Research Article

Prevalence of metabolic syndrome in drug-naive patients with schizophrenia

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Abstract

Background: Asians are physiologically and genetically at a higher risk of metabolic syndrome. India is at the top with highest prevalence of metabolic syndrome. In recent times, it is established that antipsychotics, especially second generations, increases the risk of metabolic syndrome – which could be an already existing co-morbidity of schizophrenia in drug-naïve patients.

Objective: This was a hospital-based cross-sectional study with the aim to know the prevalence of metabolic syndrome in the antipsychotic naïve schizophrenia patients.

Material and Methods: Following pre-decided inclusion and exclusion criteria, 65 patients were selected and assessed using socio-demographic and clinical data sheet, physical examinations like blood pressure, waist circumferences, and biochemical with normal values prescribed by API.

Results: The prevalence of metabolic syndrome in patients with schizophrenia was 15.6% but major concern was the higher percentage of subsyndromal metabolic syndrome 1 and 2 (SMS1 and SMS2, 46.2% and 32.3%, respectively). Hypertension topped the list (65%) followed by low 'high-density lipoproteins' (HDL) (50%). Gender did not appear to be affecting the metabolic syndrome in schizophrenia but metabolic syndrome (MS) was commoner in those with age > 35 years while SMS was commoner in those with age < 35 years.

Conclusion: Even in drug-naïve schizophrenic, metabolic syndrome is more often full blown than none at all – sub-syndromal status is the commonest. Triacylglyceride (TAG) and fasting blood sugar (FBS) impairments are rare (< 5% occurrence) unless full blown MS. HDL anomaly is commoner in SMS1 while waist circumference (WC) and blood pressure (BP) anomaly is commoner in SMS2. Age appears to be the only independent factor in the prevalence (but not the duration of the disease). Diagnosis and awareness about these co-morbidities can help primary, secondary or tertiary prevention.

KEY WORDS: Schizophrenia, metabolic syndrome, subsyndromal, SMS1, SMS2

Introduction

Asian Indians are physiologically and genetically known to be at a higher risk of developing complications of metabolic syndrome even at lower levels. India is gradually leading into the top of list of countries with highest prevalence of metabolic syndrome[1].

In recent years, it has become apparent that antipsychotics, especially second generations, increases the risk of metabolic syndrome. Metabolic syndrome is a major co-morbidity in patients with schizophrenia, adding on to the burden of the disease[2–8].

Patients with schizophrenia may have impaired decision making capacity, are more likely to indulge in behavior like smoking, drug abuse, lack of physical exercise, and poor dietary habits which make them more vulnerable for many physical illnesses[3,9,10].

Schizophrenia, although, is a psychiatric disorder, have high physical co-morbidities with a mortality rate twice as high

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as in general population[11]. Unnatural causes like suicide and accident account for only a portion of increased mortality and more than 2/3rd of variance has been explained by natural causes including a variety of physical illness[12].

Patients with schizophrenia are reported to be more likely to die from cardiovascular illness than those in general population. They are at a greater risk for developing new age pandemics of chronic non infectious diseases including obesity, diabetes mellitus-type 2, hypertension, and dyslipidemia[13].

Metabolic syndrome is a complex of such disorders characterized by central obesity, dyslipidemia, abnormal glucose tolerance, and hypertension[14]. Individuals with metabolic syndrome have higher rates of coronary artery diseases, myocardial infarction, and cerebrovascular accident than individual with any one component of hypertension, diabetes mellitus, dyslipidemia, or obesity[15,16]. Nevertheless, disturbance in one component heralds the onset of other components over a period of time.

At present, metabolic syndrome is believed to be precipitated by multiple underlying factors. Metabolic syndrome can be attributed to the sedentary lifestyle, lack of physical exercise, chronic stress, smoking, alcohol, substance abuse as well as abnormal hypothalmic–pituitary–adrenal axis[2,13,17–19].

In recent times, it is established that antipsychotics, especially second generations, increases the risk of metabolic syndrome – which could be an already existing co-morbidity of schizophrenia in drug-naïve patients, especially in more vulnerable population of Asia (and more so in India).

Here it is noteworthy that Asians are physiologically and genetically known to be at a higher risk of developing complications of metabolic syndrome even at lower levels. Herein, India has highest prevalence of metabolic syndrome. In recent years, it has become apparent that antipsychotics especially second generations, increases the risk of metabolic syndrome[2–8].

