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Source / Izvornik: *Collegium Antropologicum*, 2008, 32, 113 - 117

Journal article, Published version

Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:105:486400>

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Download date / Datum preuzimanja: **2024-07-11**



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# Serum Cholesterol Concentrations in Suicidal and Non-Suicidal Male Patients Suffering from Persistent Delusional Disorder

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## ABSTRACT

*Suicidal behavior is a major health risk in psychiatric disorders, especially in affective and psychotic disorders. The neurobiology of suicidal behavior is still unclear. Suicidality has been related to a reduced cholesterol levels. The aim of this study was to evaluate serum cholesterol concentrations in suicidal and non-suicidal men suffering from persistent delusional disorder and in healthy volunteers. Results showed that serum cholesterol concentrations were significantly lower in suicidal than in non-suicidal patients and healthy controls. Also, level of psychopathology (measured by Brief Psychiatric Rating Scale) is significantly marked in the group of suicidal patients, which indicates the importance of detecting some clinical symptoms in patients with persistent delusional disorder in order to prevent suicidal behavior.*

**Key words:** *suicidality, persistent delusional disorder, cholesterol, men*

## Introduction

Persistent delusional disorder is characterized by the development either of a single delusion or of a set of related delusions which are usually persistent and sometimes lifelong. Other psychopathology is characteristically absent, but depressive symptoms may be present intermittently, and olfactory and tactile hallucinations may develop in some cases. Clear and persistent auditory hallucinations (voices), schizophrenic symptoms such as delusions of control and marked blunting of affect, and definite evidence of brain disease are all incompatible with this diagnosis. Onset is commonly in middle age but sometimes, particularly in the case of beliefs about having a misshapen body, in early adult life<sup>1</sup>. The suicidal behavior is a major risk in psychotic patients such as patients suffering from persistent delusional disorder<sup>2</sup>. The rate of suicide in psychotic patients is more than 20 times higher than that in the general population<sup>3-4</sup>. The neuro-

biology of suicide in psychoses is still unclear. Various studies<sup>5-6</sup> aimed at identifying the possible peripheral markers that might help in the early detection of suicidal behavior. While there are a lot of data regarding the biology of suicidality in schizophrenia<sup>7</sup>, the data considering biology of suicidality in the persistent delusional disorder are missing.

Among the biological hypotheses of suicidality, low blood cholesterol level has been extensively explored. Consistent findings from the large epidemiological studies provide strong evidence in support of a putative relationship between low cholesterol levels and suicidal behavior, including a completed suicide<sup>8</sup>. In the early 1990's, analysis of mortality rates in the primary prevention clinical trials revealed an association between low cholesterol and unnatural death<sup>9-11</sup>. The relationship be-

tween serum cholesterol and suicidality does not seem to be limited to individuals with certain psychiatric disorder. Patients who survived a violent suicide attempts were found to have lower cholesterol levels than patients who survived a non-violent suicide attempts<sup>12</sup>, or than non-suicidal controls<sup>13</sup>. This is in line with our previous reports showing an association between low concentration of serum cholesterol and violent suicide attempts in schizophrenic men<sup>14–15</sup> and suicidal patients in the first episode of psychosis<sup>16</sup>.

Searching the literature, we could not find papers regarding neurobiology of suicidal behavior in persistent delusional disorder. Since the knowledge of the underlying neurobiology of suicide might contribute to the prevention of the suicidal act, we hypothesized that male suicidal patients suffering from persistent delusional disorder will have different serum cholesterol than non-suicidal patients.

## Materials and Methods

### Subjects

Participants were male patients, mean age of 32.02±8.21 years, admitted to the Department of Psychiatry, University Hospital Zagreb, during the period of 18 months. The diagnosis of the persistent delusional disorder was done according to the ICD-X criteria<sup>17</sup>.

Their demographic data are given in Tables 1 and 2.

### Inclusion and exclusion criteria

All patients were free of all medications in the previous 4 weeks. Within patients, 20 patients were consecutively admitted suicidal men with diagnosis of persistent delusional disorder, and 20 patients were consecutively admitted men with same diagnosis, without suicidal behavior. Healthy male subjects (N=20) with no history of psychiatric illness and suicidal behavior were randomly selected as a control group. They were closely matched for age. All subjects gave written informed consent to participate in the study. This study was approved by the Clinical Hospital Center Medical Ethics Committee.

None of the patients or control subjects included in the study had used any cholesterol-lowering drugs before the sampling. The exclusion criteria were: hypertension, hypothyroidism, diabetes mellitus, disorders of the lipoprotein metabolism, diagnosis of substance abuse, including alcoholism, eating disorders and organic brain syndrome.

### Biochemical determination

Blood samples were collected from all subjects at 8.00 a.m. after an overnight fasting, and serum concentration of cholesterol was determined enzymatically, immediately after the blood collection. The assays were done using commercial kits (Olympus Diagnostic GmbH, Hamburg, Germany) on Olympus AU 600 automatic analyzer. Body mass index (BMI) was used as a marker of the dietary habits.

