

ORIGINAL RESEARCH

Medicine Science 2018;7(4):826-30

The relationship between serum lipid levels and lifetime suicide attempts in patients with schizophrenia

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Received 25 April 2018; Accepted 11 May 2018

Available online 29.07.2018 with doi: 10.5455/medscience.2018.07.8849

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Abstract

Patients with schizophrenia have a higher risk of suicide than the general population. Due to these high rates, researchers are investigating biomarkers associated with suicidal behavior to prevent suicide. Conflicting findings have also been reported in studies investigating the relationship between cholesterol and suicide in patients with schizophrenia. The aim of our study was to compare schizophrenia patients with and without a history of suicide attempt in terms of total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels and to investigate the relationship between cholesterol levels and lifetime suicide attempts. A retrospective, cross-sectional study was carried out in a psychotic disorders outpatient clinic at a psychiatric hospital in Turkey. Two hundred and twenty-eight patients with schizophrenia were evaluated. We present a retrospective analysis of longitudinal data addressing socio-demographic characteristics, metabolic parameters, lipid profile, scales. Lifetime suicide attempts were reported by %28 of patients. It was found that schizophrenia patients with suicide attempt had higher TC and TG levels than schizophrenia patients without suicide attempt. Similar findings were repeated male patients with schizophrenia. In female patients, only TG level showed a significant difference between those with and without suicide attempt. Our findings indicate an association between high cholesterol levels and lifetime suicidality. The findings of our study may indicate that lifetime suicide attempt in schizophrenia exhibits a different lipid profile.

Keywords: Cholesterol, schizophrenia, suicide

Introduction

Suicide is one of the primary causes of premature death in schizophrenia [1]. The lifetime risk of suicide in schizophrenia is reported to be 4.9%. Schizophrenia patients have a higher risk of suicide than the general population. The most important risk factors for suicide in individuals with schizophrenia are previous suicide attempts, substance abuse, and depression [2]. In the follow-up of patients who were discharged after the first episode, the patients who did not receive regular antipsychotic medication had a 37-fold increased risk of suicidal behavior [3]. Due to these high rates, researchers are still investigating biomarkers associated with suicidal behavior to prevent suicide.

The relationship between low cholesterol levels and increased risk of suicide has been first noticed by the fact that the rate of deaths from suicide has increased because lipid-lowering drugs have reduced serum cholesterol levels [4]. However, a later meta-analysis could not repeat the same results [5].

The relationship between cholesterol and suicidality was also investigated in patients with various psychiatric disorders.

However, conflicting results were obtained. While some studies have found a relationship between low cholesterol levels and increased suicidality [6,7], other studies have determined a positive relationship between lipid profile and suicide [8,9]. There are also studies that have not reported any relationship between them [10,11].

Conflicting findings have also been reported in studies investigating the relationship between cholesterol and suicide in schizophrenia patients. It has been recently found that schizophrenia patients who attempted suicide had lower cholesterol levels than schizophrenia patients who did not attempt suicide [12-14]. In a single study conducted in this field in our country, schizophrenia patients with and without suicide attempt were compared with age- and sex-matched healthy controls. It was found that schizophrenia patients with suicide attempt had lower cholesterol levels. However, the sample size was too small [12].

It should also be considered that there are also studies that have not found any relationship between lipid profile and suicide in this patient group [15-18]. Of these studies, two have been conducted in patients who have died of suicide [15,16], one has been conducted in patients who have been recently hospitalized due to suicide attempt [17], and one has been conducted in patients who have exhibited aggressive behaviors [18]. Studies conducted in schizophrenia patients often assess those with recent suicide

attempt. Only one study involving schizophrenia patients with lifetime suicide attempt was conducted in Tunisia. In this study, schizophrenia patients with recent suicide attempt and patients with lifetime suicide attempt were compared with healthy controls [14]. To our knowledge, there are no studies in our country giving information on lipid profile in schizophrenia patients with lifetime suicide attempt.

The aim of our study was to compare schizophrenia patients with and without a history of suicide attempt in terms of total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels and to investigate the relationship between cholesterol levels and lifetime suicide attempts. In addition, male and female schizophrenia patients were divided into two separate groups, and those with and without suicide attempt were compared with each other in terms of lipid profile.

Material and Methods

Sample

This retrospective cross-sectional study was conducted in patients who were followed up in the Psychotic Disorders Outpatient Clinic of Training and Research Hospital and who were diagnosed with schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) criteria [19]. Patients who were followed between 1 October 2016 and 1 January 2017 were included in the study. Patients who were not diagnosed with schizophrenia, who had missing data on blood tests and scales, who had significant neurological impairment and mental retardation, who had metabolic syndrome according to the Adult Treatment Panel III (ATP III) criteria [20], who received anti-hyperlipidemia drugs, who had alcohol and substance use disorder and major depression between the start and end dates of the study period, and who attempted suicide within the last 3 months were excluded from the study. The study was approved by the Ethics Committee of Training and Research Hospital. Informed consent form was obtained from the patients.

