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ORIGINAL ARTICLE

Metabolic Syndrome, 10year – Coronary Heart Disease and 8 year-Diabetes Mellitus Prediction in the Patients with Schizophrenia

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ABSTRACT
Objective: We sought to determine whether individuals with schizophrenia are at greater risk form metabolic syndrome, coronary heart disease (CHD) and diabetes mellitus (DM). Methods: A total of 105 subjects meeting DSM-IV criteria for Schizophrenia were assessed for their base line characteristics, BMI, blood pressure, waist circumference, FBS and lipid profile. Results: 25.7 % of total subjects have met metabolic syndrome criteria. Among those who have metabolic syndrome (27), 82%were female and only18%wasmale (p: 0.001). Abnormal waist circumference was seen in33 (64.7%) of females and 9(19.6%) of males (P: 0.000). The same results was observed for low HDL cholesterol in 25 (46.3%) and 0(P: 0.000) and high triglycerides in 14 (25.9%) and 22(45.8%) (P: 0.036) of studied women and men respectively. Overall10-year coronary heart disease risk was 5.7±4.7% (7.2%in male gender versus 4.4%in female) which was significantly higher in them ales (P: 0.003). Total 8-yearDM risk prediction of45-65years old patients were 7.8%±8.2% (P: 0.002). 8–year DM risk in the patients with metabolic syndrome was remarkably higher (11.8%) than the patients without that (5.5%) (P: 0.004). Conclusions: Our findings add to the importance of screening and intervention programs for metabolic disorders among patients with schizophrenia.
Keywords; *Schizophrenia, Metabolic syndrome, Heart disease, Diabetes mellitus*

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INTRODUCTION

Schizophrenia occurs in approximately1% of the world's population [1]. Medical co-morbidities are associated with and people with schizophrenia and they are more vulnerable to medical illnesses in general [2, 3]. The risk of developing metabolic risk factors has supposed to be greater in patients with mental illnesses; for instance, patients with schizophrenia are susceptible to diabetes and obesity from 1.2 to 2 times more common than in the general population [4].Previous studies indicated that individual with schizophrenia are prone to a significant increased risk of coronary heart disease and diabetes mellitus [5-8]. Recent researches among patients with schizophrenia demonstrated that they suffered from elevated rates of metabolic syndrome risk factors such as dyslipidemia, reduced HDL cholesterol and hypertension. Poor lifestyle, inadequate physical activity, overweight, cigarette are the most important predisposing factors [9-10]. In spite of being one of the most interesting topics of research, few studies focused on coronary heart disease and diabetes mellitus prediction in the patients with schizophrenia. In this report, we assessed metabolic syndrome risk factors and CHD and their correlation with diabetes mellitus risk in patients with schizophrenia.

MATERIAL AND METHOD

Subjects:

A total 186 diagnosed schizophrenic patients according to DSM–IV criteria (American Psychiatric Association 1994) were evaluated for this study. They all had admission history in Shahid-Beheshti hospital, as a psychological disease referral centre in Zanjanin 2011-2012. As shown in figure 1, 57 were living in rural and 45 in urbans outpatients. Also, 84 patients who have taken care in Hakim institute at least in previous year. Inclusion-exclusion criteria were includingage18-74, no other simultaneous psychological disease, metabolic abnormality due to secondary causes such as cancer, high dose corticosteroid, and uncontrolled thyroid disease, end stage cardiac, liver or renal disease. Finally, totalnumber105 individuals were enrolled in this study. Patients' socio-demographic and clinical information including their lifestyle (alcohol and coffee consumption, smoking) were registered in a questionnaire. All patients or their caretakers gave written informed consent. The study was approved by Zanjan University of medical sciences ethical committee and conducted in Metabolic Disease Research Centre.

Measurements

Blood pressure was measured by a digital barometer (OMRON made in China) after 10 min resting in sitting position with the accuracy of 0.1mmHg; weight was measured in minimum dressing by digital scale (TEFAL made in France) with the accuracy of 0.1kg. Height of the subjects was measured by standard methods and body mass index (BMI) was calculated. Waist circumference of the patients was measured by standard methods. Blood samples were collected at base line to measure BUN, Cr, serum lipid profile (TG, total cholesterol, HDL-C), fasting plasma glucose (FBS).All blood samples for the assessment of lipid profile were obtained after 14 hours of fasting. All the laboratory measurements were conducted at the central laboratory of Shahid-Beheshti hospital.

