METABOLIC SYNDROME IN THE POPULATION OF PSYCHIATRIC PATIENTS IN NOVI SAD

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Summary: OBJECTIVES: The aim of this study is to determine the prevalence of metabolic syndrome (MetS) in a sample of hospitalized patients and to relate it to socio-demographic characteristics, psychiatric diagnosis and psycho-pharmacotherapy. **METHODS:** The study was conceived as a retrospective cohort study. Data of interest for this research were collected from the medical history of hospitalized patients at the Clinic for Psychiatry KCV in the period from January 2018 to January 2020. **RESULTS:** Out of a total of 2409 patients hospitalized at the Psychiatric Clinic, 1327 patients had criteria for metabolic syndrome, with a high prevalence of 55.1% among this population. Although there are more respondents in the sample (55.7%), males with a diagnosis of MetS (58.1%) dominate. The data show that the prevalence of metabolic syndrome increases statistically significantly with the age of psychiatric patients. However, the prevalence of metabolic syndrome in the study population younger than 30 years is about 33%. Among patients with incomplete primary school, 67% have a diagnosis of metabolic syndrome, which is statistically significantly higher than other compulsory profiles (p <0.001). The study sample shows a statistically significantly higher prevalence of metabolic syndrome among patients treated for psychotic disorders, with as much as 67% prevalence. Therapy with atypical antipsychotics was most associated with metabolic syndrome in 67.5% of patients, followed by a combination of 2 or more antipsychotics with 60.7% (χ^2=26.99, p<0.0019). Abdominal obesity is the strongest predictor of the response that the subjects will suffer from the metabolic syndrome, the quotient of which is 1.34 by logistic regression. Another important predictor refers to triglyceridemia, whose probability quotient is 1.12. **CONCLUSION:** The prevalence of metabolic syndrome in psychiatric patients in Novi Sad is alarmingly high, in more than half of patients, especially those treated for psychotic and mood disorders and using atypical antipsychotics and combinations of antipsychotics. In a patient with metabolic syndrome there is male dominance, low educational profile and the prevalence increases statistically significantly with increasing age of psychiatric patients
Keywords: Abdominal Obesity, Metabolic Syndrome, Mental disorders

INTRODUCTION

Mass non-communicable diseases are in the first place in terms of morality and morbidity within the general population. In this group of diseases, metabolic diseases such as obesity and diabetes predominate, which are accompanied by an increased risk of cardiovascular and cerebro-vascular incidents, and a consequent fatal outcome. In the population of psychiatric patients, however, it is known that the rate of premature mortality from all causes is far higher than in the general population. Studies have shown that the life expectancy of patients with significant psychiatric disorders is reduced by 7 to 24 years [1,2,3,4]. On the other hand, about 60% of premature deaths of psychiatric patients occur due to somatic illnesses, predominantly due to cardiovascular diseases. The risk of cardiovascular diseases, increased by comorbidities such as diabetes, obesity, stroke, is multiplied in patients with several different psychiatric diseases such as psychotic disorders, mood disorders and anxiety disorders. [1,2,3,4,5].

MetS is defined as a combination of multiple comorbid conditions such as abdominal obesity, high arterial blood pressure, low "good", HDL cholesterol, hypertriglyceridemia and hyperglycemia. MetS is therefore the first step on the so-called. A "metabolic pathway" that ultimately ends in premature death. This concept of MetS is in line with the recommendations of the International Diabetes Federation. The concept of MetS has proven to be the most appropriate universal predictive

factor that allows to select groups with increased risk and to prevent the progression of the "metabolic pathway" by timely medical and nutritional action [6,7].

The prevalence of MetS in the general population is between 10% and 15%, while in the population of psychiatric patients the value is many times higher and ranges from 30% to as much as 60% [8,9,10]. Most of the world's research points to psychotropic therapy as one of the main causes of the multiple incidence of MetS within a group of psychiatric patients [11,12]. Weight gain is often a side effect of a large number of psychotropic drugs. Today it is clear that some drugs used in psychiatry as a side effect disrupt fat and sugar metabolism [13,14].

