



## Screening for metabolic syndrome in patients with bipolar disorder

Maryam Maddineshat<sup>1</sup>, Hamid Reza Bayati<sup>2</sup>, Atefe-Sadat Davudi<sup>3</sup>, Sepideh Frozesh<sup>4</sup>, Masoumeh Taherpour<sup>5</sup>

1. Ph.D. Student in Nursing, School of Nursing, North Khorasan University of Medical Sciences, Bojnurd, Iran
2. M.D in Psychiatry, Imam Reza Hospital, North Khorasan University of Medical Sciences, Bojnurd, Iran
3. Imam Ali Hospital, North Khorasan University of Medical Sciences, Bojnurd, Iran
4. Imam Ali Hospital, North Khorasan University of Medical Sciences, Bojnurd, Iran
5. M.Sc in Biostatistics, Faculty of Biostatistics, North Khorasan University of Medical Sciences, Bojnurd, Iran

### Corresponding Author:

School of Nursing,  
North Khorasan University of Medical Sciences,  
Bojnurd,  
Iran,  
E-mail: neshat\_maryam@yahoo.com

### Article History

Received: 14 December 2017  
Accepted: 31 January 2018  
Published: March-April 2018

### Citation


Maryam Maddineshat, Hamid Reza Bayati, Atefe-Sadat Davudi, Sepideh Frozesh, Masoumeh Taherpour. Screening for metabolic syndrome in patients with bipolar disorder. *Medical Science*, 2018, 22(90), 181-187

### Publication License



This work is licensed under a Creative Commons Attribution 4.0 International License.

### General Note

 Article is recommended to print as color digital version in recycled paper.

### ABSTRACT

Metabolic health threat to patients with bipolar disorder is of interest to many studies. This study aimed to screen metabolic syndrome in patients with bipolar disorder in a University Hospital Psychiatry Outpatient Clinic, Bojnurd, Iran. In this cross-sectional study 124 patients with bipolar disorder were screened by sequential sampling method. Patients with bipolar disorder were

admitted from October, 2014 to November, 2015 in a University Hospital Psychiatry Outpatient Clinic. Patients were evaluated for metabolic syndrome using a checklist based on NCEP ATP III criteria. The prevalence of metabolic syndrome was higher in women with bipolar disorder (70.2%). About 22.6% of patients had high blood sugar (high fasting glucose), 68.5% had abdominal obesity, 8.1% had high blood pressure, 34.7% had high cholesterol, and 46.7% had high triglyceride. Most of patient (88.9%) were illiterate, and the most common metabolic abnormality was related to obesity. Age and BMI had a significant relationship with the prevalence of metabolic syndrome ( $P < 0.05$ ). Some criteria of metabolic syndrome coexist in bipolar patients. Screening for metabolic syndrome in bipolar patients is important in preventing the risks posed by it. Also, given that most patients with bipolar disorder and metabolic syndrome are women and most patients were illiterate, it is recommended that training classes be set up in psychiatric clinics.

