КЛИНИЧКИ ИСТРАЖУВАЊА

ПРЕВАЛЕНЦИЈА НА МЕТАБОЛИЧКИ СИНДРОМ КАЈ ПАЦИЕНТИ СО ШИЗОФРЕНИЈА ВО ЦЕНТАРОТ ЗА МЕНТАЛНО ЗДРАВЈЕ "ПРОЛЕТ", ПСИХИЈАТРИСКА БОЛНИЦА – СКОПЈЕ

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Цитирање: Исјановски В, Исјановски И. Преваленца на метаболички синдром кај пациенти со шизофренија во Центарот за ментално здравје - „Пролет", Психијатриска болница – Скопје. Арх J Здравје 2019;11(1):95-103

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Извадок

Шизофренијата е поврзана со зголемен ризик од кардио-метаболички морбидитет и морталитет. Метаболичкот синдром (МС) е релевантен предиктор за морбидитет и морталитет на кардиоваскуларните заболувања, исто така, се покажа дека е поприсутен кај пациенти со шизофренија. Цел на ова истражување беше да ја утврдиме преваленцијата на МС во примерок од пациенти со шизофренија во Центарот за ментално здравје - „Пролет", Психијатриска болница - Скопје и потенцијалните ризик фактори поврзани со него. Материјали и методи: примерокот се состои од 50 пациенти со шизофренија. Кај сите пациенти е земена венска крв за да се одреди нивото на холестерол HDL, триглицериди и гликоза, измерена е телесна тежина, телесна висина и обемот на половината. МС е дефиниран според критериумите за Национална програма за холестеролска програма за возрасни третман - панели III (NCEP ATP III). Резултати: Преваленцијата на МС кај пациенти со шизофренија изнесуваше 46,0%. Се покажа дека зголемувањето на индексот на телесна маса (BMI) е значително поврзано со преваленцијата на МС. Заклучок: Оваа студија покажала висока преваленција на МС кај пациенти со шизофренија и дека BMI може да биде фактор на ризик во развојот на МС. Оваа информација е клинички релевантна бидејќи BMI рутински се мери во психијатриска пракса и може да се користи за следење на развојот на МС кај пациентите со шизофренија.

CLINICAL SCIENCE

PREVALENCE OF METABOLIC SYNDROME AMONG PATIENTS WITH SCHIZOPHRENIA IN THE CENTER FOR MENTAL HEALTH – "PROLET", PSYCHIATRIC HOSPITAL -SKOPJE

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Abstract

Schizophrenia has been associated with an increased risk of cardio-metabolic morbidity and mortality. Metabolic syndrome (MS), as a reliable predictor of cardiovascular morbidity and mortality, has also been shown to be more prevalent in patients with schizophrenia. In this study, we investigated the prevalence of MS in a sample of patients with schizophrenia in the Center for Mental Health – "Prolet", Psychiatric Hospital -Skopje, and the potential risk factors associated with it. Materials and methods: 50 patients with schizophrenia were recruited. All subjects provided a fasted sample of venous blood to measure high-density lipoprotein cholesterol (HDL-C), triglycerides and glucose levels. Weight, height and waist circumference were measured. Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Tretmant Panel III (NCEP ATD III) criteria. Results: The prevalence of MS in patients with schizophrenia was 46.0%. Increasing body mass index (BMI) was identified to be significantly associated with the prevalence of MS. Conclusion: This study found a high prevalence of MS in patients with schizophrenia, and that BMI might be a risk factor in the development of MS. This information is clinically relevant as BMI is routinely measured in psychiatric practice today, and could be used to monitor for development of MS in schizophrenia.

Introduction

Schizophrenia has been linked to metabolic disturbances such as obesity, dyslipidaemia and hyperglycemia[1-2]. It has also been associated with a more than 3-fold increase in mortality associated with cardiovascular causes[2-3]. This increase in cardio-metabolic morbidity and mortality might be due to several factors such as inherent genetic vulnerability or environmental exposures such as smoking, sedentary lifestyle, antipsychotic medication and gaps in healthcare access[4-5]. In comparison with general population, mortality among patients with schizophrenia is 2-3 times higher[6-8] and life expectancy is 20-25% lower[9]. In addition to high incidence of suicides, the cited studies revealed high cardiovascular and type 2 diabetes associated mortality of schizophrenic patients[6-8]. One of the main reasons of elevated cardiovascular and type 2 diabetes risks in patients with schizophrenia can be the high prevalence of obesity and metabolic syndrome among that people. Thus, according to studies conducted in USA, Canada and several Western European countries, frequency of metabolic syndrome (MS) in schizophrenic patients is 1.5-2 times higher than in general population or mental healthy people [10-14]. MS is highly prevalent in patients with schizophrenia with reported prevalence that ranges from 10.1% to 69.3%[15-22]. MS was reported in 42.4% of patients with schizoaffective disorder, in 24.6–50% of bipolar patients, and in 12–36% of the patients with recurrent depression[23,24]. Heiskanen et al found that the frequency of metabolic syndrome was 2–4 times higher in a group of people with schizophrenia, treated with both atypical and typical neuroleptics, than in an appropriate reference population[12].