We did not find studies of the prevalence of MetS in a group of psychiatric patients in Serbia. Therefore, this study was conducted to assess the prevalence of MetS in a sample of patients hospitalized at the Clinic for Psychiatry of the Clinical Center of Vojvodina (KCV) in Novi Sad and linked it to socio-demographic characteristics, psychiatric diagnosis and psycho-pharmacotherapy used in psychiatric patients and to single out possible predictor risk factors for MetS screening.

MATERIAL AND METHODS

The study was designed as a retrospective cohort study. Data of interest for this research were collected from the medical histories of hospitalized patients at the Clinic for Psychiatry KCV in the period from January 2018 to January 2020. Data on 2409 patients were collected. Patients under the age of 18 were not included in the study, as well as those who did not have a primary psychiatric discharge diagnosis according to ICD-10, and those patients for whom there were no complete data from medical histories. Those patients who were treated more than once in the study period were counted only once in the total sample. There were no patients treated for addiction in the sample. Sociodemographic and clinical data are taken from the history of the disease. The primary psychiatric diagnosis was taken from the discharge card according to the code system ICD-10. All diagnoses are grouped into four categories: psychosis (F20-29), mood disorders (F30-34), anxiety disorders (F40), and other mental disorders. The MetS is determined by the criteria envisaged by the agenda of the International Diabetes Federation.
1) Waist circumference values > 102 cm for men and> 88 cm for women,
2) triglyceridemia> > 1,7mmol /L (1.5 mg / ml)
3) HDL cholesterolemia HDL< 1.03 mmol/L (men) or < 1.29 mmol/L (women) (<0.4 mg/ml for men and <0.5 mg/ml for women),
4) arterial blood pressure> 135/85 mmHg,
5) fasting glycemia> 6.1 mmol / l.

If at least three of the above criteria are met, it is considered that there is a diagnosis of MetS. Patients with a history of associated arterial hypertension and diabetes mellitus were also included in the study.

Data on psycho-pharmaceuticals that patients, included in the study, drank were also recorded. Medications are divided into five groups - classic and atypical antipsychotics, antidepressants, mood stabilizers. A large number of patients were not on monopsychopharmacotherapy, so another group was formed where patients who took 2 or more drugs were classified. It is considered that a patient is on therapy with a certain psychopharmaceutical if he has been drinking it for the last 30 days in the prescribed therapeutic dose.

Statistical data processing initially consisted of descriptive variables. Frequencies and proportions were used for their processing, while standard deviations, means and medians were used to represent quantitative variables. The chi square test was used to assess the difference in the prevalence of MetS between the sexes. Comparison of the prevalence of MetS in different diagnoses was performed using the ANOVA (F) test, and in the case of a statistically significant difference, the t and χ^2 test was applied. A binary logical regression model was applied to identify the most important factors for the dichotomous outcome - the presence or absence of MetS in the study group. For all applied statistical tests, the error level was set to an acceptable level of $p < 0.05$. Statistical data processing was done in the computer program SPSS 12.0.

The conduct of such a study was approved by the Ethics Committee of the KCV. The study is conducted according to internationally recognized ethical standards set in the field of biomedical research.

RESULTS
A total of 2409 psychiatric patients participated in the study. The prevalence of MetS among this population is 1327 and 55.1%, respectively.