Clinical evaluation

Blood samples are taken regularly every 6 months between 8:00 am and 10:00 am by nurses working at our center from patients who fast for at least 8 hours and who agree to blood drawing. These blood tests include TC, TG, HDL, and LDL levels. Body weight, waist circumference, and arterial blood pressure are measured and recorded on the date on which blood samples are taken. These values were assessed to exclude patients with metabolic syndrome and to calculate body mass index (BMI). BMI is calculated by the formula kg/m^2 to determine whether a person's weight is healthy. These information were obtained retrospectively from patient files between the start and end dates of the study period. In addition, sociodemographic information such as age, gender, duration of education, duration of illness, and antipsychotic and metabolic drugs used were collected for each patient. Life-time history of suicide attempts was questioned retrospectively. A suicide attempt was defined as a self-destructive behavior with the intention of ending one's life, independent of the resulting damage [21]. In accordance with this definition, patients who attempted suicide were addressed. Positive and Negative Syndrome Scale (PANSS), Schedule for the Assessment of Insight (SAI), and Clinical Global Impression-Severity of Illness (CGI-S) are filled out at each visit. Scale scores that were determined at follow-up visit on the date on

which blood samples were taken were assessed.

Sociodemographic data form

It is a semi-structured data form prepared by the researchers. This form contained questions about age, gender, duration of education, duration of disease, antipsychotic drugs, alcohol and other substance use, additional medical illnesses, and other psychiatric medications.

Positive and Negative Syndrome Scale (PANSS)

The PANSS is a 30-item semi-structured instrument to perform psychopathological measurements related to positive, negative, and general symptoms of schizophrenia [22]. This scale included 30 items, 18 items for the Brief Psychiatric Rating Scale (BPRS) and 12 items from the Psychopathology Rating Schedule (PRS). The 30 items are arranged as seven positive symptom subscale items (P1 - P7), seven negative symptom subscale items (N1 - N7), and 16 general psychopathology symptom subscale items (G1 - G16). All 30 items are rated on a 7-point scale (1 = absent; 7 = extreme). It consists of four measures including PANSS total score, PANSS positive subscale score, PANSS negative subscale score, and PANSS general psychopathology subscale score. The validity and reliability study of the Turkish version of this scale was performed by Kostakoğlu et al. [23].

Schedule for the Assessment of Insight (SAI)

It is a semi-structured clinician-administered instrument developed for assessment of insight in schizophrenia by David in 1990 [24]. The validity and reliability study of the Turkish version of this scale was performed by Arslan et al. [25]. It is composed of four components including awareness of mental illness, ability to re-label psychotic experience as abnormal, adherence to treatment, and awareness of previous mental disorders. The items are rated on 3-point scales ranging from 0 to 2 points. Higher scores indicate higher levels of insight.

Clinical Global Impression-Severity of Illness (CGI-S)

It was developed by Guy et al. [26] to assess the clinical course of all mental disorders at all ages for clinical research purposes. It is filled out during a semi-structured interview conducted by the physician to assess the treatment response of individuals with psychiatric disorders. This scale yields three different measures: Severity of illness, overall improvement, and therapeutic index. The CGI-Severity (CGI-S), which is the first component of the scale, was assessed in our study. The CGI-S asks the clinician one question: "Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?" which is rated on the following seven-point scale: 1=normal, not at all ill; 2=borderline mentally ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=among the most extremely ill patients.

Statistical Methods

The distributional properties of the variables were examined by the Kolmogorov-Smirnov test. Since the parameters were not normally distributed, Mann Whitney U test was used to compare quantitative data of the two groups (suicide attempters and non-suicide attempters). Chi-square (X^2) test was used to compare categorical data. Furthermore, male and female patients were divided into the two groups separately as suicide attempters and

non-suicide attempters and evaluated in terms of total cholesterol, TG, HDL and LDL. The results were assessed at a 95% confidence interval, at a significance level of $p<0.05$, and at high significance levels of $p<0.01$ and $p<0.001$. The Statistical Package for the Social Sciences 18.0 (SPSS, SPSS Inc., Chicago, IL, USA) was used to analyze data.

Results

Two-hundred twenty-eight patients with schizophrenia participated in the study. Lifetime suicide attempts were reported by 28% of patients. In the total sample, 43 (18.8%) male patients and 21 (9.2%) women patients reported a history of attempted suicide.

