



# Differences in cholesterol and metabolic syndrome between bipolar disorder men with and without suicide attempts

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## ABSTRACT

Patient with mental illnesses such as schizophrenia and bipolar disorder have an increased prevalence of metabolic syndrome (MetS) and its components compared to general population. Among psychiatric disorders, bipolar disorder ranks highest in suicidality with a relative risk ratio of completed suicide of about 25 compared to the general population. Regarding the biological hypotheses of suicidality, low blood cholesterol level has been extensively explored, although results are still conflicting. The aim of this study was to investigate whether there were differences in the serum cholesterol levels in hospitalized bipolar disorder men patients with history of suicide attempts ( $N=20$ ) and without suicide attempts ( $N=20$ ). Additionally, we investigated if there were differences in the prevalence of MetS according to NCEP ATP-III criteria in these two groups of patients. Results of the study indicated significantly lower serum cholesterol levels ( $p=0.013$ ) and triglyceride levels ( $p=0.047$ ), in the bipolar disorder men with suicide attempts in comparison to bipolar disorder men without suicide attempts. The overall prevalence of MetS was 11/40 (27.5%). On this particular sample it was higher in the non-attempters 8/20 (40.0%) than in attempters 3/20 (15.0%) bipolar men group, but without statistical significance. Lower concentrations of serum cholesterol might be useful biological markers of suicidality in men with bipolar disorder.

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## 1. Introduction

Patient with mental illnesses such as schizophrenia and bipolar disorder have an increased prevalence of metabolic syndrome (MetS) and its components, risk factors for cardiovascular disease and type 2 diabetes (Ryan and Thakore, 2002; Newcomer, 2007) compared to general population in which incidence of MetS is also rising at an alarming rate (Nugent, 2004). Although in the past years more attention has been devoted to the medical burden suffered by patients with schizophrenia, very recently similar concern have arisen for bipolar disorder patients. Previous studies on the prevalence of MetS in bipolar patients found 30% and 49% prevalence of MetS in US bipolar patients (Fagiollini et al., 2005; Cardenas et al., 2008), 32%

prevalence of MetS in Turkish bipolar patients (Yumru et al., 2007) and 22.4% in Spanish bipolar patients (Garcia-Portilla et al., 2008). The etiology associated with this increased risk of MetS in bipolar disorder is unknown. In addition to psychosocial factors such as poverty, poor diet, lack of physical activities, increasing concern has focused on the association between second generation antipsychotics, weight gain and subsequent risk of hyperlipidaemia and diabetes. Patients with bipolar disorder have an additional risk for developing MetS because of hyperphagia and psychomotor retardation in atypical depression or comorbid conditions such as eating disorders, particularly within the bulimia/binge eating spectrum (McElroy et al., 2006).

Fagiollini et al. (2005) found that bipolar patients with MetS and patients endorsing the obesity criterion were more likely to report a lifetime history of suicide attempts.

Among psychiatric disorders, bipolar disorder ranks highest in suicidality with a relative risk ratio of completed suicide of about 25 compared to the general population (Baldessarini and Tondo, 2003). During their lifetime 80% of patients with bipolar disorder exhibit suicidal behaviour and 51% attempt suicide (Valtonen et al., 2005). The high lethality of suicidal acts in bipolar disorder is suggested by a much lower ratio of attempts: suicide (3:1) than in the general population (30:1) (Baldessarini et al., 2006). Compared with unipolar patients, suicide attempts in bipolar patients tend to be more lethal, particularly in males (Zalsman et al., 2006).

**Abbreviations:** MetS, metabolic syndrome; NCEP ATP-III, National Cholesterol Education Program, Adult Treatment Panel; US, United States; HDRS, Hamilton Depression Rating Scale; YMRS, Young Mania Rating Scale; BPRS, Brief Psychiatric Rating Scale; CGI-sev, Clinical Global Impression Scale-severity; SUAS, Suicide Assessment scale; HDL-c, High density lipoprotein cholesterol; LDL-c, Low density lipoprotein cholesterol; BMI, body mass index; cm, centimeter; mm, millimeter; mmol, mmol; L, liter; M-W, Mann-Whitney; 5-HT, five hydroxy tryptamin.

