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Psychiatry

PREVALENCE OF METABOLIC SYNDROME IN FIRST EPISODE DRUG NAÏVE SCHIZOPHRENIA PATIENTS

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ABSTRACT **BACKGROUND**: It is well established that schizophrenia is associated with higher morbidity and mortality due to the nature of illness itself and cardiovascular risk factors. Among cardiovascular risk factors metabolic syndrome has been discussed extensively in psychiatric literature. However most of the studies focused on the recent pharmacological interventions are possible etiological factors of metabolic syndrome. In our study we are trying to find out any association of metabolic syndrome with schizophrenia in drug naïve patients.

METHOD: Eighty consecutive drug naïve first episode patients with schizophrenia presenting at a tertiary care hospital in Western India were studied. They were assessed for prevalence of metabolic syndrome as per the criteria set by the NCEP (ATPIII) in Adults.

RESULT: A high prevalence of metabolic syndrome in drug naïve first episode patients with schizophrenia was found as compared to that in general population.

CONCLUSION: There should be mandatory screening for the possibility of hyperlipidemia, high glucose levels and metabolic syndrome in drug naïve first episode patients with schizophrenia before prescribing antipsychotic drugs.

KEYWORDS : Metabolic Syndrome, Schizophrenia, Drug Naïve, First episode psychosis

INTRODUCTION

It is well established that schizophrenia is associated with higher morbidity and mortality due to the nature of illness itself and cardiovascular risk factors. A systematic review and meta-analysis of 11 studies in all inhabited continents except South America, showed that, on average, people with schizophrenia die 14·5 years (95% CI 11·2–17·8) earlier than the general population. The number of years of potential life lost was greater for men than women (15·9 years, 95% CI 13·8–18·0 *vs* 13·6 years, 11·4–15·8). Most people in developed countries can expect to live into their late 70s or early 80s, but in the analysis people with schizophrenia died much earlier, with a mean age at death of 59·9 years (95% CI 55·5–64·3) for men and 67·6 years (63·1–72·1) for women. [1] [2] Coronary heart disease (CHD) and mental illness are among the leading causes of morbidity and mortality worldwide. Decades of research has revealed several, and sometimes surprising, links between CHD and mental illness, and has even suggested that both may actually cause one another. However, the precise nature of these links has not yet been clearly established. A large body of epidemiological prospective data has show that people with severe mental illness, including schizophrenia, bipolar disorder, and major depressive disorder, as a group, have an increased risk of developing CHD, compared with controls.[3]

Numerous studies from different countries and ethnic backgrounds have reported the prevalence of metabolic syndromes in patients with schizophrenia. A meta-analysis of several studies comprising over 25,000 patients with schizophrenia and related disorders showed an overall rate of metabolic syndrome at 32.5%[4]. Studies mentioning prevalence of metabolic syndrome in the drug naive schizophrenia patients has been very less specially in Indian population. A systematic review and meta-analysis of studies on Metabolic syndrome in antipsychotic-naïve patients with first-episode psychosis in 2021 showed an increased rates of Metabolic Syndrome in naïve first-episode psychosis patients, especially in those of non-Caucasian origin and that the altered metabolic parameters in FEPs are not exclusively due to antipsychotic treatments.[5].

A cross-sectional study in 2007 to determine whether there is an association between Type 2 diabetes mellitus and schizophrenia, independent of medication, oral glucose tolerance test on 38 non-obese white Caucasians who fulfilled the criteria for first-episode drug-naïve schizophrenia, 38 control subjects (matched for age, gender, smoking status, alcohol intake and ethnicity) and 44 first-degree relatives of the patients. The frequency of impaired glucose tolerance (IGT), defined by World Health Organization criteria, was 10.5% (n = 4) in patients with schizophrenia, 18.2% (n = 8) in unaffected relatives and 0.0% in healthy control subjects. The high point prevalence of IGT in never-treated patients and relatives supports either shared environmental or genetic predisposition to IGT[6].

In a study done in Japan in 2021, it was found that apart from these common risk factors and risk factors unique to schizophrenia, accumulating evidence suggests the existence of common susceptibility genes between schizophrenia and T2DM. Functional proteins translated from common genetic susceptibility genes are known to regulate neuronal development in the brain and insulin in the pancreas through several common cascades. Many genetic and epidemiological studies have reliably associated the comorbidity of schizophrenia and T2DM, and it is probably safe to think that common cascades and mechanisms suspected from common genes' functions are related to the onset of both schizophrenia and T2DM. On the other hand, even when genetic analyses are performed on a relatively large number of comorbid patients, the results are sometimes inconsistent, and susceptibility genes may carry only a low or moderate risk.[7].