Currently, there are at least 7 different classification criteria for MS developed by various expert panels World Health Organization (WHO); The European Group for the Study of Insulin Resistance (EGIR); The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATD III); The American Association of Clinical Endocrinology; The International Diabetes Federation (IDF); The American Heart Association National Heart, Lung and Blood Institute (AHA]NHLB); A Joint Interium Statement[25].

Meanwhile the prevalence of MS among patients with schizophrenia in Macedonia has been

never assessed. Therefore the present study was performed in order to display MS frequencies (prevalence) in patients with schizophrenia, examined in the Center for Mental Health – "Prolet", Psychiatric Hospital –Skopje.

Materials and Methods

This is a cross sectional study conducted from August 2018 until December 2018. This study was conducted at the Center for Mental Health – "Prolet", Psychiatric Hospital –Skopje. 50 patients with diagnosis of schizophrenia (ICD-10) were enrolled. We included data from 50 patients, 36(72.0%) males and 14(28.0%) females). All selected patients received antipsychotic drugs, and 49.7% of them – atypical antipsychotics (clozapine, olanzapine, risperidone). The antipsychotic use patterns were recorded by the types and number of administered antipsychotic drugs. As clozapine and olanzapine have the highest potential to cause metabolic abnormalities[26-29] and weight gain[28], we classified the types of antipsychotic drugs into a clozapine/olanzapine group (yes or no). The number of antipsychotics used was categorized as monotherapy, currently using only one kind of antipsychotic drug, and combination, currently using more than one kind of antipsychotic. Patients aged 30 and above were enrolled into the study.

Arterial blood pressure, height, weight, and waist circumference were measured. Waist circumference was measured in the standing position. Subjects were seated when blood pressure was measured. Body mass index (BMI) was calculated according to Kettle's formula: BMI (kg/m2) = weight (kg)/height2 (m2). BMI was further categorized into underweight (BMI <18.5 kg/m2), normal (BMI 18.5 to 24.9 kg/m2), overweight (25.0 to 29.9 kg/m2) and obesity (BMI ≥30 kg/m2) according to the World Health Organization (WHO) public health action. Duration of illness for patients with schizophrenia was defined as the duration from onset of first psychotic symptom to the date of recruitment.

Patients were fasted for 12 h before the

venous blood was collected for determination of laboratory parameters and plasma glucose, total cholesterol, high density lipoprotein cholesterol (HDL-C), and triglycerides levels were measured.

We adopted the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII) criteria for metabolic syndrome in our study. This criterion included elevated triglycerides (≥ 1.7 mmol/l or on drug treatment for elevated triglycerides), reduced HDL-C(<=1.03mmol/l in males <=1.29 mmol /l in females or on drug treatment for reduced HDL-C), elevated blood pressure (≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure), and elevated fasting glucose (≥ 6.1mmol / l). We used waist circumference cut-offs of >=102 cm for males and ≥88 cm for females. Individuals are considered to suffer from metabolic syndrome if they fulfilled at least 3 of the above mentioned criteria.

Descriptive statistics for all study variables were computed. These descriptive statistics included frequencies and percentages for all categorical variables in addition to means, standard deviations and ranges for all normally distributed continuous. In statistical analysis we applied for the relative parameters (e.g. %) -the chi-squared test for categorical variables and Fisher's exact test in the case of independent groups. We estimate the odds ratio (OR) of MS in patients with schizophrenia, the presence of MS was used as the dependent categorical variable. The similar approach was used to identify factors associated with MS in the patient sample. We used Mann-Whitney U test to determine statistically significant differences in numerical series. The group differences were assumed to be statistically significant at p value less than 0.05.

Results

Во оваа студија беа вклучени 100 A total of 50 patients diagnosed with schizophrenia were recruited for this study. The investigation group had a higher proportion of males- 72.0% and females-18.0%. Mean age of the patients was 48.1 ± 9.3 years. All of them were from urban residence. Table 1 shows the demographics and metabolic characteristics of the study sample, the general characteristics of the sample. The group had a higher proportion of males, smokers, low socioeconomic level, and metabolic disturbances such as obesity, hypertension, hypertriglyceridaemia and fasting hyperglycaemia. Olanzapine/ Clozapine was received by 70.0% of patients and 54.0% of patients were on combination therapy.