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**Table 1**  
Differences in demographic, biological and clinical parameters between bipolar disorder men with suicide attempts ( $N=20$ ) and bipolar disorder men without suicide attempts ( $N=20$ )

Characteristics	Suicide attempters			Non-attempters			$U^{\ddagger}$	$P$	Effect size (for significant results only)
	Mean $\pm$ SD*	95% CI <sup>†</sup> for mean	Median	Mean $\pm$ SD	95% CI for mean	Median			
Age (years)	36.4 $\pm$ 9.95	31.69–41.01	32.0	36.7 $\pm$ 14.43	29.94–43.46	29.5	176.5	0.529	–
Duration of illness (year)	10.6 $\pm$ 7.01	7.27–13.83	9.5	8.8 $\pm$ 7.05	5.45–12.05	5.5	154.0	0.221	–
BMI (kg/m <sup>2</sup> )	26.9 $\pm$ 4.88	24.64–29.21	25.7	27.3 $\pm$ 3.83	25.48–29.06	26.4	178.0	0.565	–
Waist circumference (cm)	94.1 $\pm$ 12.14	88.42–99.78	92.5	97.3 $\pm$ 9.22	92.94–101.56	96.5	155.5	0.231	–
Cholesterol (mmol/L)	4.0 $\pm$ 0.83	3.6349–4.42	3.9	5.1 $\pm$ 1.58	4.33–5.8	4.8	109.0	0.013	0.15
Triglycerides (mmol/L)	1.4 $\pm$ 0.52	1.1749–1.66	1.3	2.3 $\pm$ 1.74	1.44–3.06	1.6	119.5	0.028	0.10
LDL-c (mmol/L)	2.7 $\pm$ 1.50	1.9982–3.40	2.3	3.1 $\pm$ 1.32	2.46–3.7	3.0	157.5	0.253	–
HDL-c (mmol/L)	2.3 $\pm$ 2.98	0.9498–3.74	1.2	2.1 $\pm$ 2.67	0.83–3.33	1.2	197.0	0.947	–
GUK (mmol/L)	6.4 $\pm$ 3.99	4.482–8.22	4.8	6.2 $\pm$ 2.53	4.97–7.34	5.5	148.0	0.165	–
CGI severity	4.5 $\pm$ 1.00	4.03–4.97	5.0	4.6 $\pm$ 0.76	4.19–4.91	4.5	198.5	0.968	–
BPRS (score)	62.0 $\pm$ 9.93	57.35–66.65	64.5	63.3 $\pm$ 10.58	58.35–68.25	64.0	186.5	0.718	–
HDRS-17 (score)	24.6 $\pm$ 10.29	19.78–29.42	26.5	19.4 $\pm$ 10.5	14.49–24.31	15.5	144.0	0.134	–
YMRS (score)	17.7 $\pm$ 15.67	10.32–24.98	14.0	26.8 $\pm$ 17.25	18.73–34.87	33.0	139.5	0.102	–
SUAS (score)	54.9 $\pm$ 6.83	51.65–58.05	55.5	47.7 $\pm$ 9.96	42.99–52.31	50.5	116.0	0.023	0.16

\* Standard deviation.

<sup>†</sup> 95% Confidence interval.

<sup>‡</sup> Mann-Whitney U test with exact statistical significance ( $P$ ).

Suicidal behavior varied markedly between different phases of bipolar disorder and it is predominantly associated with depressive and mixed phases of the illness, rarely with pure manic phase. (Goldberg et al., 1999; Oquendo et al., 2000; Valtonen et al., 2007).