**Keywords:** Bipolar disorder; Metabolic syndrome; Obesity

## 1. INTRODUCTION

Metabolic syndrome is defined by concurrent development of three disorders associated with metabolism, including: increased waist circumference or abdominal obesity, hypertension, dyslipidemia, and hyperglycemia (O'Callaghan et al., 2011, Zarzavadjian Le Bian et al., 2017). Metabolic syndrome is a group of risk factors that can predict lethal diseases like cardio-vascular diseases (CVDs) and diabetes in different communities. It has been suggested for more than a century in psychiatric literature that metabolic syndrome is common in patients with mental disorders and plays a role in premature mortality of patients with mental disorders (Margari et al., 2013, Carliner et al., 2014). It is estimated that mortality rate from CVDs are two-folds in patients with bipolar disorder than healthy people and they develop metabolic syndrome 4-6 years earlier than healthy people. Patients with bipolar disorder have unhealthy lifestyles, caused by excessive intake of calories and cholesterol, smoking and a sedentary lifestyle; also long-term use of medications for treatment of bipolar disorder may accelerate metabolic syndrome and obesity (Murray et al., 2009, Fiedorowicz et al., 2008). In Italy, a two-year follow-up of 70 patients with bipolar disorder showed an increase in the prevalence of metabolic syndrome from 28.6% to 44%. Aging, increased BMI, and atypical antipsychotic medications predicted metabolic syndrome in this study. The findings of other studies suggest that metabolic syndrome in bipolar patients is the adverse effects of antipsychotic medications and mood stabilizers (Salvi et al., 2012). Some studies have reported that it has not been determined yet what exactly stimulates vascular inflammatory process and makes the patients with bipolar disorder prone to metabolic syndrome (Leboyer et al., 2012, Weiner et al., 2011). Bipolar disorder affects patients' quality of life, and most psychiatrists have confirmed that they concern metabolic health, as two-thirds of doctors have changed the medical practice of bipolar patients (Bauer et al., 2008). Even some studies have reported higher prevalence of metabolic syndrome in patients with bipolar disorder than other psychiatric disorders, such as schizophrenia. While other studies have described that the use of some medications and lifestyle of patients with bipolar disorder increases the risk of metabolic syndrome and CVD-related mortality in these patients (Bly et al., 2014, Lee et al., 2010). Despite this evidence, unfortunately, no Iranian study was found to address patients with bipolar disorder and metabolic syndrome, through a search in Persian sources, including Magiran, SID, Iranmedex, Medlib, and Google. Only in one study by Sadatyan et al. 2012, among 130 Iranian women with psychiatric disorders, regardless of the type of disease, 39.8% was reported based on criteria NCEP ATP II (Saadatian et al., 2012). In Iran, there are little strong evidence about metabolic syndrome, which address patients with bipolar disorder indicating that patients with mental disorders pay less attention to their physical health, compared to patients without the disorder (O'Callaghan et al., 2011). Considering the high prevalence of metabolic syndrome in bipolar patients and the importance of reducing the complications of metabolic syndrome, the present study aimed to screen metabolic syndrome in patients with bipolar disorder in a University Hospital Psychiatry Outpatient Clinic, Bojnurd, Iran.

## 2. MATERIALS AND METHODS

A normal screening program for metabolic syndrome was conducted in University Hospital Psychiatry Outpatient Clinic, Bojnurd, Iran. This cross-sectional analytic study included all male and female patients diagnosed with bipolar disorder based on DSM-IV-TR criteria and psychiatrist's consultant. After approval by Ethics committee (Code: 567/P/91), The number of participants was estimated at 200 and after commencement of the study, 124 patients with bipolar disorder were selected by non-probable convenient sampling method, from those who participated in the screening program for one year from October 2013 to November 2014. Inclusion criteria for this study were as follows: 1) Patients referring to Psychiatry Outpatient Clinic, 2) aged over 18 years, 3) Minimum treatment period for at least 3 months, and 4) willingness to participate in the study. Exclusion criteria were as follows: 1) Current pregnancy, 2) concurrent mental diseases (such as schizophrenia), 3) severe physical diseases, and 4) history of treatment for

metabolic disorders. The total number of patients who met the inclusion criteria was 124 patients, from whom verbal and written consent was obtained. The participants were assured of confidentiality of their information and scientific honesty and trustworthiness were met in line with prevention of revealing the name of the subjects. Ethical principles, in accordance with the guidelines of the Declaration of Helsinki, were taken into consideration. For patients with bipolar disorder participating in the study, two checklists were completed, including socio-demographic data (age, gender, single or married, living place, educational level, employment status, duration of disease, disease history, number of relapses, duration of medication consumption, type and dose of the medication, number of the medications, etc.) and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (2002), used in recently published studies (Saadian et al., 2012, 2002, Babic et al., 2010, Salvi et al., 2008, Vuksan-Cusa et al., 2010, Chackrewarthy et al., 2013). To measure the risk of metabolic syndrome, the criteria provided by Program Adult Treatment Panel III (NCEP ATP III) was used, including:

- Abdominal obesity: waist circumference  $\geq 102$  cm in men, and  $\geq 88$  cm in women
- Hypertriglyceridemia:  $\geq 150$  mg/dl or on lipid-lowering medication
- Low HDL-C:  $<40$  mg/dl in men and  $<50$  mg/dl in women
- High blood pressure: systolic pressure  $\geq 130$  mmHg and/or diastolic pressure  $\geq 85$  mmHg or on antihypertensive medication
- High fasting glucose:  $\geq 100$  mg/dl

To complete the measures of NCEP ATP III, blood samples were collected after 8 hours' fasting and evaluated for cholesterol, glucose, triglycerides, HDL-C by introducing a research team member to the laboratory of hospital. Waist circumference was measured from iliac crest at umbilical level and body mass index, and blood pressure were measured in the psychiatric clinic. Since these measures are standard, the scores were compared with criteria of metabolic syndrome for each patient. The relationship between metabolic syndrome and its components with demographic and clinical variables was analyzed using chi-square tests, t-test and nonparametric tests (Mann-Whitney U). The results were considered to be significant at  $p = 0.05$ . Data analysis was performed using SPSS16 software.

### 3. RESULTS

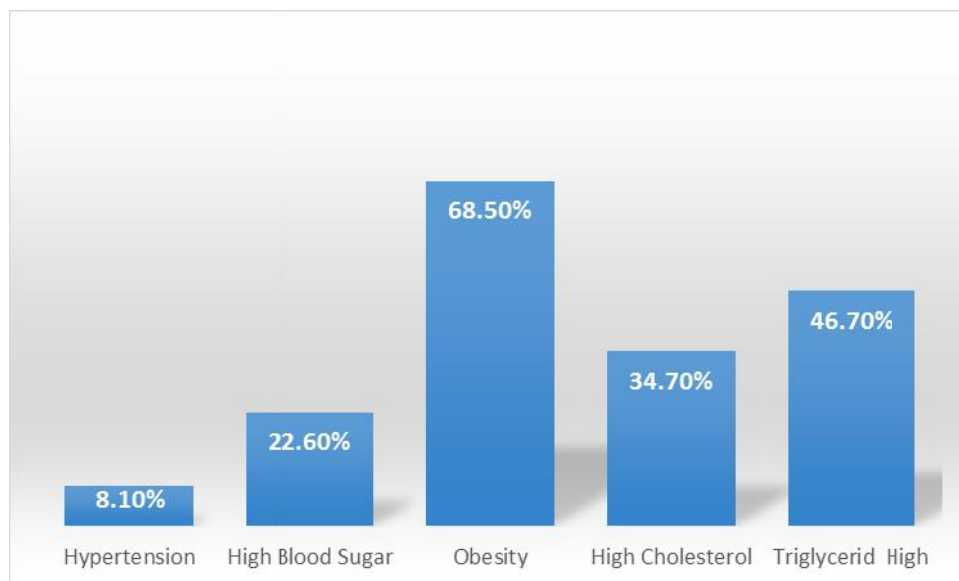
The information of 124 patients who were diagnosed based on DSM-IV-TR criteria by psychiatrist's consultant with bipolar disorder were examined. Screening revealed that 70.2% of participants were women, 88.9% were illiterate, and most used two or more antipsychotic medications, mainly classic antipsychotic medications (Table 1).

**Table 1** Sociodemographic and clinical characteristics of outpatients with Bipolar disorder

Characteristics	Value
Age (years), Mean $\pm$ S.D	43.91 $\pm$ 9.9
Females, n (%)	70.2%
Married, n (%)	88.7%
Education years	
Illiteracy	30%
Primary school	58.9%
Diploma and more	11.1%
Duration of illness, Mean $\pm$ S.D	6.05 $\pm$ 5.46
Number of medications for BD	
Old antipsychotics*, n (%)	22.6%
Antidepressants, n (%)	37.7%
Mood stabilizers, n (%)	21.5%
Benzodiazepines, n (%)	14%
Anticholinergic, n (%)	4.2%
patients were taking two drugs	56.5%
patients were taking three drugs	24.2%
patients were taking four drugs	3.2%
BMI, Mean $\pm$ S.D.	36.51 $\pm$ 22.82 kg.m <sup>2</sup>

\* First generation antipsychotic drugs or typical antipsychotics

Clinical reports of risk factors related to metabolic syndrome were as follows: 22.6% of participants had high fasting glucose, 68.5% abdominal obesity, 8.1% hypertension, 34.7% high cholesterol, and 46.7% had high triglycerides (Figure 1).