Despite the added risk, many patients with schizophrenia have limited access to general healthcare with less opportunity for cardiovascular risk screening and prevention than would be expected in a non-psychiatric population[8,20–22]. Diagnosis and awareness about these co-morbidities can help primary (prophylactic), secondary (ameliorative), or tertiary (mitigating) prevention.

India arising as diabetes capital of the world, metabolic syndrome had been redefined with new criteria for Indian population by the Association of Physicians of India. This would be the first study in drug-naïve patients with schizophrenia using the newly approved consensus statement for diagnosing metabolic syndrome for Indian population.

Material and Methods

Defining Schizophrenia

International Classification of Diseases (ed. 10)-Diagnostic Criteria for Research [ICD-10 DCR, version 16][23] relies on Schniderian symptoms in diagnosing schizophrenia. One month duration of persistence of listed symptoms is required. Symptoms are classified into 9 different groups.

The first four involves first rank symptoms, viz., disordered thought possession, made phenomenon, certain specific hallucinations and specific delusions. The next four are the second rank symptoms namely, other hallucinations and delusions, formal thought disorder, catatonic symptoms, and negative symptoms. Last group are the symptoms specific for simple schizophrenia, which has to persist for duration of one year to make the diagnosis of schizophrenia.

Defining Metabolic Syndrome

Metabolic syndrome is a complex disorder characterized by central obesity, dyslipidemia, abnormal glucose tolerance, and hypertension[16]. Three out of five factors have to be abnormal for diagnosis of the metabolic syndrome as per Table 1.

The Present Study

The study was conducted at the Institute of Mental Health and Hospital, Agra. It is a tertiary referral center and a post-graduate teaching hospital. The study was cross-sectional and hospital based, in which, subjects were included using the purposive sampling method. In total, 65 patients were taken up from December 2012 to January 2014. All patients were diagnosed as a case of schizophrenia as per the criteria laid by ICD-10, DCR.

Inclusion criteria:

1. Patient with schizophrenia diagnosed according to ICD-10 (DCR).
2. Patient age between 20 and 50 years of either sex.
3. Patient giving written and informed consent/consent obtained from guardian.
4. Patient who are anti-psychotic drug naïve.

Table 1: Association of Physicians of India (API) criterion for metabolic syndrome.[24]

Factors	Defining level
1. Abdominal obesity, given as Waist circumference	
Men	>90cm
Women	>80cm
2. Triglyceride	>150mg/dl
3. HDL Cholesterol	
Men	<40mg/dl
Women	<50mg/dl
4. Blood pressure	
Systolic	>130 mm Hg
Diastolic	>85 mm Hg
5. Fasting glucose	>100 mg/dl

Exclusion criteria:

1. Patients younger than 20 years/older than 50 years.
2. Patients/guardians not giving informed consent.
3. Patients suffering from any other psychiatric or neurological co-morbidity.
4. Patients who have received anti-psychotic treatment in past.
5. Patients with substance dependence syndrome, except tobacco and caffeine.

Socio-demographic profile of all patients were taken in a semi-structured study profile containing name, age, sex, education, socio-economic status, and marital status. Clinical data sheet includes information like duration of illness, past history, detailed treatment history, substance intake, family history of medical illness, etc. Patients were assessed on the following parameters:

1. Blood pressure
2. Waist circumference
3. Fasting blood sugar
4. Fasting triglyceride
5. Fasting high density lipoproteins (HDL)

For measuring the blood pressure, standard protocol was followed[25]. Waist circumference was measured just above ileac crest, at the end of normal expiration, in the fasting state, with the subject standing erect and looking straight forward with feet shoulder width apart and arm crossed over the chest in a relaxed manner and observer taking a position to the right side of patient's body on one knee, by using a non-stretchable flexible tape with a spring loaded mechanism to standardize tape tension during measurement[26].

The patients were told to fast at least for 8–12 h before serum investigations. Triglyceride, high-density lipoprotein, and blood sugar were measured, with subjects in fasting state (8–12 h), in routine biochemistry laboratory at the Institute of Mental Health and Hospital, Agra by using autoanalyzer. Value of result was assessed on basis of API consensus guidelines for diagnosing metabolic syndrome[24].

The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for windows, version 16.0) and Microsoft Excel. Descriptive statistics were used to define the sample characteristics.