**TABLE 1**  
AGE, BMI AND CHOLESTEROL (X±SD) IN MALE SUICIDAL AND NON-SUICIDAL PATIENTS SUFFERING FROM PERSISTENT DELUSIONAL DISORDER AND IN HEALTHY CONTROL SUBJECTS

Characteristic	Suicidal (N=20)	Non-suicidal (N=20)	Healthy controls (N=20)	One-way ANOVA; F	p
Age (years)	33.70±7.40	31.40±8.26	30.95±9.03	0.638	0.532
BMI (kg/m <sup>2</sup> )	24.78±2.07	25.16±1.92	25.32±1.76	0.417	0.661
Cholesterol (mmol/L)	4.37±1.00	5.23±1.00	5.09±0.53	5.618	0.006

**TABLE 2**  
SOCIO-DEMOGRAPHIC CHARACTERISTICS OF MALE SUICIDAL AND NON-SUICIDAL PATIENTS

Characteristics	Suicidal	Non-suicidal	$\chi^2$ test	p
Family status:	N		0.235	0.118
Living alone	2	6		
Living with family	18	14		
Education:			3.034	0.552
Elementary school	3	4		
High school	16	15		
Faculty	1	1		
Family history of suicide or suicide attempt:			1.600	0.206
Positive	8	12		
Negative	12	8		

**TABLE 3**  
BPRS (X±SD) IN MALE SUICIDAL AND NON-SUICIDAL PATIENTS SUFFERING FROM PERSISTENT DELUSIONAL DISORDER

Scale or symptom	Suicidal	Non-suicidal	Student's test; t	p
BPRS total score	79.10±11.93	67.70±9.30	3.370	0.002
Items of BPRS (9 items that significantly differ between groups):				
Depression	3.90±1.33	2.65±0.88	3.504	0.001
Suicidality	4.90±1.65	1.00±0.00	10.563	0.000
Unusual thought content	3.85±1.04	2.95±1.04	2.660	0.011
Self-neglect	3.70±0.80	2.50±1.15	3.835	0.000
Conceptual disorganisation	3.10±0.85	2.55±0.83	2.073	0.045
Blunted affect	4.30±1.38	2.45±1.10	4.689	0.000
Tension	4.25±1.29	3.20±1.11	2.761	0.009
Distractibility	4.25±1.12	3.05±1.00	3.580	0.001
Motor hyperactivity	4.05±1.23	3.30±1.08	2.044	0.048

### *Clinical Evaluations*

The trained psychiatrists performed clinical evaluation. The Brief Psychiatric Rating Scale – BPRS<sup>18</sup>, was administered to assess a broad range of psychopathology. Patients were classified as suicidal at the hospital admission if a suicidal ideation, or a suicide attempt, or both, were present. Suicidality was defined if patients had 2 or more scores on the BPRS, on the item 4 (item on suicide). Non-suicidal patients had score 1 on the BPRS item 4.

### *Statistical analysis*

The results were expressed as mean ± SD. All data were evaluated using one-way analysis of variance (ANOVA) followed by a Scheffé's multiple comparison test. When two groups were compared, Student's t-test was used. Because age and BMI might influence cholesterol levels, these variables were included as covariates within analysis of covariance (ANCOVA) in the comparison of serum cholesterol levels. The differences in the socio-demographic variables between suicidal and non-suicidal groups were assessed using Chi square ( $\chi^2$ ) test. A significance was accepted when  $p < 0.05$ . Statistical analyses were performed with the statistical package SPSS version 10 for Windows.

Age of the patients and body mass index (BMI) did not differ significantly between suicidal and non-suicidal patients and healthy control groups (Table 1). Serum cholesterol levels were significantly different ( $F=5,618$ ;  $df=2$ ;  $p=0.006$ , ANOVA) between suicidal ( $4.37 \pm 1.00$  mmol/L), non-suicidal ( $5.23 \pm 1.00$  mmol/L) patients and healthy ( $5.09 \pm 0.53$  mmol/L) male subjects (Table 1). Serum cholesterol levels were significantly reduced in suicidal when compared to non-suicidal patients ( $p=0.011$ , Scheffé's test), and healthy controls ( $p=0.038$ , Scheffé's test). These results remained after controlling for age and BMI (ANCOVA).

The demographic characteristics of the subjects are shown in Table 2. There were no significant differences in the occurrence in the socio-demographic variables between suicidal and non-suicidal male patients: in the

family status (living alone or in family), degree of education, and family history of suicide or suicide attempt (Table 2). Suicidal patients, compared to non-suicidal patients, had more cases of family history of suicidal behavior, but these differences were not significant (Table 2).

