



## Serum lipids, recent suicide attempt and recent suicide status in patients with major depressive disorder ☆☆☆



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### ABSTRACT

**Objective:** Major depressive disorder (MDD) is associated with suicide. Although several studies have reported its association with low serum lipid, few studies have investigated relationships between current suicidality and lipid profiles, comparing with other blood measures in MDD patients.

**Methods:** The study population consisted of 555 subjects with MDD who were  $\geq 18$  years old, evaluated by the Mini International Neuropsychiatric Interview (MINI) with the suicidality module. At the evaluation visit, we measured serum lipid profiles including total cholesterol, triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very low-density lipoprotein (VLDL), and blood measures such as fasting glucose, total protein, albumin, blood urea nitrogen, creatinine, thyroid hormones, red and white blood cells, platelet count, hemoglobin, and hematocrit.

**Results:** Recent attempters who had attempted suicide within the past month showed significantly lower TG and higher HDL levels than lifetime and never attempters, using *Tukey's post-hoc* analysis. Recent attempters exhibited lower TG and higher HDL than those with recent suicide ideation and wish to self-harm and those without previous attempt. Linear regression analysis revealed that TG was negatively associated with current suicidality scores ( $\beta = -0.187$ ,  $p = 0.039$ ), whereas VLDL was positively associated with the recent suicide status ( $\beta = 0.198$ ,  $p = 0.032$ ) after controlling for age and sex. There were no significant differences between the groups in terms of other serum lipid profiles and blood measures.

**Conclusions:** Low serum TG, high HDL and VLDL levels are associated with recent suicide attempt or recent suicide status in patients with MDD.

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### 1. Introduction

Suicide is the most devastating outcome in psychiatry, and previous studies have examined the association between suicide and major depressive disorder (MDD). Many suicidal behaviors are related to depression, but it is still challenging for clinicians to predict suicide risk in patients with depression. For this reason, increased attention has been paid to potential biomarkers for suicide in patients with MDD.

**Abbreviations:** MDD, major depressive disorder; MINI, mini international neuropsychiatric interview; TG, triglycerides; LDL, low-density lipoprotein.

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Cholesterol is an insoluble lipid that enters the blood stream in the form of lipoproteins, which are complex discoid particles that make cholesterol soluble. Very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density protein (HDL) are the most common lipoprotein and transfer lipids in the body. In the clinical setting, levels of total cholesterol, LDL, HDL and TG are measured to evaluate the level of blood lipids. Total cholesterol level reflects the sum of HDL, LDL and VLDL. Triglycerides are another blood lipid form derived from glycerol and fatty acids. In general, TG, VLDL and LDL contain pro-atherogenic lipids, whereas HDL contains anti-atherogenic lipids (Brown et al., 2007).

Since initial reports have suggested a potential relationship between excess mortality by violence and the use of cholesterol-lowering drugs (Frick et al., 1987; Muldoon et al., 1990), cholesterol has received attention as a potentially meaningful biomarker for suicide, but mixed results have been reported. Some reports showed that suicide attempters with MDD had lower cholesterol levels (Diaz-Sastre et al., 2007; Kim et al., 2002; Lee and Kim, 2003; Partonen et al., 1999; Perez-Rodriguez et al.,

2008), but others reported negative associations between suicide and low cholesterol (de Leon et al., 2011; Fiedorowicz and Coryell, 2007). This could be partially due to methodological limitations. Most previous studies with clinical population had small samples, and focused on total cholesterol as the measure of interest. Given that each lipoprotein sub-fraction has a different role in the human body, total cholesterol might not be sufficient to determine the relationship between lipids and suicidality. Additionally, it is not clear whether a lower lipid profile is either a state or trait marker for suicide. Other blood markers should be compared in the same population to investigate potential biomarkers equally and to evaluate group differences between suicide attempters and non-attempters.

In this study, we determined the effect of lipid profiles on recent suicide status in patients with MDD and evaluated the potential of lipid profiles as a meaningful marker for suicide in the clinical setting. We explored the level of lipoproteins sub-fractions and evaluated the differences between subjects with different degrees of suicidality.

## 2. Methods

### 2.1. Subjects

A total of 555 patients who were newly diagnosed with MDD by the diagnostic criteria of the DSM-IV were recruited from the outpatient clinic of the Department of Psychiatry and Depression Center of the Samsung Medical Center between July 1, 2009 and July 28, 2012. All participants were medically stable and did not require any acute interventions. Those who had bipolar disorder, schizophrenia, other psychotic disorders, alcohol use disorders, organic mental disorders, mental retardation, neurologic illness including epilepsy, and serious medical illnesses were excluded.