Table 1. Sociodemographic characteristics

		Metabolic syndrome		Statistical analysis	
	Overall	Yes	No	χ^2	P
Sex					
Male	1068 (44,3%)	621 (58,1%)	447 (41,9%)		
Female	1341 (55,7%)	706 (52,6%)	635 (47,4%)	7,045	0,008
Age					
AS+-SD	46,87±18,09	47,06+-17,97	46,64+-18,24		
< 30 years	953 (39,6%)	321 (33,7%)	632 (66,3%)		
od 31 do 50 years	817 (33,9%)	449 (55,0%)	368 (45,0%)		
> 51 yers	639 (26,5%)	357 (55,9%)	282 (44,1%)	0,230	0,891
Marital status					
Married	527 (21,9)	255 (48,4%)	272 (51,6%)		
Single	752 (31,2%)	467 (62,1,%)	285 (37,9%)		
Divorced	862 (35,8)	427 (49,5%)	435 (50,5%)		
Widowed	268 (11,1%)	178 (66,4%)	90 (33,6%)	49,157	0,000
Number of children					
AS+-SD	1,56±0,60	1,56+-0,61	1,55+-0,60		
None	1205 (50,0%)	660 (54,8%)	545 (45,2%)		
1-3 children	1062 (44,1%)	586 (55,2%)	476 (44,8%)		
> 3 children	142 (5,9%)	81 (57,0%)	61 (43,0%)	0,271	0,873
Educational level					
Illiterate	477 (19,8%)	322 (67,5%)	155 (32,5%)		
Primary/less	629 (26,1%)	344 (54,7%)	285 (45,3%)		
Secundary/less	799 (33,2%)	436 (54,6%)	363 (45,4%)		
University/other	504 (20,9)	225 (44,6%)	279 (55,4%)	57,079	0,000

Note: AS - arithmetic mean, SD - standard deviation, χ^2 - statistical, p - statistical significance

Although there are more female respondents in the sample (55.7%), there are more male respondents with a diagnosis of MetS (58.1%) than women. The average age of the patient is about 47 years. About 40% of the sample consists of respondents younger than 30 years, a third from 30 to 50 years, and a quarter over 50 years of age. In the population of patients younger than 30, one third record the criteria for the diagnosis of MetS. It can be observed that among widows and singles there are more subjects with MetS compared to patients who are married or divorced. On average, respondents have less than two children. In terms of education, one third of respondents have completed secondary school, one fifth do not even have completed primary school, and one in four respondents has only primary school, and about 20% of them have a high school diploma. Among patients with incomplete primary school, almost two thirds of them are diagnosed with MetS. It can be seen that there is a statistically significant correlation between the sex of the subjects and the prevalence of MetS χ^2 (7.045, p=0.008). Men have a relatively higher prevalence of MetS χ^2 (49,157, p=0,000). There is a statistically significant correlation between the level of education of the subjects and the prevalence of MetS χ^2 (52,079, p=0,000.)

Approximately half of the patients included in the study are being treated for psychotic disorders, a third are suffering from mood disorders, and a fifth are suffering from anxiety disorders. The study sample shows a statistically significantly higher prevalence of metabolic syndrome among patients treated for psychotic disorders, with as much as 67% prevalence. Therapy with atypical antipsychotics was most associated with metabolic syndrome in 67.5% of patients, followed by a combination of 2 or more antipsychotics with 60.7% (χ^2=26.99, p <0.0019). The diagnosis of metabolic syndrome is most common in patients

up to 5 years of age and is over 65%. The body mass index averages about 28, but is 10 units higher among the population of subjects who have MetS. The situation is similar when it comes to waist circumference. The average waist circumference among the psychiatric population in the sample was 95 cm, while among subjects with MetS the waist circumference was higher by almost 20 cm compared to those without MetS.

