



The Association Between Depression, Impulsive Behaviors and Suicidal Ideation with Serum Low Density Lipoprotein (LDL) Level in Patients with Morbid Obesity: A Cross-Sectional Study

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Abstract

The aim of this study was to compare the severity of depression, impulsive behaviors and suicidal ideation in patients with obesity with Low Density Lipoprotein (LDL) below 100 or above 100 *mg/dl*.

Methods: This was a cross-sectional study. The study population included patients with obesity referred to the obesity clinic of Rasool-e-Akram Hospital affiliated to Iran University of Medical Sciences, Tehran, Iran. Patients were divided into two groups with LDL below and above 100 *mg/dl*. The Beck scale for suicidal ideation and Depression and the Barratt Impulsiveness Scale questionnaires were filled. Finally, the score of questionnaires and demographic variables were compared between the two groups. P-values below 0.05 were considered as statistically significant.

Results: 300 patients entered the study. There was a statistically significant difference regarding the severity of depression between the two groups, as in patients with LDL over 100 *mg/dl*, depression was more severe (p-value = 0.02). Moreover, there was a statistically significant difference regarding the impulsivity score and its subgroups or the suicidal ideation between the two groups (higher in patients with LDL) above 100 *mg/dl*, p-values <0.05).

Conclusion: Elevated serum LDL levels could be associated with psychological factors such as depression or suicidal ideation and motor, cognition and unplanned impulsivity in patients with morbid obesity. This might be justified by an increase in BMI. Further clinical trials are required to assess these findings.

Keywords: Impulsivity, Low density lipoprotein (LDL), Major depressive disorder, Obesity, Suicidal ideation

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Received: Sept 30 2021

Accepted: Dec 18 2021

Citation to this article:

Ghanbari Jolfaei A, Soheilipour F, Mohammadnia F, Tajik Esmaeeli S. The Association Between Depression, Impulsive Behaviors and Suicidal Ideation with Serum Low Density Lipoprotein (LDL) Level in Patients with Morbid Obesity: A Cross-Sectional Study. *J Iran Med Council.* 2022;5(3):403-10.

Introduction

Major Depressive Disorder (MDD) is one of the most common and complicated human diseases. Since enduring an episode of depression can be very difficult and exhausting, such patients are at a high risk for suicide and other risky behaviors (1).

For almost 30 years, cholesterol has been recognized as a harmful substance to human health due to its role in cardiovascular disorders, thus the emphasis has always been on lowering blood cholesterol levels (2). On the other hand, cholesterol is an essential substance for maintaining human mental health as is present in the nerve cell membranes (3). Cholesterol participates in the activity of serotonin receptors on the surface of nerve cells as well (4). Therefore, lowering cholesterol indirectly reduces serotonin activity at least theoretically.

Some authors claimed that blood cholesterol-lowering treatments only reduce mortality due to cardiovascular complications and have no effect on the overall mortality rate as lowering cholesterol might increase the mortality rate because of suicidal attempts and violence (5). In addition, some other researchers have found a link between low serum cholesterol levels and increased rates of depression (6) or suicidal ideation (7). Inconsistently, some other articles reported that serum Low Density Lipoprotein (LDL) levels were higher in patients with episodes of major depression than those in the normal control group (8). Despite the fact, some others have not found any association between cholesterol levels and suicidal behaviours (9).

Monoamine Oxidase (MAO) has been suggested as a possible explanation for elevated serum cholesterol level in patients with depression. Some animal studies have suggested monoaminergic metabolism as the responsible mechanism in hypercholesterolemic rats. In fact, they reported increased monoamine oxidase A and B activity in the rat hippocampus (10). However, there is still a long way to understand the underlying molecular pathophysiology of depression and the effect of lipid profile on it.

Impulse-Control Disorder (ICD) is one of the psychiatric disorders defined as the inability to resist strong temptation to perform a harmful behavior. The person has a great desire to do this behavior for an immediate relief, but after a while, he or she experiences

regret and guilt (11). An inverse association has been reported between serum total cholesterol level and body mass index with patients with ICD (12).