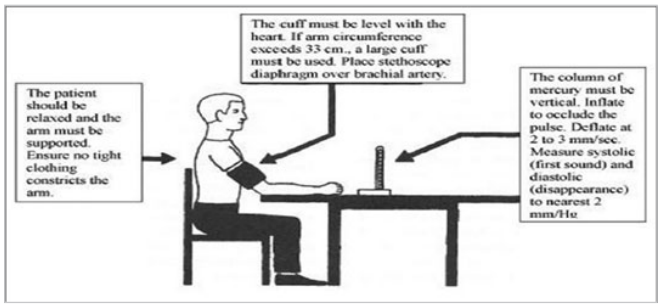

Figure 1: Measuring blood pressure.

Chi-square was used to explore the associations between sample characteristics and different levels of metabolic syndrome. Analysis of Variance (ANOVA) was used to compare the sample characteristics of clinical variables. One-way ANOVA was done with post hoc analysis using either Bonferroni test or Games–Howell test depending on homogeneity of variance of the subjects.

The comparison of clinical and metabolic parameters across the median age of 35 years was done by using Student's *t*-test. Pearson's correlation was performed to find any relation between age, gender, and age of onset with the metabolic syndrome and its components.

Results

Table 2 shows the prevalence of metabolic syndrome in patients with schizophrenia. A total of 10 subjects among 65 patients with schizophrenia had metabolic syndrome, crossing the cut-off in at least three of five criteria. Among the rest, 30 patients had met one (Sub-syndromal Metabolic Syndrome 1; SMS1) and 21 had crossed two (Sub-syndromal Metabolic Syndrome 2; SMS2) out of five parameters. Only 4 had all the criteria of metabolic syndrome within normal limits.

Tables 3–6 describe the frequency of derangement in different parameters of metabolic syndrome in patients with schizophrenia, those with SMS1 and SMS2 and metabolic syndrome (MS).

Tables 7a and b describe the socio-demographic profile of the sample population and compares them across the subjects with different levels of MS. On comparison, only age was found to be significantly different across different levels of metabolic syndrome by chi square test ($\chi^2 = 9.458$, $p = 0.025$). Fischer's exact test was used to assess the significance as expected cell count was less than 5 in three of the cells.

Table 8 compares the clinical variables across different subgroups of patients. On one-way ANOVA age of onset was found to be significantly different ($f = 2.885$ and $p = 0.043$) among the groups. Duration of illness was found to be similar across the groups with a mean duration of 2.95 years.

On post-hoc Bonferroni analysis, patients with metabolic syndrome (mean = 35.45 standard deviation = 9.45) had significantly different age of onset in comparison to those meeting only one of the criteria of metabolic syndrome (SMS1) (mean = 26.98 years and standard deviation = 8.37).

Tables 9a and b show comparison of means of the parameters defining metabolic syndrome across different groups of patients. One-way ANOVA was done with post-hoc analysis using either Bonferroni test or Games–Howell test depending on homogeneity of variance of the subjects. The comparison of clinical and metabolic parameters across the median age of 35 years using Student's *t*-test is shown in Tables 10a and b. A bimodal age of onset could be seen. Diastolic blood pressure (DBP) is found to be significantly higher in males in comparison to females.

Table 2: Frequency chart of patients fulfilling criteria of metabolic syndrome.

	Criteria Fulfilled	Frequency	Percent
No Metabolic Syndrome (No MS)	0	4	6.2
Sub-Syndromal Metabolic Syndrome 1 (SMS1)	1	30	46.2
Sub-Syndromal Metabolic Syndrome 2 (SMS2)	2	21	32.3
Metabolic Syndrome (MS)	≥3	10	15.4
Total		65	100.0

Table 3: Frequency of patients with schizophrenia across cut-off values of parameters of metabolic syndrome.

N = 65	TAG	FBS	IIDL	WC	BP	SBP	DBP
Normal	62 (95%)	62 (95%)	30(46.2%)	44 (67.7%)	25 (38.5%)	28 (43%)	36 (55.3%)
Abnormal	3 (5%)	3 (5%)	35 (53.8%)	21 (32.3%)	40 (61.5%)	37 (57%)	29 (44.7%)

Table 4: Frequency of patients with schizophrenia with SMS1 across cut-off values of parameters of metabolic syndrome.

