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Original Research Article

Metabolic Syndrome among Patients with Schizophrenia Receiving Antipsychotics at Chitwan Medical College, Nepal

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ABSTRACT

Introduction: Schizophrenia itself has been associated with an increased risk of cardio-metabolic morbidity and mortality. Treatment with antipsychotic agents has also been recognized as an additional risk factors of metabolic syndrome. This study was undertaken to find out the proportion of metabolic syndrome and factors associated with it among patients with schizophrenia receiving antipsychotics at Chitwan Medical College, Nepal.
Methodology: A cross-sectional study design was conducted among 85 clinically diagnosed patients with schizophrenia who were receiving antipsychotics for at least 6 months from psychiatric outpatients department of Chitwan Medical College Teaching Hospital. Data were collected from October 2013 to December 2013 using semi-structured interview schedule, physiological measurement and record review. Obtained data were analyzed by using descriptive and inferential statistics. Metabolic syndrome was assessed according to International Federation of Diabetes (IFD) definition criteria based on gender specific.
Results: The overall metabolic syndrome among patients with schizophrenia was 24.7%. Metabolic syndrome was common in female compared to male (31.6% vs. 17.5%). On average, study patients had 1.69 ± 0.97 metabolic abnormalities. The most common metabolic abnormalities were central obesity or abnormal waist circumference (64.7%), elevated plasma fasting glucose (54.1%), hypertriglyceridemia (44.7%), and low HDL cholesterol (18.8%) while the least prevalent metabolic parameter was elevated blood pressure 4 (4.7%). Central obesity or abnormal waist circumference and reduced HDL cholesterol were significantly higher among male compared to female patients. Moreover, multiple logistic regression analysis showed that only age and duration of treatment with antipsychotics were significant predictors of metabolic syndrome in patients with schizophrenia.
Conclusion: Quarter of patients with schizophrenia receiving antipsychotics have metabolic syndrome and notable factors associated are increasing age and duration of treatment with antipsychotics. Therefore, proper monitoring of metabolic syndrome and associated risk factors are needed for the betterment of patients.

Key words: Metabolic Syndrome, Schizophrenic patients.

INTRODUCTION

Metabolic syndrome affects a great number of people and it is estimated that approximately 20%-25% of the world's adult population suffers from it. [1] The reported prevalence of metabolic syndrome in Asians is 5%-%. [2-4] In Nepal, 22.5% of the people have metabolic syndrome based on IDF criteria and 20.7% according to the National Cholesterol Education Program-

Adult Treatment Panel (NCEP ATP) criteria. [5]

The prevalence of metabolic syndrome in patients with schizophrenia is approximately two to four times higher than that in the general population [6,7] and also found to be higher among patients with schizophrenia than the patients with other different psychiatric disorders (41.0% vs. 38.0%). [8]

Metabolic syndrome not only entails serious health complications but also places individuals at a greater risk of other serious medical conditions such as Cardiovascular Disorders (CVD) and diabetes. [9,10] People with metabolic syndrome are twice as likely to die from it and three times more likely to have a heart attack or stroke compared to people without it. [11] Furthermore metabolic abnormalities not only have an impact on physical health but also on a poorer health related quality of life, [12] non-compliance, subjective distress, [13] lower functional [14] and cognitive performance. [15]

Antipsychotic drugs have revolutionized the management of serious mental illnesses such as schizophrenia and bipolar disorders; they have provided countless individuals with an enhanced quality of life and improved psychosocial functioning. [16] Besides its therapeutic effects, it has been recognized as an additional risk factor for the development of metabolic abnormalities in patients with schizophrenia. [17] Evidence based study reported that the frequency of metabolic syndrome is 2-4 times higher in a group of people with schizophrenia treated with both atypical and typical antipsychotics. [18] In Thailand, 20% of patients with schizophrenia receiving long-term antipsychotic treatment developed metabolic syndrome within a year of follow-up. [19] Similarly, 46.7% of patients with schizophrenia receiving antipsychotic medications for at least one year developed metabolic syndrome in Malaysia. [20] Likewise, 18% of patients with schizophrenia in India developed metabolic syndrome (IDF criteria) after six weeks of antipsychotic treatment. The prevalence of metabolic syndrome (IDF criteria) was highest with olanzapine (26%) followed by risperidone (24%) and least with haloperidol (3%). [21]

