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ORIGINAL RESEARCH ARTICLE

STUDY OF METABOLIC SYNDROME IN SCHIZOPHRENIC PATIENTS TREATED WITH ANTIPSYCHOTICS

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ABSTRACT

Background: There are limited data on the prevalence of metabolic side effects with the antipsychotic drugs in Nepal. The objective was to study the prevalence of metabolic syndrome in schizophrenia patients treated with antipsychotics drugs. The second objective was to test the relationship of metabolic syndrome with different socio-demographic and clinical variables

Methods: This was hospital based cross sectional study conducted in the outpatient's unit of Department of Psychiatry, Manipal Teaching Hospital, Pokhara. Ethical approval was taken from the Institutional Review Committee of Manipal College of Medical Sciences, Pokhara. A total of 60 patients (age between 16 and 65 years) who had fulfilled the diagnostic criteria of schizophrenia according to International Classification of Disease – 10 guidelines and who had taken a single antipsychotic drug for at least 6 months were enrolled after taking informed written consent. Data were collected from April 2020 to July 2020.Patients were diagnosed to have metabolic syndrome according to adapted National Cholesterol Education Program Adult Treatment Panel III criteria by the American Heart Association (NCEP ATP III-A). Data entry and analysis was done using SPSS version 16.0. The statistical method used were percentage and chi-square test.

Results: The prevalence of metabolic syndrome was 30%. There was association of metabolic syndrome with socioeconomic status. There was no statistical association of metabolic syndrome with gender, residence, type and duration of antipsychotics use.

Conclusions: The prevalence of metabolic syndrome was high. Therefore, proper monitoring of metabolic syndrome and adequate treatment of cardio-metabolic risk factors are required for optimum long-term management.

INTRODUCTION

Schizophrenic person have shorter life span when compared to general population. A majority of persons with schizophrenia die of coronary heart disease (CHD) which is an endpoint of metabolic syndrome.[1] A review of thirty eight studies conducted on the metabolic syndrome in schizophrenic patients found approximately 2 to 3 times greater prevalence and incidence of metabolic syndrome in people with schizophrenia than in general population.[2]

In psychiatry care, the use of antipsychotic medications has caused widespread revolutionary changes to many lives. While the benefits of these medications are evident, it is important to recognize the harmful effects like the metabolic syndrome which leads to significance decrease in life expectancy for people with serious mental illness. The premature loss of life, mainly due to cardiovascular incidents experienced by people with serious mental illness taking antipsychotic medications is of grave concern. The situation is serious and demands urgent attention. There is only one study conducted till now in Nepal, from the Chitwan District.[3] The studies from other geographical region of Nepal were lacking. This study is conducted to fulfill this research gap.

The objective was to study the prevalence of metabolic syndrome in schizophrenic patient treated with antipsychotics attending Psychiatry OPD of Manipal Teaching Hospital, Pokhara. The second objective was to test the association of metabolic syndrome with different sociodemographic and clinical variables.

METHODS

This was hospital based cross-sectional study conducted in the Psychiatry Outpatient department of Manipal Teaching Hospital. Manipal Teaching Hospital is situated in Pokhara, the capital of the Gandaki Province of Nepal. The ethical clearance of the study was taken from Institutional Review Committee of Manipal College of Medical Sciences, Pokhara before the start of study. The informed written consent was taken from the patients. The consent was taken from the patient party if the patient had unstable mental status. The study was conducted from April 2020 to July 2020.

The sample size was calculated by using the formula $1.96^2pq/d^2$ (where; p=prevalence, 24.7%[3]; q=100-p, 75.3%; d=margin

of error, 11). The sample size according to this formula was 59.025. Hence, 60 samples were taken as a final sample size.
The total of 60 patients who had fulfilled the diagnostic criteria of schizophrenia according to ICD-10 Classification of Mental and Behaviour Disorder Diagnostic Criteria for Research (ICD-10 DCR) was selected. ICD-10 DCR was developed by Division of Mental Health of WHO in 1992. It was derived from ICD 10 Clinical and Diagnostic Guidelines. It provides operational criteria for diagnosis of Mental and Behavioral Disorders in a clearly defined and specific manner in contrast to more narrative equivalents statements used in Clinical descriptions and Diagnostic Guidelines. It is basically designed for research purposes.

The inclusion criteria for this study were patient age between 16 to 65 years and receiving only one antipsychotic medication in the last six month. Those patients with schizophrenia who were taking more than one antipsychotic medication, taking medication for metabolic abnormalities before the onset of illness and admitted in hospital due to physical illness in last 6 months and lastly patient with comorbid other mental illness were excluded. Similarly, patients taking mood stabilizers, steroids, antidepressants and contraceptives and pregnant and lactating women were also excluded.

