Original Article

Metabolic Syndrome in Drug-naïve Patients with Depressive Disorders

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ABSTRACT

Background: The prevalence of metabolic syndrome (MS) is found to be higher in patients with depression than in the general population. As there is lack of data from India, this study aimed to assess the prevalence of MS in patients with depression who had never been treated with antidepressants for their depressive disorder and compare the same with a matched group of healthy controls. **Materials and Methods:** Forty-three drug-naïve patients with depressive disorders and 43 age- and gender-matched healthy controls were assessed for the prevalence of MS as per the consensus definition. **Results:** The prevalence of MS in patients with depression was 37.2% and was significantly higher than that seen in the healthy controls (16.3%). Increased waist circumference was the most common abnormality in both the study groups. Compared to healthy controls, a significantly higher proportion of patients with depression had abnormal waist circumference, systolic blood pressure, or high blood pressure. Besides 16 patients with depressive disorders having MS, another 53.5% of patients fulfilled one or two criteria of MS. None of the sociodemographic variables was associated with development of MS in patients with depression. **Conclusions:** Slightly more than one-third of depressed patients who are drug-naïve have MS and this prevalence rate is significantly higher than in healthy controls.

Key words: *Cardiovascular mortality, depression, metabolic syndrome*

INTRODUCTION

Metabolic Syndrome (MS) is a cluster of abnormalities that predispose a person to develop type 2 diabetes mellitus and cardiovascular disease.[1,2] People with MS are twice as likely to die from, and three times as likely to develop myocardial infarction (MI) or stroke compared to people without MS.[3]

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Most of the studies which have evaluated the prevalence of MS in patients of depression have emerged from the West. Studies which have studied the relationship of MS with depression can be broadly be understood as: studies which have evaluated the prevalence of MS in depressed patients and as studies which have evaluated the prevalence of MS in patients attending general hospitals or the community-based population. In the latter studies, depression has been studied as a covariate which can predict the development of MS. Studies which have evaluated the prevalence of MS in depressed patients, of sample size varying between 60 and 230, have reported that prevalence rates vary from 25 to 41%.[4-6] In contrast, the studies which have evaluated the prevalence of MS and depression (as a disorder or as subsyndromal depression) in patients attending general hospitals or the community-based

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population have evaluated 215 to 6,189 subjects and have reported a prevalence rate of MS between 11.7 and 57%.[7-25] These studies suggest that the presence of depression increases the risk of development of MS by twofold.[7,20]

However, there is lack of data from eastern countries like India. One study from our center evaluated the prevalence of MS in patients with depression (first episode or recurrent depressive disorder according to the International Statistical Classification of Diseases, Tenth Revision (ICD-10)) and reported the prevalence rate of MS to be 44% according to the modified National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP) III criteria. However, this study included patients with depression who were on treatment.[26] Another study evaluated the level of serum cholesterol in patients with depression and reported a significant elevation of serum total cholesterol in depressed patients compared with normal controls and the significance of these findings persisted even after controlling for various confounders.[27] In the same study, the authors reported that patients with severe depression had a higher body mass index (BMI).[27] Occasional studies have also evaluated the prevalence of depressive disorders in patients of hypertension[28] and diabetes mellitus.[29]

Some of the antidepressants are known to cause weight gain[30-32] or weight loss[33,34] and also influence metabolic parameters.[35] Hence, to have a better understanding of the prevalence of MS, it is important to evaluate the patients who are relatively free from medications. In this background, the present study aimed at assessing the prevalence of MS in patients with depression who had never been treated with antidepressants for their depressive disorder and compare the same with a matched group of healthy controls.

MATERIALS AND METHODS

The study was approved by the Ethics Review Committee of the institute in which the study was carried out. All patients were recruited after obtaining informed consent. The study was carried out at the outpatient unit of a multispecialty tertiary care hospital in North India from August to December, 2010.

The study included two groups of subjects. The study group comprised patients diagnosed to have depressive disorders (first-episode depression, recurrent depressive disorder, and dysthymia) as per ICD-10.[36] The second group included a cohort of healthy controls, who were matched to the disease group for the sociodemographic variables of age, gender, education, and neighborhood.

Both the groups were recruited by purposive sampling. The inclusion criteria for the patients with depression were age more than 18 years, drug-naive (never received any psychotropic agent continuously for more than two weeks and not so in the last three months, ascertained by information obtained from patients and the caregiver and, wherever available, review of treatment records), and free from any psychiatric comorbidity or physical comorbidity (other than hypertension and diabetes mellitus) which can influence the metabolic profile. The healthy control group was recruited from the healthy relatives of the patients attending the psychiatry services or staff members.