Table 2. Clinical characteristics

	Overall	Metabolic Syndrome		Statistical analisys	
		Yes	No	χ^2	p
Psychiatric diagnosis					
Psychotic disorder	1098 (45,6%)	742 (67,5%)	356 (32,5%)		
Mood disorder	806 (33,5%)	429 (53,2%)	377 (46,7%)		
Anxious disorder	454 (23,2%)	142 (31,3%)	312 (68,7%)		
Other mental disorders	51 (2,1%)	19 (37,2%)	32 (62,8%)	181,05	0,000
Psychofarmacs					
Atypical antipsychotic	898 (37,3%)	594 (66,1%)	304 (33,9%)		
Antidepresive	287 (11,9%)	160 (55,7%)	127 (44,3%)		
Clasical antipsychotic	448 (18,6%)	246 (54,9%)	202 (45,1%)		
Mood stabilizator	267 (11,1%)	141 (52,8%)	126 (47,2%)		
Mix of 2 or more psychofarmacs	509 (21,1%)	309 (60,7%)	200 (43,8%)	26,99	0,0019
Bigining og illness (year)					
AS+-SD	26,18±5,46	26,14+-5,37	26,22+-5,57		
< 25	1023 (42,5%)	568 (56,5%)	455 (44,5%)		
25 – 50	1386 (57,5%)	759 (54,8%)	627 (45,2%)	0,138	0,711
Duration of psychiatric disease (years)					
AS+-SD	20,73±16,87	20,97+-16,86	20,45+-16,89		
<=1	504 (20,9%)	206 (41,0%)	298 (59,0%)		
1-5	501 (20,8%)	325 (64,9%)	176 (35,1%)		
6-10	396 (16,4%)	247 (62,5%)	149 (37,5%)		
> 10	1008 (41,8%)	509 (50,5%)	499 (49,5%)	3,653	0,312
Obesity indicators					
BMI	27,82±5,92	32,50+-3,50	22,08+-1,76		
Waist circumference (cm)	94,97±13,82	103,67+-11,90	84,28+-6,65		
Blood pressure					
Systolic (mmHg)	126,37±21,68	126,22+-21,63	126,54+-21,75		
Diastolic (mmHg)	80,72±16,41	80,88+-16,35	80,53+-16,49		
Laboratory tests					
Fasting blood glucose (mmol/L)	5,80±2,61	7,78+-2,62	5,91+-2,60		
Triglycerides (mmol/L)	2,77±1,59	2,75+-1,58	1,79+-1,62		
HDL- Cholesterol (mmol/L)	1,12±0,60	1,00+-0,59	1,23+-0,62		

Note: AS - arithmetic mean, SD - standard deviation, χ^2 - statistical, p - statistical significance

It has been shown that there is a statistically significant difference in BMI values between subjects with MetS and those who do not have this syndrome. In subjects with MetS, a significantly higher value of the mentioned index is recorded in relation to subjects without MetS, where the magnitude of the impact is large and amounts to 0.86. Also, there is a statistically significant difference in the value of the waist circumference indicator between subjects with MetS and those who do not have this syndrome.

Subjects with MetS have a significantly larger waist circumference compared to subjects without MetS, with a large impact size of 0.76.Table 3 also shows that there is a statistically significant difference in blood sugar, triglyceridemia and HDL cholesterol level between subjects with MetS and those who do not have this syndrome.

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Table 3. Mann-Whitney U test to examine differences between patients with and without metabolic syndrome in terms of body mass index (BMI) and waist circumference, arterial blood pressure values and laboratory measurements

Obesity indicator	Metabolic syndrome	Md	N	Mann-Whitney U	Wilcoxon W	Z	p
BMI	Yes	31,70	1327	0,000	585903,000	-42,278	0,000
	No	22,20	1082				
Waist circumference (cm)	Yes	102,00	1327	84069,500	669972,500	-37,327	0,000
	No	84,30	1082				
Blood pressure							
Systolic (mmHG)	Yes	125,90	1327	711884,500	1593012,500	-0,355	0,723
	No	126,90	1082				
Diastolic (mmHG)	Yes	80,90	1327	708787,500	1294690,500	-0,537	0,591
	No	80,20	1082				
Laboratory tests	**Metabolic syndrome**	**Md**	**N**	**Mann-Whitney U**	**Wilcoxon W**	**Z**	**p**
Fasting blood glucosae (mmol/L)	Yes	7,78	1327	713267,500	1594395,500	-18,273	0,005
	No	5,40	1082				
Triglycerides (mmol/L)	Yes	2,75	1327	711881,500	1593009,500	-12,355	0,200
	No	1,79	1082				
HDL-Cholesterol (mmol/L)	Yes	1,00	1327	713133,500	1594261,500	-10,281	0,000
	No	1,23	1082				

Note: Md - median, N - number of subjects, Mann-Whitney U - test value, Wilcoxon W - statistician, Z - standardized statistician, p - statistical significance

As shown in Table 4, two independent variables made a unique statistically significant contribution to the model (abdominal obesity and triglyceridemia). The strongest predictor of the answer that the respondents will suffer from the MetS is the waist circumference, whose quotient is 1.34. Thus, the probability that the subject will be diagnosed with metabolic syndrome is 1.34 times higher with an increase in abdominal obesity (waist circumference), when all other factors are equal. Another important predictor refers to triglyceridemia, whose probability quotient is 1.12. Thus, the probability that the subject will be diagnosed with MetS is 1.12 times higher with an increase in triglyceride values, when all other factors are equal.