Moreover, depression and impulsive behavior like binge eating can cause obesity and high LDL level. It has been shown that patients with obesity are more likely to have high blood cholesterol and statin use (13). Furthermore, statin reduces plasma LDL-cholesterol (LDL-C) by inhibiting the HMG-CoA reductase enzyme in the liver (14,15).

Considering the controversial data in this field and the importance of MDD, ICD and suicidal ideation in the quality of life, and lack of researches about this in Iran, the aim of this study was to compare the severity of depression, impulsive behaviors and suicidal ideation in two groups of patients with obesity with LDL below or higher than 100 *mg/dl*.

Materials and Methods

This was a cross-sectional study. The study population included 300 patients with obesity referred to the obesity clinic of Rasool-e-Akram Hospital affiliated to Iran University of Medical Sciences, Tehran, Iran. Available convenience sampling was used to enroll the patients. Participants included 238 females and 62 males. The patients were divided into two groups with LDL below and above 100 *mg/dl*. The inclusion criteria were age between 18-65 years, normal thyroid tests, no current drug use, Body Mass Index (BMI) > 35 *kg/m²*, normal FBS (Fasting Blood Sugar) and at least third grade elementary school literacy. Furthermore, the exclusion criteria were major psychiatric disorders, cognitive impairment, intellectual disability, advanced liver and kidney disease, thyroid disorders, menopause, use of psychiatric medications, alcohol or substance abuse, *etc.* The exclusion criteria were evaluated by clinical judgment of the investigator, a psychiatrist.

The Beck scale for suicidal ideation, the Beck Scale for Depression, and the Barratt Impulsiveness Scale questionnaires were filled by all participants. The patients read and answered the questionnaires themselves, but the researcher was available in case of any ambiguity. LDL levels were extracted from their documents. Demographic information including age, gender, literacy, BMI, drug use, *etc.* were also recorded.

Table 1. Demographic characteristics of the study population

Variables	LDL above 100 mg/dl	LDL below 100 mg/dl	p-value
Age, (Mean ± SD), year	41.1 ± 11.2	41.5 ± 12.3	0.6
Gender, n			
Male	32	30	0.7
Female	118	120	
BMI, (Mean ± SD), kg/m ²	45.6 ± 6.2	42.1 ± 4.7	0.001
Literacy, n			
High school	40	40	0.8
Diploma	62	60	
Associate degree	20	16	
Bachelor	26	30	
Master and higher	2	4	
Statin use, (yes),n	23	18	0.4

Table 2. Depression severity, impulsivity and suicidal score in the study participants

Variables		LDL below 100 mg/dl	LDL above 100 mg/dl	p-value
Depression severity, (n)	None	104	79	0.02
	Mild	27	36	
	Moderate	13	25	
	Severe	6	10	
Impulsivity, (mean ± SD)	Cognitive	59.8 ± 14	64.7 ± 14.7	0.004
	Motor	16.7 ± 4.2	18.3 ± 4.6	0.003
	Unplanned	24.9 ± 6.5	26.5 ± 6.6	0.04
	Total score	18.2 ± 5.4	19.9 ± 5.5	0.006
Suicidal ideation, (mean ± SD)		1.4 ± 3.7	2.6 ± 4.9	0.02

The Beck Scale for Suicidal ideations (BSSI)
Beck Scale for Suicidal ideations (BSSI) is one of the most common self-report questionnaires to evaluate suicidality. The reliability and validity of the BSSI in English language have been frequently reviewed and almost always the Cronbach's alpha coefficient was higher than 0.85 (16). In the Iranian population, the psychometric features of the BSSI was evaluated by Esfahani *et al* and the Cronbach's alpha coefficients were satisfactory (>0.8) and reliability coefficient was acceptable (17).

The Beck Depression Inventory-Second Edition (BDI-II)

The Beck Depression Inventory (BDI) is perhaps the most commonly used screening self-report instrument for depression in the general population. In an Iranian

sample, Ghassemzadeh *et al* indicated that the BDI-II-Persian had high internal consistency (Cronbach's alpha=0.87) and acceptable test-retest reliability (r=0.74) (18).