N = 30	TAG	FBS	IIDL	WC	BP	SBP	DBP
Normal	29 (96.7%)	30 (100%)	13 (43.3%)	29 (96.7%)	19 (63.3%)	20 (66.7%)	26 (86.7%)
Abnormal	1 (3.3%)	0(0)	17 (56.7%)	1 (3.3%)	11 (36.7%)	10 (33.3%)	4 (13.3%)

Table 5: Frequency of patients with schizophrenia with SMS2 across cut-off values of parameters of metabolic syndrome.

N = 21	TAG	FBS	IIDL	WC	BP	SBP	DBP
Normal	21 (100%)	20 (95.2%)	11 (52.4%)	9 (42.9%)	2 (9.5%)	4 (19%)	5 (23.8%)
Abnormal	0 (0)	1 (4.8%)	10 (47.6%)	12 (57.1%)	19 (90.5%)	17 (81%)	16 (76.2%)

Table 6: Frequency of patients with schizophrenia with (MS) across cut-off values of parameters of metabolic syndrome.

N = 10	TAG	FBS	IIDL	WC	BP	SBP	DBP
Normal	8 (80%)	8 (80%)	2 (20%)	2 (20%)	0 (0)	0 (0)	1 (10%)
Abnormal	2 (20%)	2 (20%)	8 (80%)	8 (80%)	10 (100%)	10 (100%)	9 (90%)

Table 7a: Socio-demographic profile of patients with schizophrenia with different levels of metabolic syndrome (a. Expected cell count less than 5, Fischer's exact test was used.)

		Total	NO-MS	SMS1	SMS2	MS	χ^2	P
Gender	Male	46	3 (6.5%)	20 (43.5%)	18 (39.1%)	5 (10.9%)	4.7	0.18
	Female	19	1 (5.3%)	10 (52.6%)	3 (15.8%)	5 (26.3%)		
Age	Above 35 years	24	1 (4.2%)	9 (37.5%)	6 (25%)	8 (33.3%)	9.46	0.03
	Below 35 years	41	3 (9.7%)	21 (51.2%)	15 (36.6%)	2 (4.8%)		

Table 7b: Socio-demographic profile of patients with schizophrenia with different levels of metabolic syndrome (a. Expected cell count less than 5, Fischer's exact test was used.)

Marital Status	Married	42	2 (4.8%)	18 (42.9%)	12 (28.6%)	10 (23.8%)	6.64	0.48
	Single	23	2 (8.7%)	12 (52.2%)	9 (39.1%)	0		
Religion	Hindu	60	4 (6.7%)	28 (46.7%)	18 (30%)	10 (16.7%)	2.5	0.68
	Others	5	0	2 (40%)	3 (60%)	0		
Occupation	Agriculture	29	1 (3.4%)	12 (41.4%)	12 (41.4%)	4 (13.8%)	7.87	0.47
	White Collar Job	8	1 (12.5%)	4 (50%)	2 (25%)	1 (12.5%)		
	Housewife	16	1 (6.2%)	7 (43.8%)	3 (18.8%)	5 (31.2%)		
	Unemployed	12	1 (8.3%)	7 (58.3%)	4 (33.3%)	0		
Socio-Economic Status	Low	55	3 (5.5%)	26 (47.3%)	18 (32.7%)	8 (14.5%)	0.56	0.77
	Middle	10	1 (10%)	4 (40%)	3 (30%)	2 (20%)		
Habitat	Rural	61	4 (6.6%)	27 (4.2%)	21 (34.4%)	9 (14.8%)	2.66	0.51
	Urban	4	0	3 (75%)	0	1 (25%)		

Table 8: Clinical profile of patients with schizophrenia with different levels of metabolic syndrome (post-hoc Bonferroni).

	Total	NO MS	SMS1	SMS2	MS	f (df = 3,61)	P	Post-hoc
Age of Onset (Years)	28.55 ± 8.53	26.25 ± 11.30	26.98 ± 8.37	27.93 ± 6.57	35.45 ± 9.45	2.89	0.04	MS>SMS 1
Duration of Illness (Years)	2.95 ± 2.70	3.00 ± 0.82	2.70 ± 2.05	2.49 ± 1.95	4.65 ± 5.08	1.67	0.19	

Table 9a: Comparison of parameters of metabolic syndrome in patients with different levels of metabolic syndrome.