Initially, psychiatrists with more than three years' clinical experience evaluated the participants' psychiatric and medical histories, and confirmed their eligibility. A trained psychologist blinded to the psychiatrists' judgment separately explored the participants' psychiatric diagnoses and current mood states using the following measures: the Korean version of the Mini International Neuropsychiatric Interview's (MINI) (Sheehan et al., 1998), the Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1967), the Mood Disorder Questionnaire (MDQ) (Hirschfeld et al., 2000) and the Hypomania Symptom Checklist-32 (HCL-32) (Tomaszewski et al., 1992). In the Korean version of the MINI, Cohen's kappa values, a measure of the inter-rater reliability, of the depression and suicide module were 0.71 (You et al., 2006). The MDQ and the HCL-32 were used for evaluating potential bipolarity. All study procedures were approved by the Institutional Review Board of the Samsung Medical Center.

### 2.2. Measure of suicidality

Recent suicide status was assessed with the Korean version of the MINI suicidality module (Sheehan et al., 1998). The MINI suicidality module was composed of six questions with a different weight: wish for death ("In the past month did you think you would be better off dead or wish you were dead?"; weight 1), wish for self-harm ("In the past month did you want to harm yourself?"; weight 2), suicidal thought ("In the past month did you think about suicide?"; weight 6), suicide plan ("In the past month did you have a suicide plan?"; weight 10), suicide attempt in the past month ("In the past month did you attempt suicide?"; weight 10), and lifetime suicide attempt ("In your lifetime did you ever make a suicide attempt?"; weight 4). Recent suicide-related questions were all asked based on the symptoms during the past 1 month. The MINI suicidality score was estimated from the sum of the weighted score of the six questions.

All participants were divided into three groups based on their history of suicide attempt: recent (suicide) attempters, lifetime (suicide) attempters and never attempters. Recent attempters were defined as

individuals with MDD who had attempted suicide within the past month; lifetime attempters were defined as those who have attempted suicide in their lifetime except for the past month. Additionally we divided subjects depending on their recent suicide status. Recent suicide ideation was defined as individuals having a serious suicide ideation and no attempt within the past month. Recent wish to self-harm was defined as having a serious idea of self-mutilation but no suicide ideation or attempt at that time within the past month.

### 2.3. Blood sample collection and testing

After a clinical evaluation, blood samples were taken when the subjects had fasted for at least 12 h. High-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG) were measured by an enzymatic colorimetric method using a Modular D2400 analyzer (Roche Diagnostics, Basel, Switzerland). And the level of very-low-density lipoprotein cholesterol (VLDL-C) was calculated using the equation of  $VLDL-C \text{ (mg/dl)} = \text{Total cholesterol} - (\text{LDL-C} + \text{HDL-C})$  according to the formula of Friedewald et al. (Friedewald et al., 1972).

In order to exclude the medical conditions or nutritional status that could affect lipid profiles, the following blood chemistry levels were also measured: fasting glucose, total protein, albumin, blood urea nitrogen (BUN), creatinine (Modular D2400 analyzer, Roche Diagnostics, Basel, Switzerland), T3, T4 (ADVIA Centaur automated analyzer, Siemens Healthcare Diagnostics, NY, USA) and complete blood count (CBC) including RBC, WBC and platelet count, hemoglobin (Hb) and hematocrit (Hct) (XE-2100 automated hematology system, Sysmex Corporation, Kobe, Japan).

### 2.4. Statistical analysis

The demographic data, current mood symptoms, blood measures and lipid profiles between recent attempters, lifetime attempters and never attempters were compared. Parametric variables were compared by means of an analysis of variance (ANOVA) followed by post-hoc pairwise comparisons using Tukey's test. Categorical data were analyzed using a chi-square test, and the Bonferroni correction was applied for the post-hoc pairwise comparisons. To determine the relationship between the degree of recent suicide status and lipid profiles, all blood measures including lipid profiles were additionally compared among recent attempters, subjects who had experienced suicide-related symptoms recently (i.e. there was a recent report of wish to self-harm, suicide ideation and attempts during the past month) and those who had not reported any suicide-related symptoms during the past month. To examine the influence of lipid profiles on suicidality, linear regression analyses were performed using the MINI suicide score as a dependent variable. In model 1, lipid profiles were entered as independent variables; in model 2, age and sex were additionally entered as covariates; in model 3, age, sex and other blood measures associated with recent suicide attempts were entered as covariates. The null hypothesis was rejected at  $p < 0.05$ . The statistical package used for the analysis was SPSS 17.0.

## 3. Results

Table 1 shows the demographic and clinical characteristics of the participants. A total of 555 participants were included in the analysis. Recent attempters were younger than lifetime and never attempters. No significant difference was observed in terms of demographic characteristics including gender, education years, employment, and marital status, except for age. As expected, the MINI suicide scores and the HAM-D scores were the highest in recent attempters, followed by lifetime attempters and never attempters ( $P < 0.001$ ). No significant differences were detected in MDQ and HCL-32 among the groups.

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