The diagnosis of metabolic syndrome was made according to the criteria of adapted National Cholesterol Education Program Adult Treatment Panel III by the American Heart Association (NCEP ATP III-A). According to this criteria, metabolic syndrome is diagnosed when 3 or more of criteria were met: elevated waist circumference (>40 inches or >102 cm in men and >35 inches or >88 cm in women), elevated fasting TG (>150 mg/dl), reduced HDL (<40 mg/dl in men and < 50 mg/dl in women), elevated BP (> 130/85 mm Hg) or taking antihypertensive medication, and elevated fasting glucose (>100mg/dl) or taking insulin or hypoglycemic medication.[4]

A self-designed proforma was used to record the socio-demographic and clinical variables of the patients. This proforma includes age, gender, residence, type of antipsychotic drug and duration of treatment. The socioeconomic status was assessed using modified Kuppuswamy's socioeconomic status scale. Data entry and analysis was done on SPSS version 16.0. The p-value less than 0.05 were considered significant in this study.

RESULTS

The total of 60 patients was analyzed. The age of the participants ranged from 17 to 56 with mean age of 32.16 years (SD=9.59 years). Table 1 showed that the prevalence of metabolic syndrome was 30% among the patient with schizophrenia treated with antipsychotics drugs. In females, 39.3% have metabolic syndrome and while in men, 21.0% have metabolic syndrome. The prevalence of metabolic syndrome was seen slightly more in patient living in rural area (31.3%) as compared to urban area (29.5%). The patients from the lower socioeconomic status had high prevalence of metabolic syndrome. There was significant association of metabolic syndrome with socioeconomic status of the patients.

Table 1: Frequency of metabolic syndrome and its association with different variables

Variables		Metabolic Syndrome (Present) N (%)	Metabolic Syndrome (Absent) N (%)	p-value
Gender	Female	11 (39.3)	17 (60.7)	0.142
	Male	7 (21.0)	25 (79.0)	
Residence	Urban	13 (29.5)	31 (70.5)	0.896
	Rural	5 (31.3)	11 (68.7)	
Socioeconomic status	Upper and Middle	5 (14.7)	29 (85.3)	0.003
	Lower	13 (50.0)	13 (50.0)	
Total		18 (30.0)	42 (70.0)	

Table 2: Relationship of metabolic syndrome with types of antipsychotics and duration of treatment

Variables		Metabolic syndrome present N (%)	Metabolic syndrome absent N (%)	p-value
Types of antipsychotics	Typical	1(16.7)	5(83.3%)	0.65
	Atypical	17(31.5)	37(68.5)	
Duration of treatment	< 2 years	7(27.0)	19 (73.0)	0.64
	> 2 years	11(32.4)	23 (67.6)	
Total		18 (30.0)	42 (70.0)	

Table 2 showed that 31.5% and 16.7% of patients who had taken atypical and typical antipsychotic drugs had metabolic syndrome respectively. Among those who had taken antipsychotics for less than 2 years, 27% had metabolic syndrome while those who had taken antipsychotics for greater than 2 years, 32.4% had metabolic syndrome. However, this association was not statistically significant.

Table 3 showed the various clinical parameters of participants. The mean systolic blood pressure among them was found to be 118.36 mm of HG (SD ±13.79) with minimum of 90 mm of Hg and maximum of 150 mm of Hg. Similarly, the mean diastolic blood

pressure among them was found to be 78.6 mm of Hg (SD ±10.75) with minimum of 60 mm of Hg and maximum of 100 mm of Hg. The mean height was found to be 161.57 cm (SD ±8.49) and mean weight was found to be 65.51 kg (SD ±13.71). Among participants the mean BMI was observed to be on the higher side which was 25.04 (SD ±4.57). The mean waist circumference in male was 87.03 cm (SD ±10.43) and in female was 92.18 (SD ±12.4). Similarly the mean hip circumference in male was 94.31 cm (SD ±7.54) and in female was 100 cm (SD ±9.24). The mean waist hip ratio in male was 0.91(SD ±0.058) whereas in female was 0.91 (SD ±0.076).

Table 4 below showed the different laboratory parameters among the participants. The mean fasting blood sugar (FBS) was found to be 93.57 mg/dl (SD ±16.49) and post prandial blood sugar was found to be 127.95 mg/dl (SD ±47.66). Among the lipid profile, the mean triglyceride was observed to be 126.78 mg/dl (SD ±74.1), mean Low density lipid was 99.56 mg/dl (SD 36.69), mean cholesterol was 153.43 mg/dl (SD ±40.2) and mean High density lipid in male was 43.03mg/dl (SD ±8.06) whereas in female it was found to be 45.14 mg/dl (SD ±11.09)

Table 3: Showing clinical parameters of the study participants

Variable		Minimum	Maximum	Mean	Standard Deviation
Systolic BP (mm of Hg)		90	150	118.36	13.79
Diastolic BP (mm of Hg)		60	100	78.6	10.75
Height (cm)		145	176	161.57	8.49
Weight (kg)		43	95	65.51	13.71
BMI (kg/m^2)		16.33	36.11	25.04	4.57
Waist circumference (cm)	Male	67	106	87.03	10.43
	Female	70	118	92.18	12.40
Hip Circumference (cm)	Male	77	107	94.31	7.54
	Female	84	120	100	9.24
Waist Hip Ratio	Male	0.77	1.04	0.91	0.058
	Female	0.78	1.10	0.91	0.076

