Dr Buckshey Award Paper

Prevalence of metabolic syndrome in unipolar depression : An exploratory study

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Abstract

Background: *Metabolic syndrome is a risk factor for the development of coronary heart disease and type -2 diabetes mellitus. Depression and diabetes share a two way relationship. Only a few studies have evaluated the prevalence of metabolic syndrome in depression and there is none from India.* ***Aim:*** *To study the prevalence of metabolic syndrome in patients with unipolar depression.* ***Methods:*** *A total of 166 patients diagnosed with unipolar depression were evaluated for the presence of metabolic syndrome according to International Diabetes Federation (IDF) and National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATP III) criteria.* ***Results:*** *Of the total sample, 41.6% and 44% of patients had metabolic syndrome according to IDF and NCEP-ATP III criteria respectively. Increased waist circumference (69%) was the most common abnormality followed by hypertension (51%). Abnormal fasting blood glucose was the least common abnormality (28.9%). Metabolic syndrome was found to be higher in subjects who were older and had higher BMI. No significant association was found between the prevalence of metabolic syndrome and type of antidepressant used. On regression analysis, high BMI was found to be strongest predictor of development of metabolic syndrome.* ***Conclusion:*** *Monitoring of BMI, waist circumference and blood pressure can be helpful for early detection of metabolic syndrome.*

Key words: *Metabolic syndrome, depression, prevalence*

Introduction

Metabolic syndrome (MetS) is a cluster of disorders/risk factors which include obesity, dyslipidaemia, insulin insensitivity, deranged glucose metabolism and hypertension. It is of immense clinical relevance because these metabolic risk factors are associated with development of coronary heart disease, cerebrovascular disease, as well as type-2 diabetes mellitus.[1,2] Depression and metabolic syndrome share a two way relationship. Depression has been associated with the development of diabetes and poor glycemic controls in those with preexisting diabetes.[3] Studies have shown that metabolic syndrome and its various components, especially central obesity and dyslipidemia are predictors of depressive symptoms.[4,5] Similarly studies in patients with depression have reported abnormalities of lipid profile,[4,8-11] higher prevalence of obesity and increased waist circumference[4,6] and hypertension.[11,12] It is suggested that presence of obesity and other

markers of metabolic syndrome can promote a chronic, sub acute state of inflammation.[13] This can cause the release of cytokines and dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis which can produce a state similar to that of depression.[14,15] It is also suggested that presence of central obesity (i.e., increased waist circumference) may be the key mediator or pathogenic factor responsible for higher prevalence of metabolic syndrome in patients with depression.

Western data suggests prevalence of metabolic syndrome in subjects with depression to vary from 30.4% to 48.8%.[6,16,17] Studies also suggest that depression increases the risk of developing metabolic syndrome by about 2 folds.[18-20] The prevalence of metabolic syndrome in subjects with depression was not influenced by factors like the number of depressive episodes, age at first episode and presence of a current episode.[17-19,21,22]

However, there is lack of data from eastern countries like India. There are occasional studies which have evaluated the prevalence of depressive disorders in patients of hypertension[23] and diabetes mellitus[24]. There is one study which has evaluated the prevalence of various subcomponents of metabolic syndrome in depressed patients. In a small sample study (n=30), Das et al[25] reported 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. In the same study, authors reported that patients with severe depression had higher body mass index. However, there is lack of data with regard to prevalence of metabolic syndrome in depressed subjects from India. In this background, the present study aimed at assessing prevalence of metabolic syndrome in subjects with depression in an Indian setting.

Method

To be included in the study, the patients were required to be 18 years or above, of either gender and diagnosed with a depressive disorder (first episode or recurrent depressive disorder according to ICD-10).[26] Patients were selected by purposive random sampling, i.e., a random table was generated using SPPS (3:2 ratios in favour of inclusion into the study) and the patients were allocated to the inclusion or exclusion group. For this, 270 patients diagnosed with first episode or recurrent depression were approached by purposive sampling, of which 20 declined to participate. Of the remaining 250 patients, a study sample of 166 patients was selected on the basis of pre-generated randomization number table.

Metabolic syndrome was ascertained by using both International Diabetes Federation (IDF) criteria and modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) criteria (see box 1). NCEP ATP-III criteria has been modified for Asians and accordingly the waist circumference criteria for Asians is restricted to >90 cm for males and > 80 for females (in contrast to NCEP ATP-III where the cut-off is 102 cm and 88 cm for males and females respectively). IDF also defines metabolic syndrome by using similar cutoffs for various components and requires presence of 3 components but the waist circumference criteria is essential.

All patients found to have metabolic abnormalities (i.e. metabolic syndrome, or any specific abnormality like hypertension, raised blood sugar, dyslipidemia) were informed, educated about the need for proper diet and regular exercise, and were referred for specialist care.