	NO MS	SMS1	SMS2	MS	Total	f (clf = 3,61)	P	Post hoc Bonfcrroni/ Games-Howell
SBP	1 17.5 ± 6	120.3 ± 13	134.4 ± 10.3	137.8 ± 4.37	127.4 ± 13.31	11.13	0.00	MS. SMS2>SMS 1. NO MS
DBF	77.5 ± 5	79.2 ± 9.1	92.7 ± 9.3	94.8 ± 5	85.9 ± 1 1	15.56	0.00	MS.SMS2>SMS 1. NO MS

Table 9b: Comparison of parameters of metabolic syndrome in patients with different levels of metabolic syndrome.

HDL	47.50 ± 6.25	42.53 ± 4.71	42.33 ± 5.14	42.1 ± 5.7	42.7 ± 5.1	1.27	0.29	
TAG	86.00 ± 17.8	93.33 ± 23.6	97.62 ± 14.7	122.6 ±46.1 7	98.8 ± 27.3	3.63	0.02	MS>SMS 1
FBS	79.5 ± 5.97	80 ± 8.2	82.6 ± 10.5	102.6 ± 62.41	84.3 ± 26	2.1	0.1 1	
WC	72.5 ± 6.1	76.3 ± 8.4	87.7 ± 9.3	87.8 ± 12.	81.5 ± 10.9	9.17	0.0	MS,SMS2>SMS1, NO MS

Table 10a: Comparison of clinical profile and parameters of metabolic syndrome in patients with schizophrenia aged above and below median.

	ABOVE 35 YEARS	BELOW 35 YEARS	t (df = 63,l)	P
Age Of Onset	37.85 ± 6.19	23.10 ± 3.47	12.345	0.000
Duration Of Illness	3.77± 3.69	2.47 ± 1.80	1.912	0.060
Systolic BP	130.79 ± 12.00	125.37 ± 13.76	1.606	0.113
Diastolic BP	83.33 ± 11.38	80.46 ± 10.53	1.029	0.307

Table 10b: Comparison of clinical profile and parameters of metabolic syndrome in patients with schizophrenia aged above and below median.

	Above 35 years	Below 35 years	*t* (df = 63,1)	*p*
High density lipoprotein	89.25 ± 11.75	83.85 ± 10.23	1.942	0.057
Triacylglycerides	42.79 ± 4.87	42.66 ± 5.34	0.100	0.921
Fasting blood sugar	105.83 ± 33.70	94.63 ± 22.23	1.614	0.111
Waist circumference	89.83 ± 40.80	81.05 ± 9.91	1.320	0.191

As per Table 11a and b, on comparing the clinical and metabolic factors across gender, diastolic BP is found to be significantly higher in males (85.37 mm of Hg) in comparison to females (72.21 mm of Hg). Rest all is comparable.

In Tables 12a and b, Pearson's correlation was done to find any relation between age, gender and age of onset with the metabolic syndrome and its components. Age of onset is found to be significantly correlating ($r = 0.913$, $p = 0.001$) with age of the patient. Systolic BP, diastolic BP, and waist circumference correlated highly among themselves and with level of metabolic syndrome. Metabolic syndrome highly correlated with all of its parameters except for HDL.

Discussion

It had been established unambiguously that schizophrenia has a widely common co-morbidity of metabolic syndrome[27]. Studies indicate that the cardiovascular risk factors associated with metabolic syndrome and cardiovascular diseases in schizophrenia are to a certain extent genetically determined[27].

At the same time, most of the antipsychotics, the drugs used in treatment of schizophrenia, are notoriously known to negatively affect different parameters of metabolic syndrome. In recent years, it has become apparent that antipsychotics especially second generations, increases the risk of metabolic syndrome[5,7,8,20–22,28].

Despite the risk, many patients with schizophrenia have limited access to general health care with less opportunity for cardiovascular risk screening and prevention than would be expected in a non-psychiatric population[28–31].

It would thus be extremely difficult to determine the extent to which the metabolic syndrome is attributable purely on the disorder; without any effect of antipsychotics in patients with schizophrenia on treatment. The study was thus formulated to assess the prevalence of metabolic syndrome in patients with schizophrenia.

The effect on metabolic profile can persist for a longer time and antipsychotics can be a precipitant for pre existing vulnerability. A study on unmedicated or antipsychotic naive patients would provide a clear picture of the association between schizophrenia and metabolic syndrome.

In a North Indian study by Grover and colleagues prevalence of metabolic syndrome was seen in 46 drug-naïve patients suffering from schizophrenia[32].

Other studies have assessed metabolic syndrome in first episode psychosis (including psychotic disorders other than schizophrenia), thus able to take more than 100 patients, like nearly 145 patients with first episode psychosis in a study by Perez-Iglesias and colleagues[33].