Metabolic syndrome was defined if three or more of the following five risk factors of the criteria of the modified NCEPIII were present:(1)triglycerides≥150 mg/dl, (2)HDL cholesterol<40 mg/dl in men and<50 mg/dl in women, [3] systolic blood pressure ≥130mmHgor diastolic blood pressure ≥85mmHg, [4] fasting plasma glucose≥100 mg/dL and [5]Truncal obesity (waist circumference more than 102 cm in men and>88 cm in women).10-year cardiovascular risk was estimated using the Framing ham function [11] to estimate the overall risk of any fatal or nonfatal CHD (including, in addition to the fatal CHD events mentioned above, any type of angina, myocardial infarction, other type of coronary ischemia, congestive heart failure, intermittent claudication, or peripheral arterial ischemia) within 10 years.In this protocol, population of interest is 30 to 74 years old, without overt CHD At the baseline examination. Predictors are age diabetes, smoking, blood pressure categories, total cholesterol categories, HDL cholesterol categories. Then we estimated risk of CHD in women and men separately.8-year Diabetes mellitus prediction was done by prediction of diabetes mellitus in cadence in middle-aged adults [11]. The predictors is age, gender, fasting glucose above100 mg/dl, BMI, HDL cholesterol categories, triglyceride above 150mg/dl, and blood pressure categories, parental history of diabetes.

Statistical analysis

Data are expressed as mean ±SD. We analyzed mean percentage changes from baseline in Fasting and postprandial TG, total cholesterol, HDL-C. Differences between the two groups were evaluated byt-test or Chi-square. P values less than 0.05 were considered statistically significant. The statistical analysis was performed according to standard methods using the Statistical Package for Social Sciences software16.

RESULTS

Baseline characteristics

Total of105 individuals with schizophrenia were assessed in this study. 57(54.3%) were women. Mean age was 39.7±9.6years old. Mean duration of disease was13.9±8.5.

50.5%were smoker at least 5 cigarettes per day for 5 years that 95.8%of them were male smoker (P: 0.000). Baseline characteristics and physical evaluation are demonstrated in table 1.

Table1: Socio-demographic and clinical characteristics of the patients with schizophrenia

Variables	Male (%)	Female (%)	Total	P value
Baseline characteristics				
Sex (%)	48(45.7)	57(54.3)	105	
Age 30-34 35-39 40-44 45-49 50-54 55-59 60-64	 14(29.2) 9(18.8) 11(22.9) 6(12.6) 3(6.2) 3(6.2) 2(4.2)	 12(21.1) 11(19.3) 8(14) 16(23.1) 4(7) 5(8.8) 1(1.8)	 26(24.8) 20(19) 15(14.2) 26(24.7) 7(6.7) 8(7.6) 3(2.8)	0.64
Cigarette smoking	47(86.8)	7(13.2)	50.5	0.000[1]
Duration of schizophrenia (years)	14.02	13.96	13.98	0.53
Impaired fasting glucose/Diabetes mellitus history	22(40.7)	17(35.4)	39(38.2)	0.58
Clinical and Laboratory findings				
Weight(kg)	73	66.5	69.5	0.034[1]
BMI(total) <24.9 25-29.9 30<	*24.5* 22 17 4	*27.0* 20 11 20	*25.9* 42 28 24	0.027[1]
WC(cm)	92.08	94.5	93.3	0.45
SBP(mmHg)	106.3	107.4	106.9	0.72
DBP(mmHg)	72.1	73.6	73.0	0.1
FBS(mg/dl)	108.3	95.2	101.3	0.52
Total Cholesterol(mg/dl)	190.8	169.0	169.9	0.87
TG(mg/dl)	146	118	131.1	0.055
HDL(mg/dl)	52	49	50.5	0.069

1- P value <0.05 is considered statistically significant

Metabolic syndrome:

25.7%of individuals with schizophrenia suffered from metabolic syndrome, 22(81.5%) were female and 5(18.5%) were male (P: 0.001). 26.7%had no risk factors and 1%met all risk factors. The rate of patients with metabolic syndrome increased from 0 within the30-35year-old group to 50% in people more than 60-64years of age. Distribution of abnormal metabolic components was compared among subjects with metabolic syndrome and those without metabolic syndrome in table2. In total sample, abnormal waist circumference was found in 42(43.3%), hypertension in19 (19.4%), low HDL cholesterol in25 (24.5%), high triglycerides in36 (35.5%) and, and impaired fasting glucose or diabetes in30 (38.2%) of individuals (Table 2).

