) and a high degree of variability is characteristic for all categories, including patients from 20 to 81 years.

The distribution by residence does not serve as either a protective or a risk factor according to the present survey.

Focusing on education levels, higher education is not protective either. In fact, 61% of the subjects with university degree were classified in the 3. category having pronounced suicidal tendency (11 out of 18 cases).

In terms of living conditions, which determine one's financial existence can be related to the risk of suicidal behavior. Regarding to the total unemployed examined, 25 out of 39 cases can be classified as having severe suicidal behavior (64%). This trend is similar for all of the low-income categories. But, no statistically significant result can be detected due to the low number of cases, such as disabled pensioners: 2 cases, those with social assistance: 3 cases.

Examining marital status, the following conclusion can be drawn: 73,68% of single patients and 60,86% of the divorced can be classified in the 3. category. Only 29% of married female patients and 36,84% of widows were in the high-risk group.

In summary, in terms of the quality of the social support network, which is largely determined by interpersonal relationships and financial background, 55,4% of cases with insufficient circumstances are classified as at high risk (41 out of 74 cases), while only 24,48% with a sufficient social safety net are at high risk (12 out of 49 cases).

We also recorded the presence of somatic comorbidities from the anamnesis, which variant does not significantly affect the distribution between different risk groups.

The most common somatic diseases were: cardiovascular - 43 cases (arterial hypertension, chronic heart failure, angina pectoris), type 2 diabetes - 11 cases, gastrointestinal - 10 cases (chronic gastritis, gastric or duodenal ulcer, liver steatosis, chronic hepatitis, gastroesophageal reflux disease), thyroid disease (autoimmune thyroiditis, thyroid cancer, hypothyroidism or hyperthyroidism) - 10 cases, neurological - 7 cases (from which epilepsy: 4 cases, 2 cases of vertigo and 3 cases of spondylosis), cancer or chronic terminal disease - 4 cases, respiratory disease - 2 cases, and other, statistically insignificant diseases. The incidence of comorbidities is also characterized by multiple accumulation: in 18 cases only one somatic disease was recorded, but in 20 cases 2, 12 cases 3 and 4, and in two cases 5 comorbidities were diagnosed. The vast majority of the medications used by these patients had no demonstrated effects on the serum cholesterol level. Cases with medications known with proven influence on cholesterol level were not included in this study. Regarding to the terms of specific diet, theoretically patients with diabetes should have followed hypoglycemic diet and those with gastrointestinal affections gastro- and liver-protective diet, but, during the interview - they all confessed that they're not following any.

Table 2 illustrates the characteristics of the psychiatric indicators of our cases: mental disorders in family history,

**Table 2. Psychiatric variables in the studied sample, distributed in 3 subcategories based on the achieved MSSl score**

Parameter	Sample (n=123)	1. category (n=38)	2. category (n=32)	3. category (n=53)
Mental disorders in family history (n, %)	46 (23%)	10 (19,23%)	15 (30,61%)	21 (21%)
Individual psychiatric antecedents (n, %)	105 (85,36%)	33 (86,84%)	30 (93,75%)	42 (79,24%)
Main psychiatric diagnose (n, %):				
- depression	67 (54,47%)	25 (65,78%)	23 (71,87%)	19 (35,84%)
- schizophrenia-spectrum disorder	14 (11,38%)	5 (13,15%)	3 (9,37%)	6 (11,32%)
- bipolar disorder	13 (10,56%)	1 (2,63%)	4 (12,5%)	8 (15,09%)
- adjustment disorder	12 (9,75%)	3 (7,89%)	1 (3,12%)	8 (15,09%)
- personality disorder	5 (4,06%)	2 (5,26%)	1 (3,12%)	2 (3,77%)
- acute psychosis	9 (7,31%)	2 (5,26%)	0	7 (13,2%)
- other	3 (2,43%)	0	0	3 (5,66%)
Chronic psychiatric treatment (n, %)	93 (75,6%)	35 (92,1%)	27 (83,37%)	31 (58,49%)
Suicide attempts in medical history (n, %)	34 (27,64%)	3 (7,89%)	3 (9,37%)	28 (52,83%)
Number of previous suicide attempts (n, %):				
- none	89 (72,35%)	35 (92,1%)	29 (90,62%)	25 (47,16%)
- one	18 (14,63%)	3 (7,89%)	2 (6,25%)	13 (24,52%)
- two	8 (6,5%)	0	1 (3,12%)	7 (13,2%)
- three	6 (4,87%)	0	0	6 (11,32%)
- four	0	0	0	0
- five	2 (1,62%)	0	0	2 (3,77%)

individual psychiatric antecedents, psychotropic treatment, number of earlier suicide attempts.

Familial psychiatric history, seen as a learned pattern of behavior or as a genetic inheritance, is a risk factor itself in developing self-harming behavior. In our sample, there was a family history of psychiatric diseases in 46 cases, which showed an even distribution in the different risk categories.

Individual psychiatric history could be registered in 105 cases (85,36% of the total number of cases), showing an equal distribution: 33 cases in 1. category, 30 in the 2. risk category and 42 cases were classified in category 3 (40%). Regarding to the most frequent main psychiatric diagnoses, we found that the most frequent were: depression – remarkably high, 67 cases (43.5%), followed by schizophrenia spectrum disorder (14 cases), bipolar disorder (13 cases), adjustment disorder (12 cases), acute psychosis (9 cases), personality disorders (5 cases) and other (3 cases). There weren't any cases registered with alcohol abuse related or with other substance consumption related. These data reflect only the referral main diagnose, but the accumulation of mental diseases is more likely characteristic to our studied sample. Suicidal thoughts with different intensity were present in every referred patient, regardless of their shown clinical aspect: whether as a command perceived during auditive hallucination, or as a maladaptive solution in mood or adjustment disorders or as making part of a delusion.