The duration of education was significantly shorter in the non-suicide attempter group than in the suicide attempter group (9.07 ± 3.33 years vs. 9.27 ± 3.81 years, $p<0.05$). There was no significant difference between the suicide attempter group than the non-suicide attempter group in terms of age, type of the

antipsychotic drugs, clozapine/olanzapine usage, BMI, and scale scores (Table 1).

The mean TC levels (219.58 ± 43.39 mg/dL vs. 200.00 ± 44.95 mg/dL, $p<0.05$) and TG levels (182.43 ± 124.05 mg/dL vs. 147.42 ± 101.27 mg/dL, $p<0.05$) who attempted suicide was significantly higher than that of the patients who did not attempted suicide (Table 2).

Male patients with schizophrenia with suicide attempts reported higher levels of TC (223.47 ± 44.88 mg/dL vs. 199.18 ± 46.34 mg/dL, $p<0.05$) and TG (203.11 ± 141.15 mg/dL vs. 159.13 ± 111.07 mg/dL, $p<0.05$) (Table 3).

The only significant difference was found in TG levels between female group of patients and higher levels was reported in suicide attempters (140.09 ± 61.91 vs. 111.12 ± 46.55 mg/dL, $p<0.05$) (Table 4).

Table 1. Demographic and clinical characteristics of schizophrenic patients with and without suicide attempts

Patient Characteristics	Patients without suicide attempt (n=164)	Patients with suicide attempt (n=64)	χ^2	U	P value
Male	124(54.3%)	43 (18.8%)	2.211		.095 ^a
Female	40 (17.5%)	21 (9.2%)			
Age (years $\pm$ SD)	41.29 ($\pm$ 9.9)	43.20 ($\pm$ 8.41)		4339.50	.054 ^b
Duration of education (years $\pm$ SD)	9.27 ($\pm$ 3.81)	9.07 ($\pm$ 3.33)		5131.00	.088 ^b
Duration of disorder (years $\pm$ SD)	18.13 ($\pm$ 7.87)	21.77 ($\pm$ 8.78)		3804.50	.002 ^{b*}
First-generation AP	19 (8.6%)	7(3.2%)	.007		.570 ^a
Second-generation AP	162(71.1%)	63 (27.6%)	1.161		.377 ^a
Klozapin/olanzapin	113 (49.6%)	54 (23.7%)	5.624		.012 ^{a*}
BMI	26.98($\pm$ 4.68)	27.30($\pm$ 4.14)		4910.00	.450 ^b
Smoking	79 (34.6%)	37(16.22%)	2.148		.094 ^a
PANSS-positive symptom subscale($\pm$ SD)	9.75($\pm$ 3.42)	9.87($\pm$ 3.76)		5136.50	.855 ^b
PANSS-negative symptom subscale	13.40($\pm$ 4.38)	12.69($\pm$ 4.96)		4442.00	.086 ^b
PANSS-general psychopathology subscale	24.62($\pm$ 6.71)	24.00($\pm$ 7.05)		4847.00	.426 ^b
PANSS- Total	47.86($\pm$ 12.23)	46.68($\pm$ 14.04)		4664.50	.231 ^b
SAI	13.46($\pm$ 5.36)	13.61($\pm$ 5.40)		4963.50	.583 ^b
CGI-S	2.16($\pm$ 1.00)	2.11($\pm$.98)		5072.50	.762 ^b

BMI: Body mass index, PANNS: The Positive and Negative Syndrome Scale, SAI: Schedule for Assessment of Insight, CGI-S: Clinical Global Impression Severity of Illness * $p<0.05$ ** $p<0.001$

^a Statistical significance of differences estimated with the Chi square (χ^2) test

^b Statistical significance of differences estimated with the Mann-Whitney U

Table 2. Lipid profile of schizophrenic patients with and without suicide attempts

Suicide attempt	N	Mean ($\pm$ SD)	U	P
TC (mg/dL)	without 164 with 64	200.00 (44.95) 219.58(43.39)	3947.50	.004*
TG(mg/dL)	without 164 with 64	147.42(101.27) 182.43(125.05)	3989.00	.005*
HDL(mg/dL)	without 164 with 64	47.89(14.86) 47.6(13.51)	5237.50	.981
LDL(mg/dL)	without 164 with 64	124.58(40.89) 129.84(43.20)	4813.00	.331

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TC: Total cholesterol, TG: Triglyceride* $p<0.05$

Table 3. Lipid profile of male patients with schizophrenia with and without suicide attempts