Table 4. Estimation of the influence of predictor variables on the probability of obtaining metabolic syndrome - binary logistic regression

Varijable	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I. EXP (B)	
							Down limes	Uper limes
Bibining of illness	-0,02	0,01	2,82	1,00	0,09	0,98	0,96	1,00
Waist circumference	0,29	0,01	516,82	1,00	0,00	1,34	1,31	1,38
Triglycerides	0,12	0,05	6,47	1,00	0,01	1,12	1,03	1,23
Constant	-26,39	1,18	497,05	1,00	0,00	0,00		

Note: B - regression coefficient, S.E. - standard error, Wald - indicator value, df - number of degrees of freedom, Sig. - statistical significance, Exp (B) - odds ratio, 95% C.I. for EXP (B) - 95% confidence interval for the probability quotient

DISCUSSION

As far as the author knows, this is the first work in the Autonomous Province of Vojvodina, but also in the entire territory of the Republic of Serbia, which deals with the examination of the prevalence of MetS in the population of psychiatric patients. It is known that patients with serious psychiatric illnesses have a far higher risk of developing MetS than the general population. In this study, the prevalence of MetS in the study population was 55.1%. This percentage is significantly higher than values from similar studies conducted worldwide where the prevalence ranges between 25 and 35% [8,14,15,16]. Although the study from the United Arab Emirates records an approximately high value of 48.1% prevalence of MetS in the group psychiatric patients [17]. Regarding the prevalence of MetS in the general population of Serbia, which is quite high and ranges from 38.4 to 42.7%, we see that psychiatric patients in Serbia are also classified as a vulnerable group in terms of metabolic status [18]. It is clear that a person with a mental

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illness is about 30% more likely to develop MetS. High rates of MetS in both the general population and the population of psychiatric patients in Serbia are certainly significantly associated with a predominantly sedentary lifestyle characterized by minimal physical activity and predominantly calorie-dense foods represented in the diet.

The prevalence of MetS increases with the age of psychiatric patients, but that in the population aged 30 to 50 and over 50 is approximately the same and amounts to about 55%. Such conclusions are in agreement with the findings of several different studies on similar topics worldwide [19]. However, what is worrying is that the incidence of MetS in the study population under the age of 30 is about 33%. The prevalence of MetS among older adolescents (16-18 years) in Serbia is 13% [20]. How much psychiatric illness is an additional aggravating factor in the life of a young person for the development of comorbid physical diseases is clear from the fact that in practically 10 years from the end of adolescence to 30 years of age the incidence rate of MetS almost urtostructs. The high prevalence of MetS in the general population in general can be explained by the high prevalence of MetS components in the elderly, such as hyperglycemia and dyslipidemia [21]. Although some studies suggest that the high incidence of MetS in the elderly is due to functional and metabolic changes which are a consequence of aging. And that would mean that the MetS is a common companion of the aging process, which practically does not stand.

In relation to the differences in the prevalence of MetS in the population of psychiatric patients in terms of gender, unlike most similar world studies, it was found that men with psychiatric diseases significantly more often meet the criteria for diagnosis of MetS [22,23]. Male, older age, single life, lower level of education and higher number of children in this study were selected risk factors for higher risk for the development of MetSin the psychiatric population. All these characteristics of the model of a psychiatric patient at risk for the diagnosis of MetS have been confirmed by studies from South Korea [24]. This deviation can be explained precisely by the characteristics of the risk population itself. Single, middle-aged men, middle and lower level of education and level of economic power, who have a psychiatric illness

and therefore insufficient and inadequate social support have all the prerequisites to practice a bad lifestyle, often accompanied by harmful habits such as smoking and alcohol use leading to metabolic development. syndrome.

