ORIGINAL ARTICLE

Metabolic Syndrome in Patients with Depression: A Cross-sectional Comparative Study

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Abstract

Background: Depression is a leading cause of disability worldwide and is also known to be comorbid with a number of medical and psychiatric illnesses. Metabolic syndrome (MS) that is now emerging as a common lifestyle illness is found to be twofold greater in patients with depression. Often, antidepressants have been considered to be the reason for this possible link, however, research from the West suggests that a direct link is plausible. There is a scarcity of literature supporting these data from the East. In this study, we have attempted to assess the prevalence of MS in depressive patients, and to determine the probable risk factors contributing to the association.

Materials and methods: Sixty consecutive patients that fulfilled the inclusion criteria were recruited from a tertiary care center in India. Sociodemographic and clinical data were obtained using a semistructured pro forma. Depressive disorder was diagnosed using International classification of diseases-10 (ICD-10), and severity was measured using Hamilton rating scale for depression (HAM-D). The weight, height, waist circumference (WC), systolic and diastolic blood pressure (BP), as well as fasting lipids and glucose were measured. Metabolic syndrome was diagnosed based on National Cholesterol Education Program/Adult Treatment Panel (NCEP ATP-III) criteria (2005 revision). The descriptive and inferential statistics were done using statistical package for social sciences (SPSS) 16.

Results and conclusion: The overall prevalence of MS among depressed patients was 35%. The prevalence among "drug-naive" patients was 30%, whereas among "on-drug" patients was 40%. The most common abnormal MS components were WC (53.33%), systolic BP (SBP) (53.3%), and high-density lipoprotein (HDL) (53.3%). Age of the patient was the only sociodemographic factor that showed significant correlation with components of MS like fasting blood sugar (FBS) and SBP. Age of onset of depression among MS cases had a negative correlation with WC. Among the MS components, the distribution of diastolic BP (DBP) and triglycerides (TG) was statistically different among the "drug-naive" and "on-drug" groups. Thus, in view of significant number of depressed patients being at risk of developing MS, it would be necessary to keep a regular check on metabolic parameters in this group of patients.

Keywords: Antidepressant, Depression, Metabolic syndrome, Waist circumference.

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Introduction

Depression is a disorder of major public health importance. Major depressive disorder has the highest lifetime prevalence (17%) of any psychiatric disorder.[1] Globally, more than 264 million people of all ages suffer from depression.[2]

Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus. The major features of MetS include central obesity, hypertriglyceridemia, low levels of HDL cholesterol, hyperglycemia, and hypertension.[3] People with MetS are twice likely to die from, and three times as likely to develop myocardial infarction (MI) or stroke compared with people without MetS.[4]

There is a bidirectional relationship between depression and MetS.[4] A recent meta-analysis by Gover et al. showed that risk of MetS in people with depression was 1.5 times more than in healthy controls. Depression is considered as a state of chronic endogenous stress that causes changes within the hypothalamic pituitary adrenal axis (HPA) and may result in the upregulation of noradrenergic activity and disturbances of cortisol homeostasis. Disturbances may also involve the metabolism of carbohydrates and lipids, as well as hemodynamic parameters, and hence may lead to MS.[5] Also, antidepressant medications are one of the widely prescribed medications worldwide. They are often associated with weight gain and metabolic abnormalities in vulnerable patients.[6]

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As there is growing consensus that the presence of depression increases the prevalence of MetS and there is a scarcity of data from eastern countries like India, the present study attempts to find the prevalence of MetS in depressive disorder patients in a general hospital setting. Different studies have found the relation of depression with different components of MetS. Hence, we tried to find the status of our population. The advent of antidepressants

has although reduced the morbidity of depressive disorder patients, they have adversely affected some of the metabolic parameters in a group of these patients. So, in order to gauge its impact on the prevalence of MetS, the study also included a group on antidepressants.

Aims and Objectives of This Study

- To evaluate the prevalence and profile of various components of MetS among depressive disorder patients.
- To compare the prevalence of MetS among "drug-naïve " with "on-drug" patients with depressive disorder.

Study Tools

- Patient health questionnaire (PHQ): self-administered version for screening patients for depression.
- Mini-International Neuropsychiatric Interview Plus (M.I.N.I. Plus) 5.0.0.
- The Rapid Assessment of Physical Activity (RAPA) – is a 9-item, self-administered questionnaire designed to assess current levels of leisure-time physical activity in the clinical setting.
- Hamilton depression rating scale (HDRS)– For assessing the severity of depression.