The sample size of 65 was taken. Considering the prevalence of metabolic syndrome nearing 10% even in the general population and much higher in the patients with schizophrenia as reported in earlier studies, it was expected to encounter patients with at least sub-syndromal metabolic syndrome if not in with syndromal level.

Although a higher sample would yield a better estimate, because of practical difficulties in getting drug-naïve patients with schizophrenia, this time-limited study was hoped to be an addition in the scientific literature on two of the major prevailing global problems.

The overall prevalence of MS even in adolescents was 4.2%, in a north Indian study among school going adolescents[34]. Hence, considering maximum yield for metabolic syndrome to be higher with advancing age, the age group of the sample was espoused to 20–50 years.

To maintain the homogeneity of the sample, those who are having comorbidities like major physical illnesses, psychiatric disorders, any regular medicine use or primary drug abuse were excluded from the study. Standard procedures and tools were used for measurement of waist circumference, blood pressure, blood sugar, and lipid profile.

A total of 65 antipsychotic drug-naive patients with schizophrenia were evaluated. Among them 46 were males and 19 females. This gender imbalance could be attributed to lower help seeking towards psychiatric care in females of Indian population and is proportional to the outpatient attendance of all patients in our hospital.

As only drug-naive were evaluated maximum (41) of the subjects were below the median age of 35 years, owing to the early onset of schizophrenia. Briefly, 42 of them were married and staying with their spouses and 60 of them following Hindu religion.

A significant proportion of patients were unemployed or home makers. Nearly half were agrarians and only one eight were in a business and white colored jobs. 90% were from rural area and 80% were from lower socio-economic background.

From the study the prevalence of metabolic syndrome in patients with schizophrenia is 15.4%.But among the rest, 46.2% had deranged parameter in one of the components

Table 11a: Comparison of clinical profile and parameters of metabolic syndrome in patients with schizophrenia across gender

	Above 35 years	Below 35 years	*t* (df = 63,1)	*p*
Age of onset	28.13±8.14	29.55±9.57	0.608	0.545
Duration of illness	2.61±2.01	3.78±3.85	1.609	0.113
Systolic BP	129.22±12.53	122.89±14.40	1.771	0.081
Diastolic BP	85.37±9.36	72.21±8.39	5.306	0.000

Table 11b: Comparison of clinical profile and parameters of metabolic syndrome in patients with schizophrenia across gender.

High Density Lipoprotein	86.87 ± 10.33	83.37 ± 12.54	1.166	0.248
Triacylglycerides	42.22 ± 4.88	43.89 ± 5.67	1.203	0.234
Fasting Blood Sugar	96.48 ± 21.77	104.32 ± 37.74	1.053	0.297
Waist Circumfcrence	85.74 ± 30.59	80.79 ± 7.28	0.694	0.490

Table 12a: Correlation of socio-demographic and clinical profile of patients with parameters of metabolic syndrome.

	Gender	Age of Onset	WC	SBP	DBP	HDL	TAG	FBS	MS
Age	.159	.913**	.069	.292*	.333**	.098	.308*	.138	.361**
Gender	1	.076	-.56**	-.218	-.145	.150	.131	-.09	.049
Age Of Onset	.076	1	.082	.283*	.286*	.032	.302*	.146	.297*

Table 12b: Correlation of socio-demographic and clinical profile of patients with parameters of metabolic syndrome.

WC	-0.556**	.082	1	.373**	.355**	-.09	.077	.123	.507**
SBP	-.218	.283	.373**	1	.746	.210	.296	.138	.560
DBP	-.145	.286*	.355**	.746**	1	.135	.306*	.069	.607**
HDL	.150	.032	-.090	.210	.135	1	.035	-.04	-.144
TAG	.131	.302*	.077	.296	.306	.035	1	-.05	.347**
FBS	-.087	.146	.123	.138	.069	-.04	-.051	1	.254*
Metabolic Syndrome	.049	.297*	.507**	.56**	.607**	-.14	.347**	.25*	1

and 32.3% in two of the components. Grover et al has called those crossing the limits in less than 3 of the components as having subsyndromal metabolic syndrome.

Trying to analyze the risk in different levels, subsyndromal metabolic syndrome1 (SMS1) is used here for those having abnormal levels in any one of the parameters and subsyndromal metabolic syndrome2 (SMS2) for those with abnormality in two of the five parameters.