The differential prevalence of metabolic syndrome associated with various atypical antipsychotic medications have been evidenced across numerous studies, with higher effects seen for certain antipsychotic medications on weight gain, waist circumference, fasting triglyceride level, and glucose levels. In our knowledge, limited data are available so far on the prevalence of metabolic syndrome and factors associated with it in patients with schizophrenia in Nepal. Though antipsychotics are used in wide range for the treatment of patients with schizophrenia, proper monitoring and screening is lacking. Hence, this study addressed this gap, assessing the proportion of metabolic syndrome and factors associated with it among patients with schizophrenia who were receiving antipsychotics which provided the necessary information with rationale for the justification of above mentioned problems.

MATERIALS AND METHODS

This is the cross-sectional study conducted at Chitwan Medical College Teaching Hospital (CMC-TH) in Chitwan, Nepal. All patients attending psychiatric outpatient department during the study period and with the following criteria were invited to participate: (1) patients aged 18 years old or more (2) who are clinically diagnosed as schizophrenia as defined by DSM-IV (3) receiving antipsychotic medications for at least 6 months. Those patients with schizophrenia who were taking medications for metabolic abnormalities, admitted in hospital due to physical illnesses 1 month prior to the visit, receiving more than one antipsychotic were excluded from the study.

In order to estimate with sufficient precision the prevalence of metabolic syndrome, we hypothesized that the

estimated prevalence rate of metabolic syndrome to be 41%. We calculated the sample size with a 95% confidence interval and of a 10% width. Based on this, we needed a sample size of at least 85 patients.

Data were collected from October 2013 to December 2013 using semi-structured interview schedule, physiological measurement and record review. Semi-structured interview schedule was developed for recording socio-demographic information and disease related variables of the respondents. Physiological measurement was used to measure the height, weight and waist circumference, blood pressure and collection of sample for lab test. After measuring height and weight, body mass index was calculated by using formula (weight in Kg÷ height in m^2). Charts were reviewed for medications used and laboratory tests were performed to find lipid profile and fasting plasma glucose level.

On the assessment day, we collected socio-demographic information and anthropometric measurements including information about the patient's smoking; alcohol and drug habits, nutrition and exercise, as well as family history of diabetes and cardiovascular disease. Body weight was measured digitally with the participants wearing light cloth and no shoes and the height measured with a simple measuring tape. Waist circumference was measured in a horizontal plane, midpoint between the inferior margin of the ribs and the superior border of the iliac crest. Participants were asked to stand with feet together and arms in a relaxed position at either side during measurement. A tape was then held in a horizontal position and wrapped around the waist, loose enough for the recorder to place one finger between the tape and the participant's body. Participants were asked to breathe normally and measurements were taken to the nearest 0.1 cm at the end of a normal exhalation. It was ascertained that participants did not contract the abdominal muscles during measurements. Blood pressure was measured twice in 10 minutes interval by using mercury sphygmomanometer in sitting position and then the mean reading was calculated and used. To assess the blood levels of triglycerides, HDL-cholesterol, and FPG, each participant was instructed to fast after midnight (at least 8 hours fasting) before giving the blood sample in the following morning. Collected blood samples were then sent to the clinical laboratory of CMC-TH for analysis as quickly as possible. After collection of blood sample, syringes were kept in puncture proof container.