Anthropometric and metabolic assessments

Physical evaluation included measurement of body weight in kilogram (Kg), height in centimeters (cm), and waist circumference (in cm) by a calibrated scale and recording of blood pressure (BP). Waist circumference was measured midway between the inferior costal margin and the superior border of the iliac crest, at the end of normal expiration in standing position. By using standard mercury manometer, at least two readings at five-minute intervals were taken to measure the BP in supine position. If BP was found to be high (≥140/90), then a third reading after 30 minutes was obtained; the lowest of these readings was taken. Fasting venous blood sample was collected under aseptic conditions to measure the blood glucose (fasting blood sugar (FBS), triglycerides (TG), and high-density lipoprotein (HDL) levels.

MS was diagnosed by using the consensus definition for MS.[37] According to this, a person is considered to have MS if he fulfills three of the following five criteria: High waist circumference (≥80 cm for females and ≥90 cm for males of Asian origin), systolic BP ≥130 mmHg and/or diastolic BP ≥85 mmHg (or on treatment for hypertension), TG levels ≥150 mg/dL (or on specific treatment for this abnormality), HDL cholesterol <40 mg/dL for males and <50 mg/dL for females (or on specific treatment for this abnormality), FBS ≥100 mg/dL (or on treatment for diabetes mellitus).

Patients and healthy subjects in the control group found to have metabolic abnormalities were informed about the same. They were explained about the need for proper diet and regular exercise, and referred for specialist care whenever required.

Statistical analysis

Analysis was done using the SPSS version 14.0 for Windows (Chicago, Illinois, USA). Frequencies with percentages were calculated for categorical variables and mean and standard deviation were calculated for

continuous variables. Those with and without MS were compared using the chi-quare test and *t*-tests. In case the data for any variable was skewed, nonparametric tests were used for comparison.

RESULTS

The study sample comprised 43 patients with depressive disorders and an equal number of subjects in the healthy control group. As per the study design, both the groups were matched for age, gender, education, and neighborhood. As detailed in Table 1, mean age of the patients with depression was 47.21 years and that of the control group was 45.88 years. The mean duration of education of the participants in the depression group was 9.05 years and that of the subjects in the healthy control group was 11.35 years. Both the groups included 22 males and 21 females. In both the groups, majority of the subjects were married, belonged to Hindu religion, came from nuclear families and urban neighborhoods. Although a higher proportion of patients in the depression group were homemakers/not on paid jobs, there was no statistically significant difference between the two groups.

The mean age of onset of the depressive disorders was 44.79 years (SD: 16.53; range: 17 to 77 years) and the mean duration of illness was 30.87 months (SD: 46.04; range: 2 weeks to 20 years). The most common psychiatric diagnosis was first-episode depression (*N*=29; 67.4%) of varying severity as per ICD-10, followed by dysthymia (*N*=7; 16.3%), and recurrent depressive disorder (*N*=4; 9.3%). A small portion of the subjects (*N*=3; 7%) had comorbid diagnosis of dysthymia along with current depressive episode. In the patient group, one participant was diagnosed with diabetes mellitus, four had a diagnosis of hypertension, and one participant had a diagnosis of both diabetes mellitus and hypertension. None of the participants in the control group had a history of diabetes mellitus, hypertension, or cerebrovascular accident.

Table 1: Sociodemographic variables of patient group vs. healthy controls

Variable	Patient group *N*=43 mean (SD)/frequency (%)	Healthy controls *N*=43 mean (SD)/frequency (%)	χ^2/*t* value
Age (years)	47.21 (16.06)	45.88 (11.4)	0.44
Education (years)	9.05 (7.07)	11.35 (3.92)	−1.86
Sex			
Male	22 (51.2)	22 (51.2)	00
Female	21 (48.8)	21 (48.8)	
Marital status			
Currently single	9 (20.9)	3 (7)	3.48
Married	34 (79.1)	40 (93)	
Occupation			
On paid jobs	16 (37.2)	27 (62.8)	5.62
Home makers/not on paid jobs	27 (62.8)	16 (37.2)	
Religion			
Hindu	33 (76.7)	33 (76.7)	00
Non-Hindu	10 (23.3)	10 (23.3)	
Family type			
Nuclear	25 (58.1)	30 (69.8)	1.26
Non-nuclear	18 (41.9)	13 (30.2)	
Neighborhood			
Urban	23 (53.5)	25 (58.1)	0.18
Village	22 (46.5)	18 (41.9)	

#Mann-Whitney U test, SD – Standard deviation

Metabolic parameters

As depicted in Table 2, 16 patients with depressive disorder (37.2%) and seven participants from the control group (16.3%) fulfilled the criteria for MS and the difference between the two groups was statistically significant. When those with a diagnosis of either diabetes mellitus or hypertension or both were removed, the prevalence of MS in the depressive disorder group was reduced to 34.14% (*N*=14).