Materials and Methods

The study was approved by the Ethics Review Committee of the institute and written informed consent was obtained from all the 60 patients included in the study. The study period was between 2013 and 2015. Initial screening was done using the PHQ-9, and MINI plus was used to rule out comorbid disorders. The inclusion and exclusion criteria for the study were as follows:

Inclusion Criteria

- Aged between 18 and 65 years.
- Depressive disorder (depressive episode, recurrent depressive disorder, and dysthymia) diagnosed as per ICD-10 guidelines.
- Both inpatients and outpatients.

Exclusion Criteria

- Depressive symptoms with psychotic disorders, alcohol dependence, obsessive compulsive disorder (OCD), and dementia.
- Depressive symptoms in bipolar disorders, neurological disorders, and pregnant or lactating.
- Past history of diagnosed diabetes mellitus/hypertension (DM/HTN) before the onset of depressive disorder.
- Obstructive sleep apnea.
- Hormonal imbalance polycystic ovarian disease (PCOD), subjects on hormone replacement therapy.

Data about sociodemographic profile and other clinical details were collected in a semistructured pro forma. The severity of depression was measured using HDRS. Physical activity was quantified using RAPA. MetS was defined using NCEP ATP III criteria (Table 1). Physical evaluation included measurement of body weight in kilogram (kg), height in centimeters (cm), WC in cm by a calibrated scale, and recording of BP. Fasting venous blood sample was collected under aseptic conditions to measure FBS, TG, and HDL levels.

The patients were further divided into two groups. One group included drug-naïve depressive disorder patients. The second group included depressive disorder patients who were on antidepressants for a minimum period of 3 weeks or had previous history of antidepressant usage. Patients in both groups found to have metabolic abnormalities were informed and explained about the need for proper diet and regular exercise, and referred for specialist care whenever required.

Table 1: Description of various metabolic syndrome (MS) components

			Cut-off values (NCEP-ATP III)	
MS components	*Mean ± SD*	*Range*	*Males*	*Females*
WC (cm)	86.92 ± 10.73	62–116	≥90	≥80
TG (mg/dL)	162.15 ± 75.15	92–576	≥150	
HDL (mg/dL)	44.93 ± 7.01	32–58	<40	<50
FBS (mg/dL)	90.95 ± 12.41	72–142	≥100	
SBP (mm Hg)	127.57 ± 13.04	90–160	≥130	
DBP (mm Hg)	84.20 ± 8.52	70–110	≥85	

Results

The mean age of our study sample ($n = 60$) was 41.38 ± 12.96 years. About 63.3% of the study subjects were females. The mean age of onset of depression was 39.63 ± 12.14 years and 43% had a past history of previous depressive episodes. The time duration of the current depressive episode was 6.07 ± 8.36 months for the drug-naïve patients and 49.43 ± 57.76 months in the "on-drug" group. The depression severity as assessed by HDRS was as follows: 23 (38%) were in very severe category, 11 (18%) in severe, 19 (32%) in moderate, and 7 (12%) in mild categories (Table 2).

The prevalence of MS among the patients with depressive disorder was 35% (21 out of 60 depressive disorder patients). The most common MetS components to be abnormal in the sample were WC (53.3%), SBP (53.3%), and HDL (53.3%) levels. The next most common abnormal MS components were TG (45%) and diastolic BP (36.7%), while the least to be deranged were FBS levels (Fig. 1). All the deranged components of MetS were toward the lower end of the range (Table 1).

Among the depressed patients, only 8 (13.3%) had no abnormal MetS components. About 86.7% (52) patients of the study group had at least one abnormal MetS component and 6.7% (4) had all the 5 MetS components as abnormal. The sociodemographic and clinical variables analyzed using Pearson correlation showed significant correlations with some of the MetS components. Age had weak positive correlation with FBS ($r = 0.263$, $p = 0.042$) and SBP ($r = 0.272$, $p = 0.036$). Age-of-onset depression had significant correlation with SBP (weak positive correlation $r = 0.315$, $p = 0.01$) as well as a trend toward significance in diastolic BP (weak positive correlation $r = 0.246$, $p = 0.05$). RAPA score had a weak negative correlation with WC ($r = -0.256$, $p = 0.04$).