Those without derangement in any of the parameters are called no metabolic syndrome (NOMS). Thus the prevalence of SMS2 is 32.3%, SMS1 is 46.2% and NOMS is only 6.2% in antipsychotic naive patients with schizophrenia.

Prevalence of the metabolic syndrome in general population as defined by National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) 5 and other criteria ranges from about 11 to 41 per cent in different regions of India[35–38].

No geographically similar study could be traced which found the prevalence using the new consensus statement. Two studies which were otherwise closer to the present study venue were the Haryana study, showing prevalence of 9.2% and in Wardha, in rural central India, 5.2 % in general population[39,40].

These show the prevalence of metabolic syndrome in patients with schizophrenia to be slightly higher or comparable to that of the local general population. A review of 12 studies of past 10 years on unmedicated and first episode psychosis patients had a mean prevalence of 10.2% among 893 patients. Indian studies too varied greatly from 3.2% to 18.2%[41].

The present study also has a comparable prevalence to those prevalence rates. Comparative studies with general population too were inconclusive regarding significant difference in the rates in schizophrenia. A recent review of three Indian studies revealed Twenty six patients (19%) meeting consensus criteria[42].

The important finding in the current study is very high percentage of patients at risk for metabolic syndrome. Prevalence of SMS2 being 32.3% and SMS1 being 46.2%, are at risk to cross the threshold for metabolic syndrome with time and/or additional risks like antipsychotic drugs or adverse life style.

Grover et al had 14 (30.43%) patients with SMS2 and 19 (41.3%) with SMS1 of total 46 drug-naïve patients. Of the 19 patients who fulfilled one criterion for MS, 18 had an abnormality other than increase in waist circumference.

The review of three Indian drug-naïve studies had 56 patients (40.9%) fulfilling one criterion and 32 patients (23.3%) fulfilling two criteria of MS out of five criteria[42].

The prevalence of SMS1 and SMS2 in general population is unclear. Nevertheless the statistical methods from which the guidelines have been evolved suggest them not to be more than 5–7%. The predictability and risk of SMS1 and SMS2 for future metabolic syndrome and its complications are also under studied.

A precipitating event like an antipsychotic exposure would lead onto a devastating course. This could also explain the cardiovascular and cerebrovascular events along with other physical problems noted to be exceedingly comorbid with schizophrenia[43].

Among the different parameters, Hypertension tops the list with 65% of drug-naive patients almost equally affecting both systolic and diastolic blood pressure. Blood pressure is higher in all the patients with schizophrenia having metabolic syndrome, suggesting it to be a key ingredient (Tables 3–5).

Whereas hypertension rates increases with number of associated derangements in other parameters, low HDL is found to be equally commonplace in almost all the subgroups – nearing 50%.

Thus low HDL possibly is the primary or the initial factor to be affected in metabolic syndrome particularly in schizophrenia. Next common factor affected is high waist circumference. Obesity marked by waist circumference is found chiefly in those with full syndromal metabolic syndrome. Thus obesity would predict full blown metabolic syndrome much specifically.

Though Insulin resistance and lipid metabolism are hypothesized to be the primary problems, raised fasting blood sugar (FBS) and triacylglycerides (TAG) were the least to be prevalent. This could be due to their appearance in later course of the illness. This could also bepointing towards presence of two different clusters of metabolic syndrome.

Blood sugar was correlating with only the presence or the absence of metabolic syndrome and HDL once again found independent of other variables. Hence it could be hypothesized that derangements of factors of metabolic syndrome in schizophrenia presents with low HDL, gradually developing hypertension followed by obesity, then diabetes and hypertriglyceridemia.

Though this linear path may not be substantiated, but needs to be evaluated in future prospective studies. From the current study gender does not appear to be affecting the metabolic syndrome in schizophrenia.

While most of the studies have shown gender differences with higher rates in female, here comparable proportions of males and females are found in all the four groups across the spectrum of metabolic syndrome. Few studies have been similar to current scenario[44–51].

On correlation analysis males were having higher waist circumference but no difference in obesity rates across gender. This justifies the gender difference in defining metabolic syndrome, taking into account the physical structural difference across gender without "pathologizing" the phenomenon.

As higher proportion (33.3%) of those above the median age of 35 years are suffering from metabolic syndrome in comparison to only 4.8% of those below 35 years (Table 6). This influence of age is similar to many earlier findings[50–54].