However, an interesting correlation can be observed between patients undergoing chronic psychiatric treatment. 105 subjects from the total of 123, had a history of psychiatric disease prior to the start of the study, whereas only 93 had prior chronic psychotropic treatment. For those in 3. category 42 (almost 80%) of the 53 cases had a prior diagnosis, but only 31 (58%) had chronic medication.

We also examined the number of suicide attempts in the medical history: 34 subjects had at least one previous suicide attempt. First-time attempters at the admission in the present study were 89 cases, equally distributed in the different risk categories: 35 cases in category 1, 29 in category 2, and 25 in category 3. 82% of multiple suicide attempts were classified in 3. category: 13 cases with one previous attempt, 7 cases with two previous attempts, 6 cases with three previous attempts, but four previous attempts were also registered in 2 cases.

Table 3 illustrates the distribution of the frequencies of the total serum cholesterol values in different risk categories based on the achieved MSSl scores. It is noteworthy that the serum total cholesterol level of the patients with the most severe risk, in the 3. category, was below 4.5 mmol/L (average: 4.06 mmol/L) - numerically 44 patients (83%). On the contrary, in the other two categories this difference is negligible: in the mild category this value can only be applied to just one patient (2,6%) and in the moderate category only 8 patients (25%). By calculating the Chi<sup>2</sup>-

**Table 3. The distribution of the frequencies of total serum cholesterol values in different categories based on the achieved MSSl scores**

Total serum cholesterol levels (mmol/L)	Sample (n=123)	1. category (n=38)	2. category (n=32)	3. category (n=53)
3-3,5	10	0	0	10
3,5-4	14	0	2	12
4-4,5	29	1	6	22
4,5-5	18	8	7	3
5-5,5	21	11	7	3
5,5-6	15	6	7	2
6-6,5	10	7	2	1
6,5-7	3	2	1	0
7-7,5	1	1	0	0
7,5-8	0	0	0	0
8-8,5	2	2	0	0

test, referring to the high and low suicide risk categories, we obtained a  $p < 0,001$ , which suggests a strong relationship between high suicide risk and serum cholesterol below 4,5mmol/L in our studied sample.

## Discussions

Our current study presents a transverse image of the sociodemographic and psychiatric characteristics of a given sample. Several parameters increase the risk of suicidal behavior. According to our survey, the social support network is outstandingly important. 74% of the analyzed subjects at risk regarding this aspect struggle with suicidal ideation and 55,4% of patients with strong verbal intent to die (3. category) have an inadequate social support network.

Another very important factor is the financial background that provides social living conditions. Interpersonal and financial problems are most often cited as the cause of suicide attempt in the literature. This covers a maladaptive problem-solving mechanism.

In this study, the protective nature of stable interpersonal relationships could not be reflected. This may be due to the relatively small number of cases, and due to the insufficient mapping of intrafamilial abuses at a national level.

Based on the level of total serum cholesterol in patients having different severity of suicide thoughts, can be stated that there is a distinct connection between suicidal behavior and low serum cholesterol.

## Conclusions

A special feature of our study was that our sample consisted only of female patients who agreed to the emergency referral, excluding those who did not seek professional help in a similar situation, or who did seek and receive only primary care (through family medicine), or who left the hospital after getting emergency patient care, refusing psychiatric care.

The limitations of our study are the followings: total cholesterol was the only lipid fraction measured and analyzed; the relatively small number of patients did not adequately reflect the expected association, and the lack of longitudinal subsequent follow-up. In addition, the studied sample consisted of a relatively homogenous group: all were referred into a psychiatric ward, majority of the subjects had previous individual- and/or familial psychiatric background etc.

The main focus of our study was on serum cholesterol levels and suicidal behavior, whereas we analyzed several similarly important parameters. One of the peculiarities of our examined sample is that education level is a neutral factor. A higher level of education is neither a protective nor a risk factor. In the same way, marital status did not serve as a protective factor either. The degree of self-harm was equally proportional among both married and single or divorced subjects.

The personal psychiatric background's parameters serve as severity indicators. The familial history of mental illness-

es are primary risk factors. All major psychiatric conditions from one's medical history are considered as risk factors. In our study, depression ranks first, followed by schizophrenia spectrum disorder, bipolar disorder and adjustment disorder. After these comes acute psychosis and various personality disorders. Recurrent self-harming behavior also carries the danger of finally realizing a suicide act. Even though more than 85% of the subjects had a chronic psychiatric diagnose, only 75% was on medication. This raises awareness as this may increase the suicide risk even more, by the inefficient monitorization and inadequate patient-doctor collaboration.

Low or medically reduced serum cholesterol levels increase the risk of suicide and suicidal/self-harm behavior, as the present study highlights. A paraclinical marker highlighting mental disorders that can be detected from a simple, inexpensive blood test is not yet routinely introduced into everyday use, so it is considered appropriate to exploit this property of cholesterol. Based on the present surveys, the idea of introducing the measurement of the total serum cholesterol as an effective, screenable suicide risk factor bio-marker is rightly recommended. Continuing this idea, it would be advisable to initiate a preliminary psychological screening before introducing cholesterol-lowering therapy. Serum cholesterol is not negligible, and is even of paramount importance due to its effects on the central nervous system, which encourages further research.

## Abbreviations

MSSI = Modified Scale of Suicide Ideation  
 IQR = interquartile range  
 n.a. = non-applicable  
 TChol = serum total cholesterol level

## Conflict of interest

None to declare.

## Contributions

DE – Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Visualization; Writing- original draft, review and editing

BE – Project administration, Supervision, Validation, Writing – review

BA – Conceptualization; Methodology; Project administration; Supervision; Validation; Writing – review and editing

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