Table 2: Comparison of metabolic syndrome components, coronary heart disease and diabetes mellitus risk in total samples and total sample

Variables	Metabolic syndrome	Non metabolic syndrome	Total (%)	P value
Waist circumference (waistcircumference102cm <males)or 88 cm <females	19(19.6)	23(23.7)	42(43.3)	0.000[1]
Hypertriglyceridemia(triglycerides≥150 mg/dl)	20(19.6)	16(15.7)	36(35.5)	0.002[1]
HDL-cholesterol<40 (males)or <50 (females) mg/dl	6(5.9)	19(18.6)	25(24.5)	0.000[1]
Hypertension (BP≥130/85)	7(7.1)	12(12.2)	19(19.4)	0.000[1]
Hyperglycemia(>100mg/dl)	19(18.6)	20(19.6)	39(38.2)	0.000[1]
CHD riskin10 years (Framingham)	5.6±4.7	6.1±4.9	5.7±4.7	0.74
DM riskin8 years (Framingham)	5.5±5.1	11.8±10.6	7.8±8.2	0.004[1]
Variables	Male (%)	Female (%)	Total (%)	P value
Waist circumference (waistcircumference102cm <males)or 88 cm <females	9(9.3)	33(34)	42(43.3)	0.000[1]
Hypertriglyceridemia(triglycerides≥150 mg/dl)	22(21.6)	14(13.7)	36(35.3)	0.036[1]
HDL-cholesterol<40 (males)or <50 (females) mg/dl	0	25(24.5)	25(25.5)	0.000[1]
Hypertension (BP≥130/85)	6(6.1)	13(13.3)	19(19.4)	0.13
Hyperglycemia(>100mg/dl)	17(16.7)	22(21.6)	39(38.2)	0.58
Metabolic syndrome (%)	5(10.4)	22(38.8)	27(25.7)	0.001[1]
CHD riskin10 years (Framingham)	7.2±5.5	4.4±3.6	5.7±4.7	0.049[1]
DM riskin8 years (Framingham)	6.2±4.6	9.1±10	7.8±8.2	0.002[1]

1- P value <0.05 is considered statistically significant

Among total 27men and women with metabolic syndrome, abnormal waist circumference was detected in 3(11.1%) of males and 20 (74.1%) of females (P: 0.000), hypertension in 4(14.8%) and 8(29.6%), low HDL cholesterol in0 and 19 (70.4%)(P:0.00), high triglycerides in 5(10.55%) and 11(40.7) (P: 0.04), and impaired fasting glucose or diabetes in4 (14.8%) and 16 (59.3%) respectively. Waist circumference, serum TG, and HDL were significantly different between two genders. Abnormal waist circumference was the most common metabolic abnormality in both sexes. Mean WC was 102.6cm in those with the metabolic syndrome and 89.7cm in normal individuals (P: 0.000).Abdominal obesity was found in 43.3% of patients and compared to men, women suffered much more from obesity (P: 0.000). Serum TG was more than 150md/dl was found in 35.5% and this risk factor was dominant in the males (P: 0.036). 24.5%of total individuals who consisted of 70% with metabolic syndrome had significant lower level of HDL in comparison to patients without metabolic abnormality (P:0.000) and all of them were women.10

year-Coronary heart disease and 8 year-Diabetes mellitus risk: According to Framingham function risk assessment, total10 year –coronary heart disease risk in both genders was estimated 5.7% risk. The sex breakdown represented this risk7.6%in the males and 4.4%in the females (P: 0.003). As 8-year diabetes risk prediction protocol includes subjects aged over 45years, 59 of our schizophrenia patients over age45were eligible for risk assessments. Diabetes mellitus risk of subjects with mean age of 46.7±6.6 was calculated 8.3±8.6%.It was remarkably greater in the women with schizophrenia (9.1%) compared with the men (6.2%) (P: 0.037). Diabetes mellitus risk was predicted 11.8±10.8% among individuals with metabolic syndrome in comparison to those without (5.5±5.1%) (P: 0.04).But, CHD risk was not different within two groups (table2).Our results revealed coronary heart disease risk had direct correlation with age, FBS, TG and reverse with HDL level. Similarly BMI, waist circumference showed direct correlation with 8 years diabetes mellitus risk (table3).Multi variable regression analysis confirmed aging (Betar:0.38, P: 0.000), and impaired fasting glucose (Betar: 0.49, P: 0.000) preserved this positive correlation with 10-year coronary heart disease and BMI increasing kept the same relation with diabetes mellitus (Beta: 0.49, P: 0.016).

Table3: Correlation between metabolic risk factors with CHD and DM

Variables	**CHD risk (N=105)**		**DM risk (N=59)**	
	Pearson Correlation	P value	Pearson Correlation	P value
Age	0.42	0.000[1]	0.068	0.6
Weight	0.078	0.4	0.174	0.2
BMI	0.27	0.7	0.309	0.029[1]
Waist circumference(WC)	0.019	0.8	0.296	0.035[1]
Systolic Blood pressure(SBP)	0.064	0.5	0.185	0.1
Diastolic Blood pressure(DBP)	0.186	0.06	0.085	0.5
Fasting plasma glucose(FPG)	0.54	0.000[1]	0.156	0.2
Cholesterol	0.15	0.1	0.257	0.052
Triglyceride	0.225	0.023[1]	0.095	0.4
High Density lipoprotein(HDL)	-0.243	0.014[1]	0.082	0.4