Thus as the age appears to be a major independent risk factor for metabolic syndrome in schizophrenia, age and other external factors might be confounding the results and needs to be considered before drawing a final conclusion.

Such difference could not be noted when compared across the median age group with each parameter, assessed quantitatively (Table 9). Also SMS1 and SMS2 are in comparable proportions across age (Table 6).

These signify the persistence of risk for metabolic syndrome in patients of schizophrenia despite age; thereby appearing that schizophrenia and age have a cumulative effect on risk enhancement.

Apart from age no other socio-demographic factors were found to be differentiating the groups (Table 9). Marital status, employment status, habitat, religion, or socio-economic factors does not seem to affect the metabolic syndrome.

Again impact by some external factor especially specific factors of life style, and limited representation of higher class, middle to higher income groups in a white collar job and people following other than Hindu religion in the study sample will necessitate future studies before generalizing.

Clinically age of onset was significantly higher in those patients with metabolic syndrome. So the age of onset would just be a function of age on metabolic syndrome rather than having an independent risk.

Similar correlations profile of age of onset and age of patients corroborates this assertion. Two studies failed to see any association between chronicity of illness and prevalence of metabolic syndrome[55,56].

But previously a study has predicted higher rates of metabolic syndrome by duration of illness[57]. The findings of this study could be attributed more to the cumulative doses of antipsychotic than any effect of illness per se.

Some of the extrinsic factors like antipsychotics have been ruled out by the nature of the sampling (only drug-naive patients). So the higher prevalence of metabolic syndrome seems to be due to intrinsic factors.

Most authors emphasized the importance of extrinsic factors (antipsychotic medication, increased calorie intake, sedentary lifestyle) in its development; however the concept of intrinsic factors being implicated (genetic links between schizophrenia and diabetes) is also supported[27].

Leucht et al[58,59], in their impressive work reviewed 52 original articles, the majority of which describe individual features of metabolic syndrome in patients with schizophrenia since 1919, the pre-neuroleptic era.

Thus psychiatrists need to be aware of metabolic side effects of antipsychotic medications and to include them in risk/benefit assessment when choosing a specific antipsychotic[60].

The cornerstone of early detection and effective management of metabolic syndrome in patients with schizophrenia is comprehensive monitoring, and a variety of guidelines provide structured schedules for this.

Despite the introduction of guidelines for metabolic screening in schizophrenia, metabolic monitoring in routine clinical practice is still low. In their impressive meta-analysis of 48 studies, Mitchell and colleagues reviewed changes in monitoring screening of patients receiving antipsychotics before and after the implementation of relevant guidelines[61].

They concluded that although guidelines can increase monitoring, most patients still do not receive adequate testing. Similar results come from another group of researchers who found that glucose and lipid screening is underutilized in patients starting on second generation antipsychotics (SGAs) [62], and the introduction of the American Diabetes Association's Consensus Statement on antipsychotic drugs and diabetes was not associated with an increase in screening rates[63].

Conclusion

In the present study, the prevalence of metabolic syndrome in patients with schizophrenia was 15.4%. But the majority of patients who did not fulfill the complete criteria have one or two deranged parameter of components of metabolic syndrome – 46.2% has 1 deranged parameter and 32.3% had 2 parameters (SMS1 and 2; i.e., sub-metabolic syndrome 1 and 2, respectively).

Thus the important finding in the current study is very high percentage of patients at risk for metabolic syndrome as these people are at risk to cross the threshold for metabolic syndrome with time and/or additional risks like antipsychotic drugs or adverse life style. A bimodal age of onset could be seen. Diastolic blood pressure (DBP) is found to be significantly higher in males in comparison to females.

Among various parameters hypertension top the list (65%) followed by low HDL (approximately 50%). Gender does not appear to be affecting the metabolic syndrome in schizophrenia but age appears to be a major independent risk factor for metabolic syndrome. In recent years, it has become apparent that antipsychotics especially second generations, increases the risk of metabolic syndrome.

Despite the risk, many patients with schizophrenia have limited access to general health care with less opportunity for cardiovascular risk screening and prevention than would be expected in a non-psychiatric population. So psychiatrists need to be aware of metabolic side effects of antipsychotic medications and to include them in risk/benefit assessment when choosing a specific antipsychotic. Thus management and minimization of metabolic risk factors are pertinent when providing optimal care to patients with schizophrenia.

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