MATERIALS AND METHOD

This was a cross sectional study which was carried out in department of the psychiatry in a tertiary care hospital in western India over a period of 03 months from July-Sep 2021. Eighty adult patients, who were diagnosed as a case of Schizophrenia as per ICD-10 criteria and who themselves/whose relatives provided written informed consent were included in the study. Cases who were having past/ family history of diabetes or cardiovascular disease, history of chronic medical illnesses, taking medications known to affect body glucose or lipids, pregnancy, history of concurrent substance use, excluded from the study. This study was approved by institutional ethical committee and no ethical issues and conflict of interest were found. The data collected was analysed using SPSS software. Chi-square test was applied to analyse the qualitative data. The two-tailed statistical significance level was set at $P \leq 0.05$.

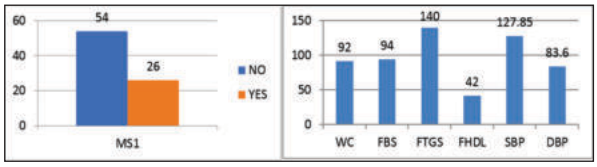
All the selected patients were then assessed for metabolic syndrome as per the criteria set by the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) and the subjects were considered to have metabolic syndrome if he/she fulfilled 03 or more of the following- 1. Waist Circumference > 102 cm in men and 88 cm in women, 2. Serum triglyceride level ≥ 150 mg/dL, 3. High density lipoprotein (HDL) < 40 mg/dL in men and < 50 mg/dL in women, 4. Blood pressure ≥ 130/85 mm Hg, 5. Fasting serum

Glucose level ≥ 110 mg/dL.

RESULTS

Of the 80 drug naïve patients recruited in this study, **26 (32.5%)** were found to fulfill the ATP-III criteria for metabolic syndrome. Their mean metabolic parameters were-

metabolic parameters	Mean	Std dev
WC	92	± 9.9
FBS	94	± 13
FTGS	140	± 52.4
FHDL	42	± 8.1
SBP	127.85	±15.676
DBP	83.60	±9.474



Age

The age of the study population ranged from 16yrs to 68yrs with mean age being 36yrs. The variation in distribution of cases of metabolic syndrome among different age groups at entry was found to be **not statistically significant**. (**P Value=0.106).** Thus we can assume that age of onset does not increase the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner.

AGE	NO	YES	Total	p Value	Significance
<=20	4(7.4)	0(0)	4(5)	0.106	Not Significant
21-30	15(27.8)	7(26.9)	22(27.5)		
31-40	14(25.9)	11(42.3)	25(31.2)		
41-50	16(29.6)	4(15.4)	20(25)		
51-60	5(9.3)	2(7.7)	7(8.8)		
>60	0(0)	2(7.7)	2(2.5)		
Total	54(100)	26(100)	80(100)		

Sex

Total number of female patients entering the study was 41 (51.2%) and that of male patients was 39 (48.8%). While 76.9% of the cases of metabolic syndrome at entry were females, only 23.1% of them were males. The variation in distribution of cases of metabolic syndrome among different sex groups at entry was found to be **statistically significant**. (**P Value=0.001**). Thus we can assume that female sex does increase the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner.

SEX	NO	YES	Total	p Value	Significance
Female	21(38.9)	20(76.9)	41(51.2)	0.001	Significant
Male	33(61.1)	6(23.1)	39(48.8)		
Total	54(100)	26(100)	80(100)		

Occupation

There were 38 (47.5%) housewives, 30 (37.5%) skilled/unskilled workers, 7 (8.8%) retired persons, and 5 (6.2%) students among the study population. While 76.9% of the cases of metabolic syndrome at entry were housewives, only 23.1% of them were from other occupational groups. The highest prevalence of metabolic syndrome was found among housewives, followed by skilled/unskilled workers, retired persons and least among students. The variation in distribution of cases of metabolic syndrome among different occupation groups at entry was found to be **statistically significant**. (**P Value=0.003**).

	Metabolic Syndrome			P Value	Significance
OCCUPATION	NO	YES	Total	0.003	Significant
Housewife	18(33.3)	20(76.9)	38(47.5)		
Retd	6(11.1)	1(3.8)	7(8.8)		
Service	25(46.3)	5(19.2)	30(37.5)		
Student	5(9.3)	0(0)	5(6.2)		
Total	54(100)	26(100)	80(100)		

35 (43.8%) of the patients entering the study had an active life style while 45 (56.2%) of them led more of a sedentary lifestyle. While 80.8% of the cases of metabolic syndrome at entry were leading more of a sedentary lifestyle, only 19.2% of them had an active life style. The variation in distribution of cases of metabolic syndrome among different lifestyle groups at entry was found to be **statistically significant**. (**P Value=0.002**, table-9). Thus we can say that the distribution of patients of the different lifestyle groups in our study, did impact the prevalence of metabolic syndrome at baseline, in a statistically significant manner and that sedentary lifestyle does increase the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner.