1- P value <0.05 is considered statistically significant

DISCUSSION:

Our results indicate 25.7% of the studied schizophrenic individuals has metabolic syndrome according to modified NCEP III criteria. When results compared with prevalence of metabolic syndrome of general population in Zanjan (23.7%) studied in 2009 by Sharifi and colleagues [12], it was revealed no significant increase in metabolic syndrome prevalence between studied selected populations with normal ones. Of course, in contrary to the general population, metabolic syndrome prevalence was considerably higher in female than male. Patients with metabolic syndrome increased from 0 with in the 30-35 year-old group to 50% in people more than 60-64 years of age. The prevalence of metabolic syndrome differs from 28.7 to 53% review papers [7-9].In US studies, prevalence of 6.7% was found in patients 20 to 29 years of age, and the highest 43.5% prevalence among patients over 60 (14). In Canadian study, this prevalence rates was 42.6%inmen and 48.5%in women [13]. Other studies conducted in England and Finland have documented values from 8 to 37%, respectively [14, 15]. Among the risk factors of metabolic syndrome, waist circumference, serum TG, and HDL were significantly different between two genders. Also, abnormality in BMI, WC, SBP, DBP, triglyceride level and HDL level were dominant in the patients with metabolic syndrome. Previous studies in consistent to our study have reported that the BMI of people with schizophrenia is higher than that of general population [16-20]. We think that underlies obesity in people with schizophrenia might be due to medications, lifestyle, and genetic vulnerability. In previous studies, patients with schizophrenia have been considered as a high-risk group of coronary

artery disease because they are easily exposed to many risk factors such as smoking, obesity, lack of regular physical exercise, and highly psychological stress [21, 22].
Interestingly, this study found a high prevalence of abdominal obesity and adiposity, and Low level of HDL particularly among females, coinciding with the findings of the CATIE study [9, 23] and CLAMORSl [24]. The prevalence of hyperrtriglycridemia was near 35.5% and was particularly high in males in the line with CAMORAL [24]. Studies indicated that lipid levels in schizophrenia are not routinely monitor and a simple blood test including a complete lipid profile enables us to detect 89% more cases with dyslipemia than were diagnosed upon admission..
Although we did not found any significant difference in prevalence of hypertension, hypertension was above N50%, and was higher in males in CLAMORS study [24]. Patients with schizophrenia have suffered from enormous clinical and public health burden of cardiovascular disease which is responsible for their reduced life expectancy. Overall risk of coronary heart disease was 5.7%. This risk was assessed 7.6%in the male gender. The risk of CHD reported in CAMROLS [24] was estimated 7.2±7.6 and also similar to the results of CATIE (McEvoy et al. 2005). Our study like CAMROLS dedicated that CHD in patients with schizophrenia were in the same range as the normal general population 10 to 15 years older. Metabolic syndrome in considered as a risk of diabetes, cardiovascular disease and death [25]. Obesity has been considered a major risk factor for coronary heart disease in large prospective studies [26, 27]. Some studies, however, reported that abdominal obesity is closely associated with increased risk of coronary heart disease, independent of total degree of obesity [28, 29]. Some other investigations showed that the most prevalent cardiovascular risk factors were smoking and hypercholesterolemia. We found prevalent factors such as hypertriglyceridemia, obesity and low HDL level in at least third of the studied population. As another interesting finding in our study, 8year DM prediction showed a higher risk for schizophrenic individuals with metabolic syndrome. Recent studies of schizophrenic patients have found that the rate of DM is higher than that of the general population [30, 31]. In fact, schizophrenia might be referred to as metabolic syndrome, for its association with visceral fat distribution, abnormal lipid metabolism, and metabolic dysfunction in the absence of medication treatment and beyond what is attributed to diet and lifestyle [32, 33].

CONCLUSION

Our findings add to the importance of screening and intervention programs for metabolic disorders and known risk of cardiovascular and diabetes mellitus among patients with schizophrenia. As a general, we may suggest on secondary treatment and modification of metabolic risk factors additionally emphasis on primary prevention of unfavourable risk factors in patients with schizophrenia. The treatment and prevention strategies should consist of healthy lifestyles, smoking cessation, appropriate diets and adequate levels of activity, and medical support and care, as well as screening and treatment.

LIMITATIONS

Our study has several limitations. First, we had not accessed to rural patient easily. Although they were recruited to this study separately by two times phone call, a few numbers of those living in villages were interested to participate in our study. So, our samples included mostly urban cases or rural population has already lived in the city. Second, many patients did not received appropriate family care, or no proper medical controls, so we had to used the patients subjective information about their medical history of diabetes, cardiovascular disease and smoking . Anyway, we attempted to use of minimum patients subjective information and sufficed to objective data.

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CONFLICT OF INTEREST/AUTHORS DISCLOSURE

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