ATD III, and the data analysis, MS is registered in 18 (36.0%) patients, and not 32 (64.0%). The prevalence of MS in the group (total sample) is 36.0%. Female patients had higher MS prevalence than male patients, female sex increases the risk for MS (tab 10.

Those with MS were significantly older with a mean age of 45.1 years compared with those without MS with a mean age of 39.3 years, age over 50 years increases the risk for MS.

More smokers and higher BMI were noted in patients with MS. Those with MS had a significantly higher BMI compared with those without MS, with the mean BMI at 31.8±3.3 kg/m^2 and 24.5±2.2kg/m^2 respectively (P <0.00). There was a trend to show that increasing BMI was associated with higher risk for MS in patients. There were a significantly higher proportion of smokers in the group. The prevalence of MS was found to be significantly associated with patients who smoked with an unadjusted OR 6.90 (1.04-76.042) compared with patients who did not smoke. Low socioeconomic level increases the risk for MS for ten times. There were no differences in duration of illness. According to the Odds Ratio(OR) familial history (registration of diseases in the family-cardiovascular, HTA and diabetes) increases the chance for MS four times. There were no differences of family history of psychiatric disorders. The average waist circumference of patients with MS is higher and it is 103.6 ± 9.2 cm, and in the group without MS it is 84.9 ± 7.6 cm, the difference is statistically significant for p <0.05 (p = 0.00). The mean value of systolic blood pressure in patients with MS is higher and was 151.1 ± 9.3mmHg, and in the group without MS it was 126.2 ± 9.6mmHg., the difference is statistically significant for p <0.05 (p = 0.00) .The average value of diastolic blood pressure in pa-

tients with MS was higher and is 91.0 ± 4.7 mmHg, and in the group without MS it was 76.1 ± 6.8 mmHg, the difference was statistically significant for p <0.05 (p = 0.00). The average triglyceride value in patients with MS was higher and was 2.5 ± 0.8 mmol/l (higher than ≥1.7mmol/l of the predicted value with NCEP ATD III), and in the group without MS it was 1.3 ± 0.3mmol/l, the difference was statistically significant for p <0.05 (p = 0.00). The average glycemic value in patients with MS was higher and was 6.5 ± 0.6mmol/l (higher than≥ 6.1mmol/l of the predicted value with NCEP ATD III), and in the group without MS it was 4.9 ± 0.4mmol/l, the difference was statistically significant for p <0.05 (p = 0.00). The mean HDL of subjects with MS was lower and was 1.1 ± 0.2 mmol/l, and in the group without MS it was1.4 ± 0.2 mmol/l (tab 2).

Table 1. Characteristics of Study Subjects

patients N=50		**p value**
Age in years, mean (SD)	48.1 ± 9.3	
Gender, n (%)		
Male	36(72.0)	0.0000
Female	14(18.0)	
Smoking status, n (%)		
Non-smokers	12(24.0)	0.0000
smokers	38(76.0)	
Body Mass Index in kg/m2, n (%)		
normal 18.5 to 24.9	8(16.0)	0.0001; 0.0263
overweight 25.0 to 29.9	15(30.0)	
obesity ≥30	27(54.0)	
Socioeconomic level, n (%)		
low	37(74.0)	0.0000
moderate	13(26.0)	
Family history of psychiatric disorders, n (%)		
yes	27(54.0)	0.4237
no	23(46.0)	
Family history of DM, of cardiac diseases, of cerebrovascular stroke, n (%)		
yes	20(40.0)	0.0455
no	30(60.0)	
Employed, n (%)		
unemployed	44(88.0)	0.0000
employed	6 (12.0)	
Duration of psychiatric illness , mean (SD)		15.8 ± 9.3
Elevated waist circumference, n (%)		
yes	32(64.0)	0.0051
no	18(36.0)	
Olanzapine/Clozapine, n (%)		
yes	35(70.0)	0.0001
no	15(30.0)	
Drug regimen, n (%)		
Monotherapy	23(46.0)	0.4237
Combination therapy	27(54.0)	

Elevated blood pressure, n (%)		
yes	31(62.0)	0.0164
no	19(38.0)	
Elevated fasting glucose, n (%)		
yes	36(72.0)	0.0001
no	14(28.0)	
Reduced HDL-C, n (%)		
yes	28(56.0)	0.2301
no	22(44.0)	