As far as the effect of antidepressant was concerned, the prevalence of MetS among drug-naïve patients was 30%, whereas on-drug group, patients had a prevalence of 40%. However, the difference was not statistically significant ($p = 0.294$). Amitryptiline (46.7%) was the most common antidepressant used in the sample followed by fluoxetine (40%) and escitalopram (13.3%). Among the sociodemographic factors, "on-drug" group had a female predominance (73.3%), which was statistically significant as compared with the "drug-naïve" group ($p = 0.03$). All other factors were comparable in both groups (Table 3). Among the clinical factors, the mean age of onset of depression was delayed by 1.87 years in the "on-drug" group and this showed

Table 2: Description of sociodemographic and clinical variables

Age	
Mean ± SD	41.38 ± 12.96
Range	18–64
Gender	
Male	22 (36.7%)
Female	38 (63.3%)
Marital status	
Married	36 (60%)
Single	24 (40%)
Number of years of formal education (years)	
Mean ± SD	6.83 ± 5
Range	0–20
<5 years	22 (36.7%)
5–10 years	27 (45%)
>10 years	11 (18.3%)
Family type	
Nuclear	36 (60%)
Joint	9 (15%)
Extended	15 (25%)
Locality	
Urban	43 (71.7%)
Rural	17 (28.3%)
Socioeconomic class	
Upper-middle class	10 (16.7%)
Lower-middle class	32 (53.3%)
Upper-lower class	18 (30%)
Age of onset of depression (years)	
Mean ± SD	39.63 ± 12.14
Range	18–64
Past history of depressive episode	13 (43.3%)
H/o substance dependence	9 (15%)
Total time spent in depression (months)	
1. "Drug-naïve" group Mean ± SD	6.07 ± 8.36
2. "On-drug" group Mean ± SD	49.43 ± 57.76
Family h/o psychiatric illness	19 (31.7%)
Physical activity (RAPA-1 scores)	
Sedentary	0
Light activity	2
Underactive	3
Active	55
BMI	
Normal	36 (60%)
Overweight	20 (33%)
Obese	4 (7 %)
HDRS	
Mild	7 (12%)
Moderate	19 (32%)
Severe	11 (18%)
Very severe	23 (38%)

BMI, body mass index; HDRS, Hamilton depression rating scale

a trend toward statistical significance ($p = 0.06$). The "on-drug" group had a greater duration of depressive episode at the time of the study ($p = 0.008$). Among the MS components, TG ($p = 0.0008$) and diastolic BP ($p = 0.003$) were higher in the "on-drug" group, and this difference was found to be statistically different ($p = 0.0008$) (Table 4).

Discussion

There is increasing literature to suggest the independent association between MetS and depression. The prevalence of MetS found in the general population among Asians is 14–18%,[7] whereas the prevalence of MetS among depressed patients have reported to be varying from 25 to 41%.[8] The prevalence of MetS among depressed patients in our study was 35%. These studies suggest that the presence of depression increases the risk of development of MetS by twofold, which is supported by the present study.

Heiskanen et al. found in a 6-year follow-up study that the prevalence of MS was 36%.[8] However, cross-sectional studies like Richter et al., John et al., and Teixeira et al., which evaluated larger samples of depressive patients, also found a prevalence of 35%, 46%, and 48.1%, respectively.[9–11] Our cross-sectional study also showed a prevalence of 35%.

This was also supported by the fact that 86.7% of depressed patients had at least one MetS component abnormal.

Among the few Indian studies, Grover et al. found that prevalence of MetS in 44.3% in the patients with depressive disorder included first-episode depression, recurrent depressive disorder, and dysthymia.[12] Agarwal et al. reported a prevalence of 24% in patients with bipolar depression and 26% in those with recurrent depression[13] compared with the control groups. All these studies have attempted to assess prevalence of MetS in drug-naïve patients, thus reporting an association between MetS and depression independent of the use of psychotropics.

Some of the hypotheses to explain the association between depressive disorders and MS are (1) there is a bidirectional relationship between MetS and depression.[4] (2) Those with stressful life events were more at risk for developing MetS,[14] and stress could be an important factor, with depression and MetS being the end outcomes. (3) Other confounding factors like diet and lifestyle, environmental factors, socioeconomic status, and nicotine dependence can all independently cause MetS in a depressed patient. However, in our study, the depression severity scores in those with and without MetS revealed no statistical significance. In fact, the mean HDRS score among those without MetS was slightly more than those with MetS (21.5 vs 18.43).

In the present study, 65% among the depressed patients did not have MetS, which means there are some protective factors that are operating in a group of patients. This could be an area for further research.

The most common MetS components to be abnormal in the present study sample were WC, SBP, and HDL levels (53.3%). The next common MetS components were triglyceride levels (45%) and diastolic BP (36.7%), and the least common were FBS (15%) levels. These findings find support from other Indian study by Grover et al. wherein WC was the most common subcomponent of MetS that was increased.[12] Western studies like that of Richter et al. found BP to be the most common MS component.[9] In the present study, when either SBP or DBP was considered, 54 (90%) of the depressed patients had a BP in the higher range.