Before data collection, ethical approval was obtained from Nepal Health Research Council and Chitwan Medical College-Institutional Review Committee (CMC-IRC). The participants were explained about the purpose and nature of the study and benefits they get from the study. Participants were also informed that they have to give fasting blood sample for lipid profile and plasma glucose which will be done free of costs and reports will be provided to them. The verbal informed consent was obtained from all participants to maintain their right to self-determination. Those participants who were not able to give consents themselves or mentally disturbed, consent was obtained from their visitors. To maintain privacy and confidentiality, code number was given to each participant instead of name, and they were assured that their information would not be disclosed. The data were collected by researchers themselves. Collected data were kept in password protected computer and the entire information containing sheets were discarded after the publication of results.

Statistical analysis

The descriptive statistics such as frequencies, percentages, means, standard deviations, median and inter quartile range (Q1 to Q3) were computed. The percentages of participants who have metabolic syndrome were calculated. Independent sample t test was used for continuous variable to measure difference between groups while chi-square test was used for

categorical variable. Univariate analysis was carried out using binary logistic regression while multiple logistic regression was carried out on variables that showed significance in univariate analysis. In both univariate and multiple logistic regression, the presence of metabolic syndrome was used as the dependent categorical variable. All statistical analyses were conducted using statistical package for social sciences (SPSS) version 19 for window. The term statistically significant will be applied to a p-value of <0.05.

RESULTS

General Description

A total 85 patients with schizophrenia receiving antipsychotics for at least 6 months were recruited for this study. The highest percentage of patients (35.3%) was between 30-40 years of age followed by 20-30 years (31.8%). The mean age of the patients was 35.42 ±11.31 [95% CI: 20 - 60] years. Most of the patients (88.2%) were literate and 52.9% were residing in rural area of Chitwan district. The highest percentages of patients (29.4%) were housewife followed by students (20.0%) and farmer (16.5%). The median duration of schizophrenia diagnosis was 3 (Q1-Q3: 1.6 to 7.5) years and duration of treatment with antipsychotics was 2 (Q1-Q3: 1.25 to 3.0) years. The majority (75.3%) of the patients were using atypical antipsychotics and the most commonly used antipsychotic was olanzapine (31.8%), followed by quetiapine (24.7%), haloperidol (16.5%), risperidone (18.8%) and trifluoperazine (8.2%). The number of non-smokers was higher than the smoker (74.1% vs. 25.9%). The mean body mass index was 24.82 ± 4.49 and the body mass index was higher in female compared to male (26.05 ± 4.49 kg/m^2 vs. 23.44 ± 4.11 kg/m^2, p=0.007) (As shown in Table 1).

Table 1: General Characteristics of Patients with Schizophrenia n=85

Variables	N(%) or Mean (± SD) or Median (Q1-Q3)		
	Total	Male	Female
Age group in year	**35.42 (± 11.31)**	**34.60 (±10.51)**	**36.16 (±12.05)**
Education			
Illiterate	10 (11.8)	1 (10.0)	9 (90.0)
Literate	75 (88.2)	39 (52.0)	36 (48.0)
Address			
Rural	53 (62.4)	27 (50.9)	26 (49.1)
Urban	32 (37.6)	13 (40.6)	19 (59.4)
Occupation			
Not working	29 (34.1)	13 (44.8)	16 (55.2)
Working	56 (65.9)	27 (48.2)	29 (51.8)
Smoking status			
Smoker	22 (25.9)	17 (77.3)	5 (27.7)
Non-smoker	63 (74.1)	23 (36.5)	40 (63.5)
Duration of illness in year	3 (1.6-7.5)	3 (2.0-6.5)	2 (1.3-10.0)
Duration of treatment in year	2 (1.25-3.0)	3 (2-4)	2 (1-3)
Type of drugs			
Typical	21 (24.7)	9 (42.9)	12 (57.1)
Atypical	64 (75.3)	31 (48.4)	33 (51.6)
BMI (kg/m^2)	24.82 (±4.49)	23.44 (±4.11)	26.05 (±4.49)
Waist circumference	87.88 (±10.43)	86.60 (±9.99)	89.02 (±10.78)
Systolic BP	113.29 (±10.84)	115.00 (±9.34)	111.78 (±11.93)
Diastolic BP	74.35 (±8.23)	75.00 (±8.16)	73.78 (±8.34)
Triglycerides	131.0 (90.0-227.5)	130 (96.75-257.0)	131 (85-183.0)
HDL	53 (47.5-61.0)	53 (48.25-59.75)	57 (46.0-62.5)
Fasting plasma glucose	101.0 (90.5-110.0)	102.5 (97.0-110.0)	99.0 (87.5-110.0)