Table 4: Showing laboratory parameter of study participants

Variable		Minimum	Maximum	Mean	Standard Deviation
Fasting Blood Sugar (mg/dl)		72.0	181.0	93.57	16.49
Postprandial blood sugar (mg/dl)		79.0	403.00	127.95	47.66
Triglycerides (mg/dl)		25	393	126.78	74.10
High density lipid (mg/dl)	Male	23.0	56	43.03	8.06
	Female	25.0	84	45.14	11.09
Low density lipid (mg/dl)		15.0	207	99.56	36.69
Total cholesterol (mg/dl)		67	273	153.43	40.20

DISCUSSION

This was hospital based cross sectional study carried out in patients with schizophrenia attending psychiatric OPD of Manipal Teaching Hospital, Pokhara. The study mainly done to assess the prevalence and correlates of metabolic syndrome among patient with schizophrenia treated with antipsychotic drugs.

The prevalence of metabolic syndrome in this study was 30%. Our findings was consistent with the study done in Chitwan, Nepal[3] and in Japan.[5] However, the other studies done in Vietnam[6] and Australia[7] found high prevalence of 86% and 68% respectively. These discrepancies in prevalence rate may be due to difference in lifestyle of patients, operational definition of metabolic syndrome and different diagnostic criteria used.

This study showed that female (39.3%) had higher prevalence of metabolic syndrome in comparison to male (21%) which was according to study done in India, Spain and Iran. [8,9,10] Similarly another comparative study done in India found prevalence of 29% and 23% in women's and men's sample, respectively. The frequency of occurrence of the Metabolic Syndrome was similar for men (83%) and women (86%) and increased with age in both sexes.[6] There was no association of gender with metabolic syndrome in our study (p=0.142). Similarly, the study done in Spain[9] also did not found association of metabolic syndrome with gender of the patient. The high prevalence of metabolic syndrome in female is explained by the sedentary life style, poor dietary habit, lack of physical exercise, staying indoor most of the time, stress and lower education level which leads to less health seeking behavior.

There was no association between metabolic syndrome and residence in our study. One study conducted in Japan found association of metabolic syndrome with residence which contradict with our study findings.[5]

In this study, the prevalence of metabolic syndrome is noted maximum in the lower socioeconomic class samples (50%) and the association was statistically significant (p=0.003). One study done in Korea found the prevalence of metabolic syndrome maximum in the middle class sample which was contradict to our study findings. According to this study, the lower SES groups showed more tendencies to smoke and to exercise less

regularly.[11]This can also be explained by the poor health behaviors such as diet, smoking, leisure time, and heavy drinking noted more in the patient belonging to the lower socioeconomic class.[12]

In this study, patients using atypical antipsychotics had higher prevalence (31.5%) of metabolic syndrome compared to those on typical antipsychotics (16.7%). However, the association was not statistically significant (p-value = 0.65). These findings were similar to the other studies.[13,14] In one study done in Qatar the prevalence of metabolic syndrome in first generation and second generation antipsychotics was 13.4% and 67.9% respectively.[15]

With regards to duration of treatment, patient taking antipsychotic drugs for more than 2 years had higher prevalence (32.4%) than those patients taking antipsychotic drugs less than 2 years (27.0%). However, this association was not statistically significant in the present study (p value=0.64). This finding was consistent with the studies done in India and Taiwan.[16,17] There are some studies that have demonstrated that the duration of treatment does not influence the prevalence.[18-20] However, there are large body of evidences that a longer duration of illness has been demonstrated to be associated with higher prevalence of metabolic syndrome.[21-24]

There are few limitations of this study. The small sample size is the obvious limitation of this study. This provides even smaller samples when classifying the different sub variables. Due to small and uneven sampling sizes, it is difficult to standardize and infer the results. The other limitations were cross-sectional design of this study and absence of a healthy control group. A longitudinal study design and comparison with a healthy control group would have been useful in noting changes in metabolic syndrome. Furthermore, this study has got no power to examine the metabolic syndrome with combination therapy with different antipsychotic agents, dosages, and drug level in blood of patients. Factors that potentially affect the development of metabolic syndrome, such as lifestyle or genetic variations were also not investigated. The data were collected at only one hospital which might impact on generalizability of the results.

CONCLUSION

The prevalence of metabolic syndrome in the patients with schizophrenia taking antipsychotics drugs was high. There was association of metabolic syndrome with socioeconomic status. 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, it is recommended to monitor metabolic syndrome parameters regularly to identify those patients with an increased risk of metabolic syndrome, intervene appropriately when needed. Further studies with prospective design and larger samples to determine the prevalence and correlates of metabolic syndrome in schizophrenic patients are needed to corroborate our findings, in order to provide patients with schizophrenia a higher standard of medical care.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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