East et al. also found that individuals with depressive symptoms had an increased frequency of higher WC, higher TG, and lower HDL, while women with depressive symptoms also had marginally higher FBS levels.[15] FBS was the least common abnormality detected in our study, which may be because of the strict exclusion criteria wherein the already-diagnosed cases of DM were not part of the study sample. Though majority of studies had WC and BP to be the

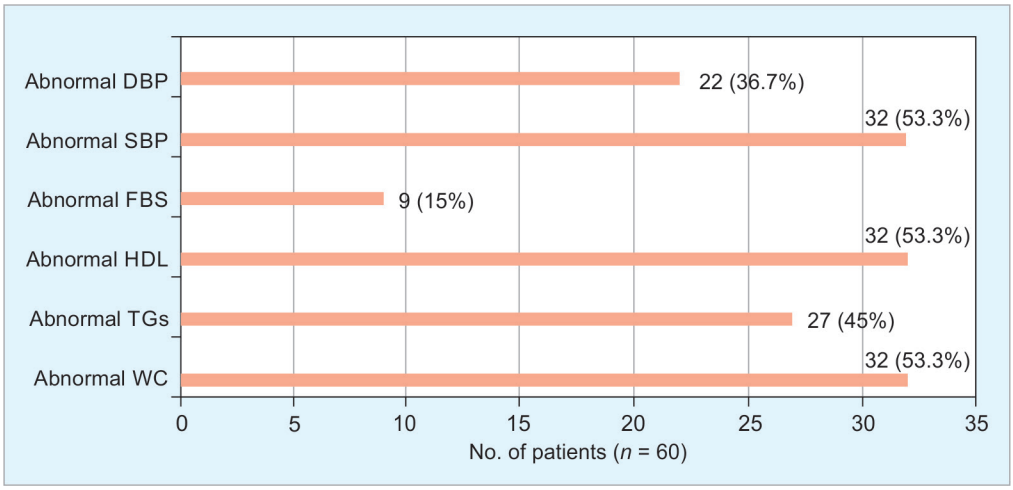

Fig. 1: Abnormal MS components in the depressive disorder patients

Table 3: Comparison of sociodemographic and clinical variables among "on-drug" and "drug-naïve" group

	Drug-naïve	*On-drug*	*p-value (t-test/Chi-square test)*
Age (years)			
Mean ± SD	39.27 ± 14.29	43.5 ± 11.33	0.209
Range	18–64	23–63	
Gender (%)			
Male	14 (46.7%)	8 (26.7%)	
Female	16 (53.3%)	22 (73.3%)	0.03
Marital status (%)			
Married	18 (60%)	18 (60%)	1
Single	12 (40%)	12 (40%)	
Family type (%)			
Nuclear	18 (60%)	18 (60 %)	
Joint	5 (16.7%)	4 (13.4%)	0.915
Extended	7 (23.3%)	8 (26.6 %)	
Locality (%)			
Urban	20 (66.7%)	23 (76.7%)	0.39
Rural	10 (33.3%)	7 (23.3%)	
MKC			
UMC	7 (23.3 %)	3 (10 %)	
LMC	16 (53.3%)	16 (53.3%)	0.288
ULC	7 (23.3%)	11 (36.6%)	
Age of onset of depression	38.33 ± 13.96	40.2 ± 9.75	0.06
Past history of depressive episode	–	13 (43.3%)	–
H/o substance dependence	5 (16.67%)	4 (13.33%)	0.718
Current depressive episode duration (months)	6.07 ± 8.36	11.83 ± 7.97	0.008
Family h/o psychiatric illness	10 (33.33%)	9 (30%)	0.781
Family h/o MS components	10 (33.3%)	7 (23.33%)	0.444
Physical activity (RAPA-1 scores)			
Sedentary	0	0	
Light activity	2	0	
Underactive	3	0	
Active	25	30	
HDRS score	21.17 ± 5.51	19.23 ± 5.54	0.9769
PHQ-9 score	20.07 ±3.83	18.67 ± 3.11	0.2679
BMI (kg/m^2)	23.36 ± 3.77	24.55 ± 4.27	0.5067
Age of onset of depression	38.33 ± 13.96	40.2 ± 9.75	0.06