Proportion of Metabolic Syndrome

According to IDF criteria, 24.7% of patients with schizophrenia met the criteria of metabolic syndrome. On average; the study patients had 1.69 ± 0.97 metabolic abnormalities (Shown in Table 2).

Central obesity or abnormal waist circumference was the most common metabolic parameter in both males and

females whereas raised blood pressure was the least common metabolic parameter in both genders. The frequency of abnormal waist circumference and reduced HDL were significantly higher in male compared to female patients. On average, metabolic syndrome was higher in female patients compared to male patients (31.1% vs. 17.5%) but it was not statistically significant (Shown in Table 3).

Table 2: Proportion of Metabolic Abnormalities Criteria among Patients with Schizophrenia n=85

Number of Metabolic Syndrome Criteria	N (%)		
	Total (n=85)	Male (n=40)	Female (n=45)
0	9 (10.6)	7 (17.5)	2 (4.44)
1	75 (88.2)	33 (82.5)	42 (93.3)
2	50 (58.8)	20 (50.0)	30 (66.7)
3	24 (28.3)	10 (25.0)	14 (31.1)
4	9 (10.6)	3 (7.5)	6 (13.3)
5	0	0	0
MS≥3 (WC+ 2 other criteria)	21 (24.7)	7 (17.5)	14 (31.1)

Average criteria= 1.69 ± 0.97

Table 3: Proportion of Metabolic Syndrome Parameters among Patients with Schizophrenia

Metabolic Syndrome IDF Criteria	Entire (n=85)	Male (n=40)	Female (n=45)	OR (95% CI)	p
Central obesity or abnormal waist circumference (BMI >30 kg/m^2 or waist circumference: men≥90 cm; women≥80 cm)	55 (64.7)	31 (77.5)	24 (53.3)	3.014 (1.171 -7.757)	0.022
Raised blood pressure (≥130/85 mmHg)	4 (4.7)	3 (7.5)	1 (2.2)	3.568 (0.356 - 35.762)	0.279
Raised triglyceride level (≥150 mg/dl)	38 (44.7)	19 (42.2)	19 (47.5)	0.808 (0.343 - 1.904)	0.625
Reduced HDL (men<40 mg/dl; women <50 mg/dl)	16 (18.8)	13 (32.5)	3 (6.7)	6.741 (1.756 - 25.879)	0.005
Raised fasting plasma glucose (≥100mg/dl)	46 (54.1)	24 (60.0)	22 (48.9)	1.568 (0.663-3.711)	0.306
Metabolic syndrome (BMI >30 kg/m^2 or WC: men≥90 cm; women≥80 cm) plus other 2 criteria	21 (24.7)	7 (17.5)	14 (31.6)	2.129 (0.759 - 5.971)	0.151

Table 4: Univariate Logistic Regression Analysis of Metabolic Syndrome among Patients with Schizophrenia n=85