With respect to the subtypes of depressive disorder, the prevalence of MS in subjects with first-episode depression was 34.5% (10 out of 29), 50% in those with recurrent depressive disorder (2 out of 4), 28.6% in the dysthymia group (2 out of 7), and 33.33% in the group with comorbid dysthymia and current depressive episode.

As shown in Table 2, among the various parameters of MS, increased waist circumference was the most common abnormality in both the study groups. In the depressive disorder group, raised waist circumference was followed by abnormal BP (46.5%) and raised TG levels, whereas in the healthy control group, the second most common abnormality was raised TG levels and this was followed by low HDL levels. Hyperglycemia remained the least common abnormality in both the groups.

Of the 43 patients, 22 (51.2%) were obese (BMI≥25). Similarly in healthy controls, increased waist circumference remained the most common abnormality and hyperglycemia the least common MS parameter.

Besides 16 patients with depressive disorders having MS, another 12 (27.9%) patients fulfilled two of the five criteria for MS and another 11 (25.6%) fulfilled one criterion for MS. Further, when the data of patients fulfilling only two criteria was analyzed further, it was seen that 10 of the 12 had increased waist circumference, and six had high BP. Of the 11 patients who fulfilled one criterion for MS, seven had an abnormality other than increase in waist circumference.

Table 2: Clinical variables and metabolic syndrome profile of patients and healthy controls

Variable	Patient group *N*=43 mean±SD/frequency (%)	Healthy controls *N*=43 mean±SD/frequency (%)	χ^2/*t* value
Body weight (Kg)	65.42 (13.89)	66.63 (11.45)	−0.44
Height (cm)	163.16 (10.65)	161.98 (7.28)	0.60
BMI	24.67 (5.21)	25.38 (4.63)	−0.66
Obesity (BMI≥25)	22 (51.2)	18 (41.9)	0.74
WC (cm)	91.11 (13.35)	86.37 (11.27)	1.78
SBP (mmHg)	124.98 (15.7)	114.19 (13.66)	3.39**
DBP (mmHg)	82.56 (10.25)	77.35 (8.80)	2.52*
TG levels (mg/dL)	135.17 (49.22)	147.09 (63.39)	0.97
HDL levels (mg/dL)	49.09 (12.2)	54.67 (13.52)	−2.0*
LDL levels (mg/dL)	113.31 (34.58)	93.81 (24.14)	3.0**
Total cholesterol levels (mg/dL)	189.94 (40.70)	173.19 (33.2)	2.09*
FBS levels (mg/dL)	104.47 (56.91)	88.34 (6.76)	1.84
Abnormal waist circumference [≥90 (M),≥80 (F)]	30 (69.8)	20 (46.6)	4.77*
SBP≥130 mmHg	18 (41.9)	8 (18.6)	5.51*
DBP≥85 mmHg	12 (27.9)	6 (13.9)	2.52
Abnormal BP≥130/≥85 mmHg	20 (46.5)	7 (16.3)	7.93**
TG≥150 mg/dl	16 (37.2)	14 (32.6)	0.20
Low HDL (<40 mg/dl M,<50 mg/dl F)	14 (32.6)	10 (23.3)	9.25
FBS≥100 mg/dl[$]	10 (23.3)	4 (9.3)	3.07
MS	16 (37.2)	7 (16.3)	4.80*
MS criteria fulfilled[$]			
0	4 (9.3)	14 (32.6)	
1	11 (25.6)	11 (25.6)	9.41
2	12 (27.9)	11 (25.6)	
3	10 (23.3)	5 (11.6)	
4	5 (11.6)	2 (4.6)	
5	1 (2.3)	0	

MS – Metabolic syndrome; BMI – Body mass index; WC – Waist circumference; SBP – Systolic blood pressure; DBP – Diastolic blood pressure; HDL – High-density lipoprotein; TG – Triglycerides; LSL – Low-density lipoprotein; FBS – Fasting blood sugar; [$]Fischer exact test; SD – Standard deviation; F – Female; M – Male; BP – Blood pressure;*$P<0.05$; **$P<0.01$

As shown in Table 2, when the prevalence of subcomponents of MS was compared between the two groups, the patient group had significantly higher systolic and diastolic BP, higher low-density lipoprotein (LDL) and total cholesterol levels, and lower HDL levels than the healthy controls. Compared to the healthy controls, a significantly higher proportion of patients had abnormal waist circumference, systolic blood pressure or high blood pressure.