Among the biological hypotheses of suicidality, low blood cholesterol level has been extensively explored, although results are still conflicting. Numerous studies showed lower cholesterol levels in patients hospitalized after suicide attempt as compared to non-attempters hospitalized patients (Sarchiapone et al., 2001; Guillem et al., 2002; Kim et al., 2002) with remained significant difference in men, but not in women, after gender stratification (Diaz-Sastre et al., 2007). On the other hand, there are some other studies showing no relationship between low cholesterol levels and suicide attempt (Roy et al., 2001; Tsai et al., 2002; Deisenhammer et al., 2004; Fiedorowicz et al., 2007) and even one recent study demonstrating higher cholesterol level in patients with suicide attempt in the past year (Brunner et al., 2006).

After several studies of our team regarding the role of low cholesterol in suicidal behavior in different psychiatric disorders (Marčinko et al., 2004, 2005, 2007a,b, 2008), the current study was created to investigate if serum cholesterol level is decreased in male bipolar disorder patients with suicide attempts compared to non-attempters. Additionally, the aim of this study was to estimate if there were differences in the prevalence of metabolic syndrome between bipolar disorder male patients with and without lifetime suicide attempts.

## 2. Methods

### 2.1. Sample

Subjects were male patients ( $N=40$ ) with bipolar disorder treated at the Department of Psychiatry, University Hospital Centre Zagreb during the period of 36 months. Within patients, 20 patients were consecutively admitted men with bipolar disorder with history of suicide attempt, and 20 patients were consecutively admitted men with bipolar disorder without history of suicide attempt. Needed sample size was calculated respecting the following parameters: alpha error level of 95% ( $p<0.05$ ), large effect size (Cohens  $d\geq 0.8$ ), infinite population, t-tests for two independent samples with homogenous variances). Needed sample size under this conditions were  $N=26$ . Due to the practical restraints (small number of patients that were free of medication during the last 3 months prior to the inclusion into the study) we accomplished somewhat smaller final sample ( $N=20$ ). The

diagnosis of bipolar disorder was made according to diagnostic criteria of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), (World Health Organization, 1996). According to ICD-10 criteria in suicide attempter group 7 patients were in depressive, 5 in manic and 8 in mixed episode. In non attempter group 6 patients were in depressive, 12 in manic and 2 in mixed episode.

Intensity of depressive symptoms was assessed by Hamilton Depression Rating Scale, HDRS-17 (Hamilton, 1960), while manic symptoms were assessed by Young Mania Rating Scale, YMRS (Young et al., 1978). Brief Psychiatric Rating Scale (BPRS-18) was used to estimate a broad range of psychopathology (Overall and Gorham, 1962). Clinical Global Impression severity, CGI sev (Guy, 1976) was performed to assess the severity of illness, and Suicide Assessment Scale, SUAS for symptoms of suicidality (Stanley et al., 1986). Suicide attempt, by definition, included intent to die, self-harm did not count. The trained psychiatrist performed clinical evaluation.

All participants were free of all psychotropic medication for the previous 3 months. Two groups of patients were closely matched for age. All subjects gave written consent for participation in the study after detailed information about the procedures. This study was approved by the Clinical Hospital Center Medical Ethics Committee.

Only patients whose biochemical analyses from the time of admission were available were included in the study. Venous blood samples were collected within 24 h of admission. The exclusion criteria were: hypertension, diabetes mellitus, inherited disorders of lipoprotein metabolism, diagnosis of substance abuse, including alcoholism, eating disorder and organic brain syndrome.

### 2.2. Assessment

Venipuncture was performed for all subjects between 8 and 9 a.m. after 12 h overnight fast. Immediately after collecting blood samples, serum concentration of total cholesterol, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides and serum glucose were determined using enzyme methods and commercial kits (Olympus Diagnostic, GmbH, Hamburg, Germany) on Olympus AU 600 automated analyzer. Inter-assay laboratory coefficients of variation were 3.2% for cholesterol, 2.5 for triglycerides and 3.0% for HDL-cholesterol. Reference intervals for the measured parameters were as follows: cholesterol  $<5.0$  mmol/L, LDL  $<3.0$  mmol/L, HDL  $>1.0$  mmol/L, triglycerides  $<1.7$  mmol/L and glucose  $>6.1$  mmol/L.

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