**Figure 1** The number and percentage of patients with abnormal metabolic criteria

The distributing factor for factors associated with metabolic syndrome was sex, as most women were obese, and had high triglycerides, cholesterol, blood pressure and blood sugar levels, compared to men. In women, the most common abnormality was related to obesity and in this study, most patients with metabolic syndrome were female. Also, comparison of women and men, based on chi-square test, showed significant association between obesity, triglycerides, cholesterol, and blood glucose levels ( $P < 0.005$ ). After screening, patients with bipolar disorder were assessed for metabolic syndrome, according to its definition (having at least three disorders associated with metabolism), indicating that 25% ( $n=31$ ) had the metabolic syndrome, and 75% of participants ( $n=93$ ) did not, representing the prevalence of metabolic syndrome at 25% (Table 2).

**Table 2** Clinical documentation of risk factor metabolic syndrome and its diagnostic in outpatients with Bipolar disorder

Components	total number (percent)	Number in men (percent)	Number in women (percent)	P-value (Level of significance)
Obesity	85(68.5%)	31(35.1%)	72(82.8%)	0.002
Triglycerides	58(46.7%)	7(18.9%)	51(58.6%)	<0.001
Cholesterol	43(34.7%)	19(51.4%)	24(27.6%)	0.01
Hypertension	10(1.8%)	2(5.45%)	8(9.2%)	0.478
Blood Sugar	28(22.6%)	15(40.5%)	13(14.9%)	0.002
At least three or more components	31(25%)	11(29.7%)	20(23%)	0.428

After screening and diagnosis of metabolic syndrome, Also, comparison between patients with bipolar disorder with and without metabolic syndrome showed that patients with bipolar disorder and metabolic syndrome were mostly >48 years old, women, consumed 3 or more medications, had a BMI >38 kg/m<sup>2</sup>, and used classic antipsychotic medications, antidepressants, and mood stabilizers. The results of chi-square test, t test and Mann-Whitney tests showed a statistically significant relationship between metabolic syndrome and demographics, including age and BMI ( $p < 0.05$ ), (Table 3).

**Table 3** The comparison of criteria in outpatients with Bipolar disorder with and without metabolic syndrome after Screening

Components	Patients with Metabolic syndrome	Patients without Metabolic syndrome	P-value (statistics)
Age (mean, standard deviation)	48.40±9.85	42.45±9.54	0.004(-2.939)
Gender (% of female)	64.5%	72%	0.428(0.629)
The number of medications	3.12±1.32	3.17±1.45	0.816
BMI	38.14±11.95	35.71± 24.08	0.046(-1.994)
Anti s old Drug (% of drug users)	21.7%(13patients)	78.3%(47 patients)	0.8329(0.376)
Anti-depressant Drug (% of drug users)	25%(25patients)	75%(75 patients)	0.827(0.380)
Mood stabilizer Drug (% of drug users)	26.3%(patients)	73.7%( patients)	0.542(0.372)