$p \leq 0.05$ taken as statistically significant

Table 4: Comparison of MS components among on-drug and drug-naïve group

Mean ± SD	*Drug-naïve group*	*On-drug group*	*p-value*
WC (cm)	86.63 ± 11.96	87.20 ± 9.54	0.2294
TG (mg/dL)	152.56 ± 49.47	171.73 ± 94.09	0.0008
HDL (mg/dL)	43.96 ± 6.79	45.63 ± 7.09	0.8175
FBS (mg/dL)	88.53 ± 10.21	93.37 ± 14.04	0.0916
SBP (mm Hg)	127.46 ± 13.33	127.67 ± 12.99	0.8903
DBP (mm Hg)	83.47 ± 7.95	93.37 ± 14.04	0.003

$p \leq 0.05$ taken as statistically significant

most common MetS components to be abnormal, the present study had additional components of HDL and TG contributing toward MS diagnosis. Some studies have concluded that MS is a predictive factor for the development of depression and that WC largely contributes to the association between MetS and depression. This could not be tested in the present study.

MetS per se is not a homogeneous group as shown in the present study. Various combinations of MetS components can result in the final diagnosis of MetS. The most common combination has been that of WC, TG, and HDL, which suggests that there are factors such as ethnicity and genetic predisposition to development of a particular MS component abnormality.

Among the sociodemographic factors, age had weak positive correlation with some of the components of MetS like FBS and SBP. This has been also observed in a study by Hakan et al. wherein MetS was correlated with age and not with any other sociodemographic factor.[16] However, in the Indian context, the study by Grover et al. showed that gender and other sociodemographic variables had no influence on metabolic parameters in patients with depression.[12]

In a study by Kinder et al., women with a history of a major depressive episode were twice as likely to have MetS unlike men.[17] This is in contrast to the present study wherein even though there was a female dominance, the gender distribution was not statistically significant in those with and without MetS.

As far as clinical factors were concerned, age of onset depression had weak positive correlation with the MetS component of SBP as well as a trend toward significance in DBP. It also had a moderate negative correlation with WC. This indicates that those with earlier age of onset of depression had a greater WC and were more likely to develop MetS in future. WC largely contributes to the association between MetS and depression.[15] As expected, body mass index (BMI) had a significant positive correlation with 3 of the MetS components – WC, TG, and FBS (Table 1).

Some of the antidepressants are known to cause weight gain or weight loss and also influence metabolic parameters.[3] The present study showed a slightly higher prevalence among the "on-drug" group (40%) as compared with drug-naïve group (30%) though it was not statistically significant ($p = 0.294$). The possible reasons for the difference not being statistically significant could be that (1) the group on medication was not homogeneous and there were no data on total duration of exposure to antidepressants. (2) The period of exposure of 3 weeks might be too short to have any impact on prevalence of MetS. The present study had 14 (46.7%) patients on a tricyclic antidepressant and the rest 16 (53.3%) on selective serotonin reuptake inhibitors (SSRIs), and the sample size was too small to assess the influence of individual antidepressant on prevalence of MetS.

Strengths of our Study

- Strict inclusion and exclusion criteria.
- Comparison of two groups, drug-naïve as well as on-drug groups for the prevalence of MetS among the depressed patients.

However, our study has certain limitations, as the data were obtained by a cross-sectional assessment, it was not possible to imply causation or to test the direction of the effects. Purposive sampling was done to recruit subjects into the study. Interviewer bias may have played a part as the interviewer was not blinded though the diagnosis of MetS was an objective assessment. Sample size was inadequate which may limit generalization and findings require replication in other settings. The study also did not evaluate the dietary and lifestyle factors that are known to contribute to the development of MetS. Other limitations include duration of antidepressant use, lack of data on the number of episodes of depression, and the treatment history, including time elapsed between the episodes and treatment adherence and lack of data on MetS components in such patients. Patients with criteria for inclusion into "on-drug" group was 3 weeks which may be too short an interval to assess the effect of medication to cause MetS.

Conclusion

The prevalence of MetS among depressed patients was 35%. The most common MetS components found to be abnormal were WC, HDL, and SBP. Age was significantly correlated with SBP and FBS in the whole sample, and age of onset of depression was significantly correlated with WC in those with MetS. The prevalence of MS among on-drug group was 40%, whereas in drug-naïve group, it was 30%. DBP and TG were statistically different among the drug-naïve compared with "on-drug" group.

Future Directions

Although the present study points toward a higher prevalence of MS among depressed patients, there are unresolved issues that still remain. The role of protective as well as risk factors and their interaction among those depressed patients who go on to develop MetS needs support from further studies. Antidepressants affect some of the metabolic parameters, so it is imperative to have a regular check on these parameters in order to prevent the development of MetS. These would have to be addressed by future research.

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