The Barratt Impulsiveness Scale-11th revision (BIS-11)

It's a self-report questionnaire that assesses three dimensions of trait impulsivity: motor, non-planning, and attentional impulsivity. The Persian version of BIS-11 has been proven to be valid and reliable (19).

Ethical issues

All patients signed a written informed consent prior to enrollment. The study goals were explained in detail to the patients and they were free to leave the study at any step without affecting their routine care. All the

study steps were performed according to the Helsinki Declaration. The patients' information was kept confidential without disclosing their identities. The study protocol was approved by the ethics committee of Iran University of Medical Sciences (Ethical code; IR.IUMS.REC.1398.1014).

Statistical analysis

Data was entered into IBM SPSS STATISTICS 22 (IBM, Inc, New York, USA) and analyzed. Mean and standard deviation were utilized to express the quantitative descriptive data and frequency and percentage for the qualitative ones. Normal distribution of the data was checked using Kolmogorov-Smirnov test. Chi-square and T-test and their non-parametric counterparts were used where necessary. p-values below 0.05 were considered as statistically significant.

Results

300 patients entered the study (150 patients with LDL less than 100 and 150 above 100 *mg/dl*). Patients in the two groups were appropriately matched as there were no statistically significant differences regarding age (p value = 0.6) and gender (p value = 0.7). However, BMI was significantly higher in those with LDL greater than 100 *mg/dl* (p value < 0.001). Besides, there was no statistically significant difference between the two groups regarding literacy or statin use (p-value > 0.05). Demographic characteristics of the participants are depicted in table 1.

Despite the fact, there was a statistically significant difference with regard to the severity of depression in the two groups, as in patients with LDL more than 100 *mg/dl*, depression was more severe (p-value = 0.02). Moreover, there was a statistically significant difference considering the impulsivity score and its subgroups including motor, cognitive and unplanned impulsivity or the suicidal ideation between the two groups (higher in patients with LDL above 100 *mg/dl*, p values < 0.05). Depression severity, impulsivity and suicidal score in patients with LDL below and above 100 *mg/dl* are shown in table 2.

There was also no statistically significant association between statin use and motor, cognitive and unplanned impulsivity in any group (p-value>0.05). Also, no association was found between the depression

severity and statin use in any group (p value > 0.05).

Discussion

In our study, we tried to assess the association between depression severity score, impulsivity score and serum LDL level in patients with morbid obesity. We matched the two groups regarding age and gender to remove their confounding effects. However, some other trials did not perform matching. Dalpino *et al* (20) reported that serum LDL levels were higher in women than men. Also, Zhao (21) claimed that serum LDL levels increased with higher age. Moreover, body mass index was higher in patients with LDL levels greater than 100 *mg/dl* in our study, which is consistent with many other reports (13). There is a known association between depression and obesity (22) and LDL level is usually higher in patients with obesity. In our study we only enrolled the patients with morbid obesity to remove the confounding effect of BMI in statistical analyses.

We found that depression was more severe in patients with LDL above 100 *mg/dl*. Besides, the total impulsivity score and its subgroups including motor, cognitive and unplanned impulsivity and suicide score were significantly higher in those with LDL above 100 *mg/dl*. Wagner *et al* (8), also reported that serum LDL levels were higher in patients with episodes of major depression than those in the normal control group, which is consistent with the present trial. However, conflicting results have been reported in previous investigations. For instance, a systematic review and meta-analysis published by Persons *et al* (23) found that serum LDL levels were lower in patients with major depression, which is contrary to our findings. Different results could be due to different sample size, socioeconomic background or genetic diversity.

Tomson-Johanson *et al* investigated the effect of LDL on impulsivity. They showed that high serum LDL levels were associated with increased impulsivity and decreased inhibition in adult girls (24). Yaylaci *et al* also confirmed more impulsivity in higher LDL levels, which is consistent with our results (25). Despite the fact, Mahmoud Shaker *et al* stated that serum LDL levels were not significantly related to impulsive behaviors (26). The reasons for such inconsistencies could be due to the study sample size, underlying

diseases, age, gender distribution, drug use, ethnicity and geographic differences, depression severity, follow-up duration, *etc.* Therefore, it is necessary to conduct reviews and meta-analyses to shed light on the issue.