Suicide attempt	N	Mean ($\pm$ SD)	U	P
TC (mg/dL)	without 124 with 43	199.18(46.34) 223.47(44.88)	1858.00	.003
TG(mg/dL)	without 124 with 43	159.13(111.07) 203.11(141.15)	1989.00	.013
HDL(mg/dL)	without 124 with 43	44.04(13.22) 41.72(9.62)	2408.50	.384
LDL(mg/dL)	without 124 with 43	125.40(40.98) 136.91(43.20)	2138.50	.054

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TC: Total cholesterol, TG: Triglyceride* $p<0.05$

Table 4. Lipid profile of female patients with schizophrenia with and without suicide attempts

Suicide attempt		N	Mean (±SD)	U	P
TC (mg/dL)	without	40	202.52 (40.78)	369.50	.443
	with	21	211.61 (40.02)		
TG(mg/dL)	without	40	111.12 (46.55)	279.50	.033*
	with	21	140.09 (61.91)		
HDL(mg/dL)	without	40	59.80 (13.39)	403.00	.796
	with	21	59.52(12.55)		
LDL(mg/dL)	without	40	122.42(41.00)	362.00	.379
	with	21	115.36(40.40)		

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TC: Total cholesterol, TG: Triglyceride *p<0.05

Discussion

This study is the first study in Turkey investigating the relationship between lifetime suicide attempts and serum lipids in a large sample of patients with schizophrenia. It was found that schizophrenia patients with suicide attempt had higher TC and TG levels than schizophrenia patients without suicide attempt. These results are different from the results of previous studies showing the relationship between low cholesterol level and suicidality. This may be due to the fact that studies in patients with schizophrenia have been conducted in those with recent suicide attempt [12-14]. Only one study involving schizophrenia patients with lifetime suicide attempt was conducted in Tunisia. It was determined that schizophrenia patients with recent suicide attempt had lower total cholesterol levels compared to those with and without lifetime suicide attempt [14]. Similar to our study, there are other studies that have found a relationship between high cholesterol levels and suicidality although they have been conducted in different psychiatric populations [8,9]. Brunner et al. [8] revealed that there was a positive relationship between suicide attempt and TC, TG, BMI in the patients with depressive symptoms for the last 12 months. Another study reported that low cholesterol levels were associated with a lower risk of recent suicide attempts. In this study, the groups with and without suicide attempt were examined [9].

In our study, similar findings found in schizophrenia patients were repeated in male schizophrenia patients. In female schizophrenia patients, only TG level showed a significant difference between those with and without suicide attempt. There are studies showing that the relationship between TC level and suicide risk in psychiatric disorders is specific for either female or male gender. In these studies it was found that low serum cholesterol levels were associated with suicide [27, 28]. A recent study found that higher TC and LDL levels might be associated with suicidal ideation only in female first-episode female patients [29].

The reasons why our study has different results from previous studies can include examining different dimensions of suicidal behavior (suicidal ideation, suicide attempt, suicide loss), conducting a study in a mixed psychiatric group by investigating only those with and without suicidal behavior, number of samples, geographical region where a study is conducted, ethnic origin of individuals, weight, different diet characteristics, and effect of antipsychotic drugs on lipid levels. Most suicide attempts occur during a depressive episode and are associated with decreased

appetite and weight loss in depressed patients [30]. Low cholesterol levels that have been detected in patients with schizophrenia with recent suicide attempt may be associated with this. The different results of our study may be due to the examination of lifetime suicide attempts and the absence of depressive episodes and thereby vegetative symptoms on the date on which blood samples were taken. In addition, high lipid levels in schizophrenia patients may be related to the use of antipsychotic drugs (mainly clozapine and olanzapine), weight gain [31,32], and smoking [33]. However, the fact that most of schizophrenia patients without suicide attempt in our study highly received clozapine or olanzapine and there was no significant difference between the groups in terms of BMI and smoking status may exclude these possible reasons. Considering all results, the findings of our study may indicate that lifetime suicide attempt in schizophrenia exhibits a different lipid profile.

Limitations

Our study has some limitations. Comparison of schizophrenia patients with lifetime suicide attempt with schizophrenia patients with recent suicide attempt and healthy controls may provide more valid results. In addition, a prospective study will make it more possible to establish a causal relationship.

Conclusion

In conclusion, unlike other studies, our study found a relationship between lifetime suicide attempts and high cholesterol levels in schizophrenia patients. Given the high suicide rate in schizophrenia patients, the identification of biological markers related to suicidal behavior will provide the early detection of patients at risk for suicide and increase the chance of early intervention.

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

The study was approved by the Ethics Committee of Bakirkoy Training and Research Hospital. Informed consent form was obtained from the patients.

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