#### 4. DISCUSSION

Many studies worldwide suggest the association of metabolic disorders in patients with bipolar patient with mortality and poor consequences (Mansur et al., 2015). The results of screening 124 patients with bipolar disorder showed that 31 patients (25% of participants) had metabolic syndrome based on NCEP ATP III criteria. Most patients with bipolar disorder are less educated and older than 48 years and have a high BMI index ( $>38 \text{ kg/m}^2$ ). Assessing criteria related to metabolic syndrome showed that abdominal obesity, triglycerides, and high cholesterol were present in patients with bipolar disorder more than other criteria. Although the exact cause of metabolic syndrome in bipolar patients cannot be associated with medications, the results of this study suggested that consuming more than three medications in patients with metabolic syndrome describes bipolar. In this study also, the majority of bipolar patients were women, and metabolic syndrome was observed more in them. In line with the results of this study, the findings of the study by Vancampfort et al., 2013 strongly suggested that patients with bipolar disorder are in high risk of metabolic syndrome and CVD-related mortality. This risk is greater in bipolar patients who receive antipsychotic medications. Grover et al., 2012 conducted a study in India, which showed that among 82 patients examined based on NCEP ATP III criteria, more than 70% were obese, 44.5% had hypertension, and 42% had high triglycerides. In this study, the most common metabolic disorder in bipolar patients was obesity and comparison of patients with and without metabolic syndrome in this study indicated that patients with metabolic syndrome have a BMI  $> 25 \text{ kg/m}^2$ , and are older than 35 years. Lee et al., 2010 showed in a study in Korea on 152 patients with bipolar disorder that 25% of bipolar patients had metabolic syndrome, 40.8% of patients had a BMI over  $25 \text{ kg/m}^2$ , 47% were obese, 33% had high triglycerides and cholesterol, and 25% had hypertension. This study suggested that older age is associated with increased prevalence of metabolic syndrome and it is expected to be observed more between the ages of 50-41 years. Salvi et al., 2008 explained in their study that aging decreases muscle mass and increases body fat, especially in the abdomen and both of these changes ultimately leads to increased insulin resistance and metabolic syndrome. Czepielewski et al., 2013 stated in a review study that although many studies have confirmed the prevalence of metabolic syndrome in bipolar patients, studies have suggested different prevalence rates that can be due to differences in sampling method, or different cultures, dietary habits, physical activity, and genetic backgrounds that can affect measurements of subcomponents of metabolic syndrome. Therefore, heterogeneity was the most important concern in the diagnosis of metabolic syndrome. In addition, although NCEP ATP III and the IDF criteria are used in many studies, there are some differences in the criteria, and of course, there are numerous confounding factors that makes it more difficult to diagnose this syndrome and analyze the results. But Weiner et al., 2011 expressed in their study that despite the complexity of diagnosis of metabolic syndrome in bipolar patients, there is great evidence for the relationship between metabolic syndrome with bipolar disorder and premature mortality that cannot be ignored; thus, a fast screening program can identify the risk of metabolic syndrome and accelerates its adjustment; although patients with less severe mental problems will be diagnosed as having metabolic syndrome. One of the typical findings of the present study was low-educated patients with bipolar disorder; although psychiatric texts confirm the association of low socio-economic situations with psychiatric disorders, studies show that illiteracy and low educational level are consistent risk factors for development of mental disorders (Lund et al., 2010). In this study, illiteracy and low educational level in bipolar patients may have caused their lack of attention to serious risks of metabolic syndrome. This study had some limitations. The biggest limitation of this study was the cross-sectional nature of this study that was conducted in a specific time point and patients were not followed to assess whether the risk of metabolic syndrome has increased or decreased in them, but this the present study provides a rational hypothesis for future prospective longitudinal

studies. In addition, this study only included patients from psychiatry outpatient Clinic with bipolar disorder and type of bipolar I or II was not separately evaluated. The study's quality may have also been affected by sample size and data were restricted to psychiatry outpatient clinic of one hospital and some variables, such as family history of hypertension and diabetes or some aspects of lifestyle, such as exercise and smoking were not measured. However, this is the first study to examine metabolic syndrome in bipolar patients. Other limitations of this study include lack of a control group for comparison. This study emphasizes on improved clinical performance in busy psychiatric clinics. Thus, it is recommended that further studies be conducted with a larger sample size and with a control group.

## 5. CONCLUSION

Some criteria for metabolic syndrome coexisted in bipolar patients. Greater attention should be paid to women. Screening for metabolic syndrome in bipolar patients is of great significance in order to prevent the risk of metabolic syndrome. Considering the low literacy of these patients and to enhance clinical performance of psychiatry outpatient clinics, psychiatric training and medical follow-up seem necessary for decreasing the risk of metabolic syndrome in these patients.