Variable	With MS N (%) or Mean ± SD	Without MS N (%) or Mean ± SD	Unadjusted OR (95% CI)
Age (yrs)	**42.24 ± 10.27**	**33.19 ± 10.78**	**1.076 (1.026-1.129)**
Gender			
Male	7 (17.5)	33 (82.5)	1
Female	14 (31.1)	31 (68.9)	2.129 (0.759-5.971)
Address			
Rural	17 (32.1)	36 (67.9)	3.306(1.00-10.930)
Urban	4 (12.5)	28 (87.5)	1
Education			
Illiterate	5 (50.0)	5 (50.0)	3.687 (0.949-14.326)
Literate	16 (21.3)	59 (78.7)	1
Occupation			
Employment	7 (22.6)	24 (77.4)	1
Unemployment	14 (25.9)	40 (74.1)	1.200 (0.425 -3.391)
Duration of illness	7.63 ± 6.71	4.93 ± 6.07	1.063 (0.987-1.145)
Family history of DM			
No	17 (24.3)	53 (75.7)	1
Yes	4 (26.7)	11 (73.3)	1.134 (0.319 – 4.029)
Family history of HTN			
No	15 (26.8)	41 (73.2)	1.402 (0.478 – 4.112)
Yes	6 (20.7)	23 (79.3)	1
Smoking history			
No	17 (27.0)	46 (73.0)	1.663 (0.492 – 5.621)
Yes	4 (18.2)	18 (81.8)	1
Type of antipsychotics			
Typical	5 (23.8)	16 (76.2)	1
Atypical	16 (25.0)	48 (75.0)	1.067 (0.337-3.378)
Duration of treatment in year	3.76 ±2.14	2.19±1.28	1.749 (1.263-2.422)

Regression Analysis

Univariate analysis (Table 4) shows that the metabolic syndrome was significantly higher among older patients, rural residence, longer duration of treatment with antipsychotics compared to younger

patients, urban residence, and having lesser duration of treatment with antipsychotics respectively. However, there was no significant difference on the development of metabolic syndrome between patients with regard to gender, education, occupation, family history of diabetes and hypertension, smoking history, and type of antipsychotics.

Further, multiple logistic regressions indicated that age and duration of treatment with antipsychotics were the significant predictors of metabolic syndrome (As shown in table 5).

Table 5: Multiple Logistic Regression Analysis Model for Metabolic Syndrome among Patients with Schizophrenia

Variables	Unadjusted B	Adjusted β	P value	95% CI	
				Lower	Upper
Age in Year	1.076	1.070	0.023	1.009	1.135
Rural Address	3.306	3.110	0.113	0.763	12.677
Illiterate Status	3.687	2.483	0.294	0.454	13.591
Duration of Treatment with Antipsychotics in Year	1.749	1.738	0.002	1.222	2.473
Constant		0.002	0.000		

R^2=0.385 Hosmer and Lemeshow Test (x^2): 3.977 p=0.782

DISCUSSION

Our results showed that 24.7% of the patients with schizophrenia had metabolic syndrome according to IDF criteria where higher proportions of female had metabolic syndrome compared to male but the difference was not statistically significant. The most common metabolic abnormalities were central obesity or abnormal waist circumference, elevated fasting glucose, raised triglyceride level, and reduced HDL cholesterol. Age and duration of treatment with antipsychotics were identified as the factors associated with metabolic syndrome.

The rate of metabolic syndrome was considerably lower (24.7%) in our study than has been observed in studies conducted in Malaysia [20] and Palestine [22] which found 46.7% and 43.6% of metabolic syndrome among patients with schizophrenia respectively. These discrepancies in rates might be due to difference in lifestyle and different diagnostic criteria used in the studies.

In this study the common metabolic abnormalities among patients with schizophrenia receiving antipsychotics were central obesity (64.7%), elevated fasting glucose (54.1%), hypertriglyceridemia (44.7%), and low HDL cholesterol (18.8%) while the least prevalent was elevated blood pressure (4.7%). Our finding almost substantiate with the result of study done in Ireland [23] which showed that the common metabolic parameters of central obesity (88%), hypertriglyceridemia (43%), hypertension (41%) and glucose deregulation (32%). Likewise, Said et al. (2012) found that the most common metabolic syndrome criteria in patients were abnormal waist circumference (98.4%), low HDL cholesterol (72.6%), raised triglycerides (67.7%) and elevated blood pressure (61.1%), while the least prevalent metabolic component was elevated fasting blood glucose. [14] Furthermore Mackin and colleagues also found obesity, dyslipidemia and abnormalities of glucose homeostasis in people receiving both typical and atypical antipsychotics. [24] The probable cause might be due to use of antipsychotics because these medications may cause weight gain or changes in blood pressure, cholesterol and blood sugar levels. [25]