Table 2. Characteristics of Patients with and without MS and non-Adjusted Risk of Schizophrenia on MS

	with MS/18	without MS/32	x2/ unadjusted OR (95% CI)
Gender, n (%)			
Female	9(50.0)	5(15.6)	6.75,p=0.000 5.4(1.43-20.38)
Male	9(50.0.0)	27(84.4)	
Age in years, n (%)			
>50	16(88.9)	17(53.1)	6.56,p=0.010 7.05(1.38-35.87)
<50	2(11.1)	15(46.9)	
BMI, n (%)			
≥30	14(77.8)	13(40.6)	6.40,p=0.011 5.11(1.37-19.07)
<30	4(22.2)	19(59.46)	
Socioeconomic level, n (%)			
low	17(94.4)	20(62.5)	6.11,p=0.013 10.20(1.20-86.69)
moderate	1(5.6)	12(47.5)	
Smoking status, n (%)			
Non-smokers	17(94.4)	21(65.6)	5.24,p=0.022 6.90(1.04-76.042)
smokers	1(5.6)	11(34.4)	
Duration of illness in years, mean (SD)	13.5 ±7.15	11.0 ±7.06	p= 0.0816
Family history of DM, of cardiac diseases, of cerebrovascular stroke, n (%)			
yes	11(61.1)	9(28.1)	5.22,p=0.022 4.015(1.18-13.62)
no	7(38.9)	23(71.9)	
waist circumference, mean (SD)	103.6±9.2	84.9±7.6	p=0.00
systolic blood pressure, mean (SD)	151.1±9.3mmHg	126.2±9.6mmHg	p=0.00
diastolic blood pressure, mean (SD)	91.0±4.7mmHg	76.1±6.8mmHg	p=0.00
triglycerides, mean (SD)	2.5±0.8mmol/l	1.3±0.3mmol/l	p=0.00
glucose, mean (SD)	6.5±0.6 mmol/l	4.9±0.4 mmol/l	p=0.00
HDL-C, mean (SD)	1.1±0.2 mmol/l	1.4±0.2 mmol/l	p=0.00

Discussion

Our investigation revealed that patients with schizophrenia had significantly higher frequency of MS and some of its symptoms. Obtained results are in accordance with similar observations in studies conducted in the USA, Canada and some countries in Western Europe[6,10-11,13,25,30]. MS was more prevalent in males. Thus, according to our study the presence of schizophrenia has a greater contribution on development of MS in males than in females and especially in persons at the age above 50 years. Meanwhile, some studies had shown that MS frequency increases in patients with schizophrenia independently of age and gender[10, 13,16]. The reasons of such discrepancies between results of our and other studies are not currently known. We did not find a relationship between the presence of MS and types of antipsychotic drug. The relationship between antipsychotic drugs and risk of developing MS has remained divergent in the literature[14,16, 35, 36]. Observed metabolic disorders in schizophrenic patients can be explained by treatment of those persons with antipsychotic drugs. It was shown that antipsychotic medication, especially treatment with atypical antipsychotics, such as clozapine and olanzapine, leads to weight gain, elevation of insulin and atherogenicity of plasma lipids[29, 30-31]. All schizophrenic patients in our study received antipsychotic medication, it's difficult to evaluate the impact of this treatment on development of MS. Besides, some authors describe elevation of visceral adiposity and insulin resistance in first-episode schizophrenic patients, who haven't received earlier antipsychotic drug therapy[32]. In recent years, it has become apparent that in patients with schizophrenia particular antipsychotic agents (AP) can have negative impact on some of the modifiable MS risk factors[33,34]. The differential effects of various AP on weight are well described with clozapine and olanzapine associated with the highest weight gain[5]. It is well known that people with schizophrenia are especially prone to stress and depression disorders. Therefore, metabolic disorders in these subjects can also be due to hyperproduction of simpatico-adrenal hormones. Our study showed that female patients had higher risk of having MS, which is a common finding in previous studies[13, 19, 35-38]. Increasing BMI was associated with increased prevalence of MS, while smoking was not. Our finding that BMI is associated with MS has important clinical relevance. BMI is an easily obtainable measurement and is routinely measured in most clinical practices. It might inform clinicians of the potential risk of MS and the consequent risks of cardiovascular morbidity and mortality. Therefore, BMI could be a useful surrogate to screen and monitor for the development of MS. The meta analyze made by Mitchell A. et al findings demonstrate that MS rates are increasing with older age35.

Conclusion

Present findings strongly support the notion that patients with schizophrenia should be considered as a high-risk group. The patients with schizophrenia should receive regular monitoring and adequate treatment of cardio-metabolic risk factors. The high prevalence of the metabolic syndrome in the present study has several clinical implications:

1. There is a crucial need to develop methods, including physical activity and nutrition, to control metabolic abnormalities among schizophrenic patients.
2. The education and training are needed to ensure that mental healthcare workers have the knowledge and skills necessary to identify schizophrenic patients with the metabolic syndrome.
3. The close collaboration between mental healthcare workers and other physicians is needed to establish better health-care for patients with schizophrenia.
4. Finally, use of anti-psychotics with lesser metabolic side effects is needed in patients at risk of developing MS.

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