## ACKNOWLEDGMENTS

This research was financially supported by North Khorasan University of Medical Sciences by the No. 567/P/91. Researchers acknowledge the Department of Research and Research Center for Addiction and Behavioral Sciences and thank all the patients participating in this study, the President, Manager, and responsible personnel of hospital laboratory of Imam Ali, North Khorasan Province.

## CONFLICT OF INTEREST

The authors declare no conflict of interest in this study.

## REFERENCE

2002. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*, 106, 3143-421.PMID: 12485966.
- BABIC, D., MASLOV, B., MARTINAC, M., NIKOLIC, K., UZUN, S. & KOZUMPLIK, O. 2010. Bipolar disorder and metabolic syndrome: comorbidity or side effects of treatment of bipolar disorder. *Psychiatr Danub*, 22, 75-8.PMID:20305595.
- BAUER, M., LECRUBIER, Y. & SUPPES, T. 2008. Awareness of metabolic concerns in patients with bipolar disorder: a survey of European psychiatrists. *Eur Psychiatry*, 23, 169-77.doi: 10.1016/j.eurpsy.2007.10.007.
- BLY, M. J., TAYLOR, S. F., DALACK, G., POP-BUSUI, R., BURGHARDT, K. J., EVANS, S. J., MCINNIS, M. I., GROVE, T. B., BROOK, R. D., ZOLLNER, S. K. & ELLINGROD, V. L. 2014. Metabolic syndrome in bipolar disorder and schizophrenia: dietary and lifestyle factors compared to the general population. *Bipolar Disorders*, 16, 277-88.doi: 10.1111/bdi.12160.
- CARLINER, H., COLLINS, P. Y., CABASSA, L. J., MCNALLAN, A., JOESTL, S. S. & LEWIS-FERNÁNDEZ, R. 2014. Prevalence of cardiovascular risk factors among racial and ethnic minorities with schizophrenia spectrum and bipolar disorders: a critical literature review. *Comprehensive psychiatry*, 55, 233-247.
- CHACKREWARTHY, S., GUNASEKERA, D., PATHMESWAREN A, WJKEKON C.N, RANAWAKA, U. K., KATO, N. & ETAL 2013. A Comparison between Revised NCEP ATP III and IDF Definitions in Diagnosing Metabolic Syndrome in an Urban Sri Lankan Population: The Ragama Health Study. *ISRN Endocrinol* 2013, 320176. doi: 10.1155/2013/320176.
- CZEPIELEWSKI, L., DARUY FILHO, L., BRIETZKE, E. & GRASSI-OLIVEIRA, R. 2013. Bipolar disorder and metabolic syndrome: a systematic review. *Rev Bras Psiquiatr*, 35, 88-93.
- FIEDOROWICZ, J. G., PALAGUMMI, N. M., FORMAN-HOFFMAN, V. L., MILLER, D. D. & HAYNES, W. G. 2008. Elevated prevalence of obesity, metabolic syndrome, and cardiovascular risk factors in bipolar disorder. *Ann Clin Psychiatry*, 20, 131-7.
- GROVER, S., AGGARWAL, M., CHAKRABARTI, S., DUTT, A., AVASTHI, A., KULHARA, P., MALHOTRA, N., SOMAIYA, M. & CHAUHAN, N. 2012. Prevalence of metabolic syndrome in bipolar disorder: an exploratory study from North India. *Prog Neuropsychopharmacol Biol Psychiatry*, 36, 141-6.
- LEBOYER, M., SORECA, I., SCOTT, J., FRYE, M., HENRY, C., TAMOUZA, R. & KUPFER, D. J. 2012. Can bipolar disorder be viewed as a multi-system inflammatory disease? *J Affect Disord*, 141, 1-10.doi: 10.1016/j.jad.2011.12.049.
- LEE, N. Y., KIM, S. H., CHO, B., LEE, Y. J., CHANG, J. S., KANG, U. G., KIM, Y. S. & AHN, Y. M. 2010. Patients taking medications for bipolar disorder are more prone to