Psychiatric patients have been shown to have a significantly higher risk of having some of the components of MetS. [8] And for the general population, the overall contribution of MetS diagnosis to overall mortality is estimated at 6-7%, 12-17% as the prevalence of arterial hypertension and 30-52% regarding diabetes mellitus [25,26,27]. This study showed that the duration of psychiatric illness plays a very important role as a risk factor for the development of MetS in patients. Over 60% of psychiatric patients treated for up to 5 years, as well as over 5 to 10 years, have a MetS. Two meta-analyzes by American authors find that the duration of psychiatric illness is the greatest risk factor for the development of MetS [27,28]. The duration of psychiatric illness is certainly related to the age of such patients, but also to the time of exposure to psychotropic medication, which both have a positive impact on the development of MetS.

According to recently published studies, there are no statistically significant differences between the prevalence of MetS among patients with different psychiatric diagnoses — studies that directly compared schizophrenic patients with patients with bipolar disorder. However, there are review studies that find a much higher incidence of MetS among the population of schizophrenic and bipolar disorders [29]. The current study sample shows a significantly higher prevalence of MetS among patients treated for psychotic disorders, with as much as 67% prevalence. While in the second place are patients with a diagnosis of mood disorders. Both samples showed a statistically significant difference in relation to the occurrence of MetS. Certainly, patients with these two psychiatric diseases are most often treated with atypical antipsychotics, mood stabilizers and antidepressants, as well as a combination of several different psychopharmaceuticals, which seems to be the strongest contributing factor to metabolic disorders, in addition to practicing unhealthy lifestyles and harmful habits. But the use of psychotropic drugs is the main difference between the population of psychiatric patients and the general population. It is certainly a mixed constellation of different risk factors such

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as the clinical characteristics of the diagnosis itself with a predominance of negative symptoms, lack of adequate social support that together condition such a somatic risky lifestyle of psychiatric patients.

Atypical antipsychotics, but also a combination of several different psychopharmaceuticals, were the only ones that stood out as statistically significantly associated with the development of MetS. Such findings agree with most of the world's findings linking the use of atypical antipsychotics and the development of metabolic anchor. The CATIE study showed that after 3 months of olanzapine exposure, there was a significant increase in the number of patients who met the criteria for MetS [28]. Metabolic deterioration was also observed during long-term research of patients treated with clozapine [29]. As the indication field for atypical antipsychotics has significantly expanded today - from affective disorders to mood disorders, the population of patients using these drugs has increased significantly. Therefore, the risk of metabolic abnormalities should be considered when choosing an appropriate psychotropic drug, especially atypical antipsychotics.

Waist circumference and triglyceridemia stand out as the two most common contributing factors for the development of MetS in psychiatric patients. The risk that a psychiatric patient is diagnosed with MetS is 1.34 times higher with an increase in waist circumference, when all other factors are equal. Another important predictor refers to triglyceridemia, whose probability quotient is 1.12. These findings agree with the findings of several world studies, which certainly find a statistically significant association between visceral obesity, waist circumference and poor mental health in patients [30]. Although some studies do not find an increased value of triglycerides in the blood as a statistically significant predictor for the development of

MetS. these are the levels of cholesterol in the blood [31]. The reasons for this finding in the current study may lie in the fat metabolism itself. If it is known that triglycerides are only the initial component in the formation of cholesterol, it can be concluded that a high value of triglycerides also significantly contributes to metabolic risk, albeit indirectly through the consequent increase in cholesterol. The main reason for the increased blood cholesterol values in the patients included in this study is the diet rich in fats and refined simple sugars that dominates in the Autonomous Province of Vojvodina.

CONCLUSION

The prevalence of MetS in psychiatric patients at the Clinical Center of Vojvodina in Novi Sad is alarmingly high. in more than half of patients, especially those treated for psychotic and mood disorders and using atypical antipsychotics and combinations of antipsychotics. In a patient with metabolic syndrome there is male dominance, low educational profile and the prevalence increases statistically significantly with increasing age of psychiatric patients. These findings once again emphasize the importance of continuous, long-term and multisystem monitoring of psychiatric patients, and the need to provide better organized social and health support, especially vulnerable from the group of psychiatric patients - the elderly, singles, singles. especially atypical antipsychotics, as drugs that have stood out as those most strongly associated with the development of MetS in a group of psychiatric patients. Waist circumference and blood triglyceride values are suggested as the best predictor factors for the development of MetS.

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