Our study found hypertension as a least common metabolic parameter whereas Said and colleagues revealed elevated fasting blood glucose as a least prevalent parameter. [20] The possible explanation for these discrepancies in findings might be due to difference in mean age, life style and food habits of the patients with schizophrenia included in the studies.

With regard to gender, relatively more female than male had met the diagnostic criteria of IDF for metabolic syndrome (31.1% vs. 17.5%) in this study, but this was not statistically significant. Similar results were also obtained in the study conducted by Said et al. (2012) which

revealed that there was no significant difference on metabolic syndrome between male and women in Malaysia. [20] However, Sweileh and colleagues revealed that female had significantly higher risk of having metabolic syndrome than the male in Palestine. [22] The reasons of higher metabolic syndrome in female might be due to sedentary life style, poor dietary habits, and lack of physical exercises and lower education level which leads to less health seeking behavior.

In between gender comparison, our study found that male had significantly higher chance of having central obesity and low HDL level in compared to female. This finding is inconsistent with the findings of study conducted in Palestine which found that female had significantly higher chance of having central obesity and low HDL level compared to male. [22] These discrepancies might be due to different lifestyles and criteria used for the diagnosis of metabolic syndrome and its parameter in the studies.

With regard to age, our study found that older age patients had significantly higher risk of having metabolic syndrome and similar finding was reported by the study conducted in Palestine. [22] This might be due to high incidence of overweight or general obesity and abdominal obesity in middle age and high carbohydrate consumption in meal.

In this study, longer duration of treatment with antipsychotic was significantly associated with the metabolic syndrome. This finding is supported by the study conducted by Srisurapanont and colleagues which revealed metabolic syndrome among 20% of patients with schizophrenia receiving long-term antipsychotic treatment within a year of follow-up. [19] Similarly, Saho et al. also found metabolic syndrome among 18% of patients with schizophrenia after six weeks of antipsychotic treatment. [21] Exposure to antipsychotics may cause an initial weight gain related to metabolic disturbances or may affect the metabolism of lipids and glucose directly.

Moreover, we didn't find a relationship between the presence of metabolic syndrome and types of antipsychotics drugs and this finding is similar with the findings of the study conducted by Sweileh and colleagues. [22] Systematizing and interpreting the results by the type of antipsychotic medication is difficult, because of small and unequal sampling sizes. This study also lacks the power to examine combination of different antipsychotic agents, dosages, and drug level in blood of patients with metabolic syndrome.

This study has certain limitations. The cross-sectional design of the study limits the ability to describe how metabolic parameters changes with time period. We recruited the patients with stable schizophrenia state while acutely ill patients were not included in the study which affects the generalization of the results. Sample size is small and provides even smaller population when classifying the different data. Therefore association between diet and exercise with metabolic syndrome could not be explored due to small sample size and smaller population in different analyzing group. This study was limited to one hospital so the findings couldn't be generalized to other settings.

CONCLUSION

Quarter of patients with schizophrenia receiving antipsychotics have metabolic syndrome. Common metabolic parameters are central obesity or abnormal waist circumference, raised fasting plasma glucose level and raised triglyceride level. The risk factors associated with metabolic syndrome are increasing age and longer duration of treatment with antipsychotics. Since metabolic syndrome is known to be associated with an increased risk of cardiovascular disease and type 2 diabetes mellitus, this will have serious implications in country's health care costs. Therefore, treating physicians and health workers are recommended to monitor metabolic syndrome parameters regularly to identify

those patients with an increased risk of metabolic syndrome, intervene appropriately when needed and refer the patients for the treatment of any other physical illnesses.

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