- metabolic syndrome than Korea's general population. *Prog Neuropsychopharmacol Biol Psychiatry*, 34, 1243-9. doi: 10.1016/j.pnpbp.2010.06.029.
12. LUND, C., BREEN, A., FLISHER, A. J., KAKUMA, R., CORRIGALL, J., JOSKA, J. A., SWARTZ, L. & PATEL, V. 2010. Poverty and common mental disorders in low and middle income countries: A systematic review. *Soc Sci Med*, 71, 517-28.
13. MANSUR, R. B., BRIETZKE, E. & MCINTYRE, R. S. 2015. Is there a "metabolic-mood syndrome"? A review of the relationship between obesity and mood disorders. *Neurosci Biobehav Rev*, 52, 89-104.
14. MARGARI, F., ZAGARIA, G., LOZUPONE, M., MINERVA, F., PISANI, R., PALASCIANO, G., PASTORE, A., PALMIERI, V. & TODARELLO, O. 2013. Metabolic syndrome: differences between psychiatric and internal medicine patients. *The International Journal of Psychiatry in Medicine*, 45, 203-226.
15. MURRAY, D. P., WEINER, M., PRABHAKAR, M. & FIEDOROWICZ, J. G. 2009. Mania and mortality: why the excess cardiovascular risk in bipolar disorder? *Curr Psychiatry Rep*, 11, 475-80.
16. O'CALLAGHAN, C., LIEW, A. Y., YUSOF, M. S. D., DUFFY, R., BREEN, E. G., KINSLEY, B. & KELLY, B. D. 2011. Screening for metabolic syndrome in long-term psychiatric illness: Audit of patients receiving depot antipsychotic medication at a psychiatry clinic. *The European Journal of Psychiatry*, 25, 213-222.
17. SAADATIAN, V., GHAREH, S., SHAKERI, M., EMADZADEH, M., TARAZ JAMSHIDI, S. & EMADZADEH, A. 2012. The Frequency of Metabolic Syndrome among Female Patients Admitted in Psychiatry Ward. *Med J Mashad Univ Med Sci* 54, 230-237.(persion).
18. SALVI, V., ALBERT, U., CHIARLE, A., SORECA, I., BOGETTO, F. & MAINA, G. 2008. Metabolic syndrome in Italian patients with bipolar disorder. *Gen Hosp Psychiatry*, 30, 318-23. doi:10.1016/j.genhosppsy.2008.04.009.
19. SALVI, V., D'AMBROSIO, V., BOGETTO, F. & MAINA, G. 2012. Metabolic syndrome in Italian patients with bipolar disorder: a 2-year follow-up study. *J Affect Disord*, 136, 599-603.
20. VANCAMPFORT, D., VANSTEELANDT, K., CORRELL, C. U., MITCHELL, A. J., DE HERDT, A., SIENAERT, P., PROBST, M. & DE HERT, M. 2013. Metabolic syndrome and metabolic abnormalities in bipolar disorder: a meta-analysis of prevalence rates and moderators. *Am J Psychiatry*, 170, 265-74.
21. VUKSAN-CUSA, B., SAGUD, M. & JAKOVLJEVIC, M. 2010. C-reactive protein and metabolic syndrome in patients with bipolar disorder compared to patients with schizophrenia. *Psychiatr Danub*, 22, 275-7. PMID: 20562761.
22. WEINER, M., WARREN, L. & FIEDOROWICZ, J. G. 2011. Cardiovascular morbidity and mortality in bipolar disorder. *Ann Clin Psychiatry*, 23, 40-7. PMID:21318195.
23. ZARZAVADJIAN LE BIAN, A., FUKS, D., CHOPINET, S., GAUJOUX, S., CESARETTI, M., COSTI, R., BELGAUMKAR, A. P., SMADJA, C. & GAYET, B. 2017. Consequences of metabolic syndrome on postoperative outcomes after pancreaticoduodenectomy. *World J Gastroenterol*, 23, 3142-3149.