The BPRS score were significantly (Student's t-test) higher in suicidal compared to non-suicidal patients (Table 3). Nine of 24 symptoms on BPRS were significantly higher in suicidal patients, compared to non-suicidal patients (Table 3). We have applied test of correlation for cholesterol and each symptom of BPRS and have not found any significant correlation for cholesterol.

The main finding of the present study was significantly lower total serum cholesterol in suicidal patients suffering from persistent delusional disorder compared to non-suicidal patients with same diagnosis and healthy control subjects. The lower cholesterol levels found in suicidal patients suffering from persistent delusional disorder in the present study agree with previously published reports<sup>14–16,19–21</sup>.

Level of psychiatric symptoms (detected by BPRS) is significantly marked in the group of suicidal patients, which indicates the importance of detecting some clinical symptoms in patients with persistent delusional disorder in order to prevent suicidal behavior. Nine of 24 symptoms on BPRS, in present study, were significantly higher in suicidal suicidal patients, compared to non-suicidal patients. Spectrum of numerous mentioned symptoms and lack of significant correlation for cholesterol implies that suicidality is very complex process containing different psychopathological elements and interaction between biological and clinical parameters. A larger sample size of suicidal delusional disorder patients would be necessary to clarify what aspect of the disorder accounts for suicidality.

An association between lower serum cholesterol concentrations and increased suicidal risk has been described in the literature. Several different mechanisms have been suggested to explain the potential effect of low cholesterol levels on suicidality. Biological evidence link-

ing cholesterol and suicidality derives from demonstrated relationships between cholesterol concentrations and serotonin measures. Serotonergic dysfunction is a well-established explanation for suicidal behavior<sup>22–23</sup>, a relationship apparently mediated by increased aggressivity<sup>8,24</sup>. Low plasma concentrations of cholesterol in turn, have been associated with low platelet 5-HT content<sup>16,25</sup>, low plasma serotonin concentrations<sup>26</sup>, and blunted neuroendocrine responses to MCPP<sup>27</sup> or fenfluramine<sup>28</sup>. Hawton<sup>29</sup> speculated on the influence of a decreased serotonergic transmission on suicidal behavior. Steegmans<sup>26</sup> described lower plasma 5-HT concentrations in men with persistent low serum cholesterol concentrations. Although the biological mechanisms of the relationship between low cholesterol levels and suicide are still unclear, reduced serum cholesterol may be accompanied by alterations in 5-HT membrane fluidity, viscosity, and function of 5-HT receptor and 5-HT transporter, and decrease in 5-HT precursor, tryptophan plasma levels<sup>30</sup>. According to high cited Engelberg's hypothesis<sup>30</sup>, low serum cholesterol levels may be associated with reduced lipid micro-viscosity in the brain-cell-membrane and may decrease the exposure of 5-HT receptors on the membrane surface, resulting in decreased serotonergic recep-

tor function. Consequently, serotonergic neurotransmission may be inhibited, which may lead to a poorer suppression of impulsive or aggressive behavior, or to a depressive state, triggering a more violent pattern of behavior in susceptible individuals.

In , our findings support the hypothesis of an association between suicidal behavior and reduced level of peripheral biological marker, serum cholesterol. Identifying biological, social, and clinical predictors of suicide might help to improve the prediction and prevention of suicide. A better understanding of the neurobiology of suicide can facilitate the detection of the population of patients who have a high risk to attempt suicide, and to develop better treatment interventions for these patients. Further prospective studies are needed to investigate whether this peripheral parameter might be used as the early predictors of suicide behavior.

### Acknowledgements

This work was supported by Ministry of Science, Education and Sport from the Republic of Croatia, grant No: 0108106.

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## **SERUMSKE KONCENTRACIJE KOLESTEROLA KOD SUICIDALNIH I NESUICIDALNIH MUŠKIH BOLESNIKA OBOLJELIH OD PERZISTIRAJUĆEG SUMANUTOG POREMEĆAJA**

### **S A Ž E T A K**

Suicidalno ponašanje jedan je od vodećih zdravstvenih rizika u psihijatrijskih bolesnika, posebno u afektivnim i psihotičnim poremećajima. Neurobiologija suicidalnog ponašanja još uvijek nije dovoljno objašnjena. Suicidalnost se povezuje sa smanjenom razinom kolesterola. Svrha ovog istraživanja bila je evaluirati serumske koncentracije kolesterola u skupini muških suicidalnih i nesuicidalnih bolesnika s perzistirajućim sumanutim poremećajem te u skupini muških zdravih kontrolnih ispitanika. Rezultati pokazuju kako kod suicidalnih bolesnika postoji značajno niža razina kolesterola nego u skupini nesuicidalnih bolesnika i zdravih kontrolnih ispitanika. Također, razina psihopatologije (na skali BPSR) značajno je naglašenija u skupini suicidalnih bolesnika, što ukazuje na važnost prepoznavanja pojedinih kliničkih simptoma u bolesnika s perzistirajućim sumanutim poremećajem zbog prevencije suicidalnog ponašanja.