On comparison, there was no significant difference between the participants of either gender on any of the metabolic parameters in the depressive disorder group and the healthy control group. There was no significant difference between those with and without MS on any of the sociodemographic parameters.

DISCUSSION

Both depression and MS are known to increase the risk of cardiovascular disease. Studies from the West which have evaluated the community sample for prevalence of MS have reported that the presence of depression (current and lifetime) increases the risk of MS.[20] Studies done in patients of depression suggest that the prevalence of MS is more in patients of depression compared to healthy controls.[6,9,20,22] Due to these factors, some authors suggest a bidirectional relationship between depression and MS.[19,38,39] However, data is mostly lacking from the developing countries with regard to the relationship between depression and MS. To our knowledge, this is the first study from India to have evaluated the prevalence of MS in drug-naïve patients of depressive disorders. The sociodemographic profile of the patients included in the present study is fairly representative of depressed patients seen in our centre[27,40] and other parts of India.[41] The lipid profiles of the patients included in the present study are also comparable to the lipid profiles reported for depressed patients in previous studies from our center.[26,27]

In the present study, slightly more than one-third of the patients with depressive disorders fulfilled the criteria of MS, and the prevalence of MS was significantly higher in the depressive disorder patients compared to the healthy control group. When those with diagnosis

of either diabetes mellitus or hypertension or both were removed, the prevalence of MS in the depressive disorder group reduced to one-third (34.14%). With respect to subtypes of depressive disorder, the prevalence of MS in subjects with first-episode depression was 34.5 and 50% in those with recurrent depressive disorder. Findings of the present study are in the reported range of 25 to 41%.[4-6]

When we compare the findings of the present study with the previous study from our center, the prevalence of MS in the present sample was less (37 vs. 44% reported by Aggarwal *et al*., unpublished), but not significantly different. Although the sample size of the present study is smaller than the previous cohort, this possibly suggests that antidepressants *per se* do not have a significant impact on the prevalence of MS in patients of depression. However, this finding needs to be replicated in a larger sample.

In the present study, the most common subcomponent of MS was increased waist circumference which is in contrast to the studies from the West which have reported raised BP to be the most common abnormality.[5,6,13] However, increased waist circumference as the most common abnormality followed by raised BP in patients with depression is supported by the findings of the previous study from our center,[26] which included depressed patients on treatment with psychotropic agents.

In contrast to the previous studies, which have reported positive associations between depression and central obesity/higher waist circumference,[7,8,12,13,16,18,22,19,42,43] we did not find any difference in the waist circumference of depressed patients and the healthy controls. However, compared to controls, patients in the depressive disorder group had low HDL levels and high BP, which concurs with the findings noted in the studies from the West.[7,11,13,14,22,25,42-44]

Some of the studies from the West and a previous study from our center suggest that certain demographic variables, especially gender, influences the prevalence of subcomponents of MS and prevalence of MS in patients of depression.[7,45] Similar association of neighborhoods (urban/rural) and metabolic parameters have also been reported. However, some of the studies also refute the influence of gender and other sociodemographic variables on metabolic parameters in patients with depression.[6,10] Findings of the present study support the latter studies.[4,46]

Nearly half (53.5%) of our patient population fulfilled the subthreshold of the MS criterion (1 or 2 criteria) and 10 of the 12 patients who fulfilled two MS criteria had increased waist circumference. This finding suggests that increased waist circumference can be considered as a clinical marker which can predict the development of MS later.

Multiple episodes of depression were not associated with a greater risk for MS than single episodes of depression[4,20], though due to the small size of the sample, we could not study this association. Moreover, the duration of depression was not found to predict future MS.

The findings of the present study must be interpreted in the light of limitations of the study which includes small size of sample, purposive sampling, and cross-sectional design. The study also did not address the relationship between metabolic parameters and MS and severity of illness, residual symptoms, treatment refractoriness, and lifestyle. The study also did not evaluate the dietary and lifestyle factors which are known to contribute to the development of MS. Future studies should try to overcome these limitations.

To conclude, the present study reveals that 37% of the patients with unipolar depressive disorder have MS. With respect to the subcomponents of MS, higher waist circumference and high BP are present more frequently than other subcomponents. These findings imply that monitoring waist circumference and BP can be useful in monitoring the development of possible MS in unipolar depression patients. Besides the presence of MS, a significant proportion of the patients in the depression group had one or two metabolic abnormalities. This suggests that clinicians should not just focus on patients who have MS, but also look at this high-risk population, which can convert to MS-positive cases. Hence, any patient who fulfills a single criterion of MS should be considered at risk for the development of MS and preventive strategies should be in place.

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