Furthermore, some studies showed an association between low serum cholesterol level and an increased risk of death from injury or suicide (27-32). On the other hand, some others reported that high cholesterol levels were associated with more suicidal ideation (33-36), which is in line with the present study. Another investigation in Mexico (37) assessed the possible association between serum cholesterol level and suicide attempt in patients with major depression. They found no difference in blood lipid profile between patients who attempted suicide and those who did not. However, this study evaluated only 33 patients with major depression (moderate to severe) compared to those who had never attempted suicide, which could justify the controversial findings. There is still no consensus regarding the role of serum lipids profile and suicidal attempts, which necessitates further efforts by larger clinical trials.

We also investigated the association between statin consumption and LDL levels. Results showed that only two underlying variables including age and BMI differed between statin and non-statin users. Czech *et al* stated that statin use had no effect on impulsivity and suicidal ideation of patients, which is in line with our study (15). Despite the fact, Köhler-Forsberg *et al* evaluated statin therapy and the risk of depression (14). In this study, a total of 193,977 statin users and 193,977 non-statin users were followed up for 2, 621, 282 people-years. They finally concluded that statin use was associated with the following outcomes; 1) increased risk of using antidepressants (Hazard Rate Ratio (HRR) = 1.33; 95% confidence interval (95% -CI) = 1.31-1.36), 2) increased risk of any other prescribed medication (HRR = 1.33; 95% -CI = 1.31-1.35), 3) an increase in the diagnosis of major depression (HRR = 1.22, 95% -CI = 1.12-1.32). However, another study by Yeh *et al* (38) found that statin users had a lower risk of anxiety and depression, regardless of age, sex, and underlying disease (anxiety; adjusted hazard ratio [aHR] = 0.34, 95% confidence interval [CI] = 0.28-0.42; depression: aHR = 0.36, 95% CI = 0.25-0.53).

The study by Davison *et al* (39), also found that the prevalence of suicidal ideation was more than 2.5 times higher in those consuming statins (PR = 2.59, 95% CI 1.27-5.31, $p < 0.05$), which is not consistent with the present study.

Finally, there is still ambiguity regarding the role of statin use or LDL level with depression or/and suicidal attempts and impulsivity. More clinical trials should be performed to elucidate the exact role of hyper- or hypocholesterinemia in major depression, impulsivity or suicidal ideation.

A number of important limitations need to be considered.

The study population included only patients with obesity which limits the generalizability of our findings. However, it could remove the bias effect of BMI in interpretation of the findings. Therefore, there is a need to conduct researches in the general population. Moreover, the follow-up duration was quite short. Regarding the role of statin use, due to the lack of exact method to evaluate the role of these medications in the current study, we could not properly conclude lack of association between statin taking and the items. In this study, having chronic disease, using any medications, past psychiatry history regarding depression and impulsive behavior, marital status, employment, income and failure in reducing weight were missed and they affected depression, suicide and impulsive behavior. However, two groups were selected from the patients referred to the obesity clinic equally, that they were divided based on LDL, and we tried to match the other factors as much as possible. Since our goal was not to assess cause and effect, and we only wanted to measure the association between depression and obesity and impulsivity and LDL, we failed to measure their precedence and latency, and our method did not allow us to do so. This is one of the cross-sectional study limitations which does not assess the cause and effect. We suggest to perform larger multi-centric longitudinal studies from different ethnicities living in different geographic areas and in the general population.

Conclusion

Elevated serum LDL levels could be associated with psychological factors such as depression, suicide and motor, cognition and unplanned impulsivity in

patients with morbid obesity. This might be justified by an increase in BMI. However, there is still no consensus regarding the role of serum lipids profile with depression, suicidal attempts and impulsivity, which necessitates further efforts by larger clinical trials.

Acknowledgements

We would like to thank Farname Inc. (Canada) to help for the native English editing of the manuscript.

Funding and support

None.

Financial disclosure

None.

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