	Metabolic Syndrome				
LIFE STYLE	NO	YES	Total	p Value	Significance
Active	30(55.6)	5(19.2)	35(43.8)	0.002	Significant
Sedentary	24(44.4)	21(80.8)	45(56.2)		
Total	54(100)	26(100)	80(100)		

Symptom Scores

65 (81.2%) of the patients entering the study had PANSS scores in the positive range, while 15 (18.8%) of them had PANSS scores in the negative range. While 88.5% of the cases of metabolic syndrome at entry had PANSS scores in the positive range, only 11.5% of them had PANSS scores in the negative range. The variation in distribution of cases of metabolic syndrome among different symptom severity groups at entry was found to be **not statistically significant**. (**P Value=0.252**, table-10). Thus we can say that the distribution of patients of the negative and positive symptom groups in our study, did not impact the prevalence of metabolic syndrome at baseline, in a statistically significant manner and that negative or positive symptom scores do not impact the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner.

	Metabolic Syndrome				
PANSS	NO	YES	Total	p Value	Significance
POSITIVE	42(77.8)	23(88.5)	65(81.2)	0.252	Not Significant
NEGATIVE	12(22.2)	3(11.5)	15(18.8)		
Total	54(100)	26(100)	80(100)		

Duration of illness

43 (53.8%) of the patients had duration of illness of up to 03 months, 28 (35.0%) of them had duration of illness of 04 to 06 months, 8 (10.0%) of them had duration of illness of 07 to 09 months, while only 1 (1.2%) had duration of illness of 10 to 12 months. While 50% of the cases of metabolic syndrome at entry had duration of illness of up to 03 months, 42.3% of them had duration of illness of 04 to 06 months, and only 7.7% of them had illness of duration more than 6 months. The variation in distribution of cases of metabolic syndrome among different duration of illness groups at entry was found to be **not statistically significant**. (**P Value=0.711**, table-11). Thus we can say that the distribution of patients of the different duration of illness groups in our study, did not impact the prevalence of metabolic syndrome at baseline, in a statistically significant manner and that duration of illness does not impact the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner.

	Metabolic Syndrome				
Duration of illness	NO	YES	Total	P value	Significance
Up to 3 months	30(55.6)	13(50.0)	43(53.8)	0.711	Not Significant
4-6 months	17(31.5)	11(42.3)	28(35.0)		
7-9 months	6(11.1)	2(7.7)	8(10.0)		
10-12 months	1(1.9)	0(0.0)	1(1.2)		
TOTAL	54(100)	26(100)	80(100)		

DISCUSSION

As seen in table 2, out of the 80 drug naïve patients recruited in this study, **26 (32.5%)** were found to fulfill the ATP-III criteria for metabolic syndrome at the entry. In a large cross-sectional survey done in 2007, on urban Asian Indians, the Chennai Urban Rural Epidemiology Study, the prevalence of the metabolic syndrome was found to be 18% using the ATP III definition[8].

The causes of the metabolic syndrome are likely to reflect a mix of genetic and environmental factors and the interactions between these. General population studies confirm that genetic factors contribute to the concentration of the metabolic syndrome and its components within family groups. Unaffected first-degree relatives of people with schizophrenia have high rates of type 2 diabetes mellitus, pointing to a genetic association between these two disorders [6,7]. Many studies have reported this increased risk for diabetes in first-degree relatives of patients with schizophrenia [9,10,11]. The association HLA locus on chromosome 6 and susceptibility of first-degree relatives of schizophrenic patients to diabetes has already been reported in earlier studies [12]. Another possibility to consider is that people with schizophrenia on average have a lifestyle which increases their risk for

the development of Metabolic Syndrome: sedentary lifestyle, lack of regular physical activity, poor food intake, substance use and high rates of smoking [9,11]. Part of these lifestyle factors are influenced by aspects of the illness such as negative symptoms and vulnerability to stress. Other studies have showed an increased liability for people with schizophrenia to develop metabolic abnormalities even in the absence of antipsychotic medication, and also, some studies have showed increased visceral adiposity, elevated glycaemia and higher cortisol levels in first-episode patients before treatment [13,14].

Our study found that patient's age at onset does not impact the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner. This is a new finding in our study as many studies of similar kind and comparable study populations have reported significantly more number of older patients having metabolic syndrome as compared to younger ones [15]. We found that female sex does increase the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner. In comparison to prevalence study from CATIE baseline sample, we found almost similar prevalence in females while markedly lesser prevalence in males. Our study found that sedentary lifestyle does increase the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner and an active lifestyle is of a preventive value in development of metabolic syndrome in patients with schizophrenia as almost 80.8% of the cases of metabolic syndrome at entry were leading more of a sedentary lifestyle, while only 19.2% of them had an active life style. This finding was on expected lines as many other studies of similar design have come up with similar results [9 ,11]. Our study found that patient's occupation does impact the risk of development of metabolic syndrome in patients with schizophrenia in a statistically significant manner which is also in expected lines as many other studies of similar designs [9,11].

CONCLUSION

There is definitely a much higher prevalence of metabolic syndrome in drug naïve first episode patients with schizophrenia as compared to that in general population. Our study (table 2) shows prevalence of 32.5% of metabolic syndrome at baseline, as compared to that in general population studies). Active lifestyle and occupations involving regular exercises reduce the risk of metabolic syndrome in patients with schizophrenia, while a sedentary lifestyle and female sex increases the risk.

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