Procedure

All the eligible patients were approached

Box 1: Metabolic syndrome: Modified NCEP-ATP-III criteria

A minimum of 3 out of the following 5 criteria:

(a) high waist circumference (> 80 cm for females and > 90 for males),
(b) systolic blood pressure e" 130 and/or diastolic blood pressure e"85 mm of Hg (or on treatment for hypertension)
(c) triglyceride levels >150 mg/dl (or on treatment for this abnormality)
(d) HDL cholesterol < 40 mg/dl for male and <50 mg/dl for females (or on treatment for this abnormality)
(e) Fasting blood sugar more than 110 mg/dl (or on treatment for diabetes mellitus).

and explained about the purpose of the study. Those who provided informed consent were included. Socio-demographic and clinical details of all the subjects were recorded in structured formats. Body weight was measured in kilograms (kg) and height was measured in centimeters (cm) by a calibrated scale and the Body mass index (BMI) was calculated from the above information. Waist circumference was measured in centimeters (cm), at a point midway between the inferior costal margin and the superior iliac crest, at the end of normal expiration while standing. Standard mercury manometer was used to measure blood pressure (BP) in supine position. Two readings at 5-minute intervals were recorded and if high blood pressure (e"130/85) was noted in one of the readings, then a third reading was taken after 30 minutes; the lowest of these readings was included for analysis. Fasting venous blood sample was collected under aseptic condition to estimate fasting blood sugar (FBS), serum triglycerides (TGA) and serum high density lipoprotein (HDL) levels.

Statistical analysis

The SPSS version 14.0 for Windows (Chicago, Illinois, USA) was used for analysis. Mean and standard deviation were calculated for continuous variables. Frequencies with percentages were calculated for nominal and ordinal variables. Chi-Square and t-tests were used for comparisons, and a binary logistic regression was performed to examine the influence of independent variables on presence of metabolic syndrome.

Results

Sample characteristics

The socio-demographic and clinical profile of patients is shown in table 1. Selective Serotonin Reuptake Inhibitors (SSRIs) as a group were the most commonly prescribed antidepressants, while venlafaxine was the most common antidepressant agent used. Twenty subjects were also receiving concomitant antipsychotic agent, olanzapine (n=9) and risperidone (n=7) being the commonest. Only one subject received augmentation with lithium.

Metabolic parameters

As shown in table 2, 44% (N=73) subjects fulfilled the modified NCEP-ATP III criteria for metabolic syndrome and 41.6% (N=69) subjects fulfilled IDF criteria. Among the metabolic syndrome criteria, waist circumference was the most common criteria (69%) followed by high blood pressure or preexisting hypertension (51.2%) and low HDL levels (45.8%). Abnormal fasting blood glucose level was the least common abnormality seen (28.9%). Besides 73 patients having metabolic syndrome, another 51 patients (30.7%) fulfilled 2 criteria of metabolic syndrome and another 31 patients (18.7%) satisfied at least 1 criterion of metabolic syndrome.

There was no difference in the prevalence of MS between male and female patients. However, in terms of various subcomponents of MS, abnormal blood pressure and high

Table 1: Socio-demographic and clinical profile of patients (N=166)

Variable	Mean±SD/ Frequency (%)
Age (years)	43.42 ± 13.41
Education (years)	11.45 ± 4.66
Total duration of illness (in months)	95.73 ± 90.68
Gender	
Male	79 (47.6%)
Female	87 (52.4%)
Marital status	
Currently	34 (20.5%)
Single Married	132 (79.5%)
Occupation	
Working/Household work	151 (91.0%)
Not working	15 (9.0%)
Religion	
Hindu	129 (77.7%)
Non-Hindus	37 (22.3%)
Family type	
Nuclear	104 (62.7%)
Non- nuclear	62 (37.3%)
Locality	
Urban	105 (63.6%)
Rural	61 (36.7%)
Antidepressants	
Sertraline	28 (16.9%)
Escitalopram	23 (13.9%)
Fluoxetine	17 (10.2%)
Mirtazapine	17 (10.2%)
Venlafaxine	45 (27.1%)
Imipramine	11 (6.6%)
Other antidepressants	24 (14.5%)
Combination antidepressant	4 (2.4%)
Antipsychotics	20 (12.1%)
Mood stabilizers	1 (0.6%)

triglyceride levels were more prevalent in males compared to females, whereas lower HDL levels and higher waist circumference levels were more common in females.

Table-3 provides details of mean values of various anthropometric measures, blood pressure, lipid profile and fasting blood glucose levels.

Relationship of Metabolic syndrome to sociodemographic variables, anthropometry and clinical variables

As shown in table 4, compared to patients without MS, patients with MS were older, belonged to urban locality, were less frequently receiving sertraline, more frequently had higher BMI and BMI more than 25. When the major groups of medications received were analyzed in terms of dose, duration and cumulative medication exposure (dose x duration of intake), as shown in table 5, no significant differences was seen for duration, dose or cumulative dose of serteraline, escitalopram and venlafaxine, which were the major medication groups in the study sample.

Predictors of Metabolic syndrome

Binary logistic regression analysis was used to assess the predictors of metabolic syndrome. All variables which had statistically significant difference in the comparison analysis were considered. As shown in table 6, metabolic syndrome was significantly predicted by marital status, urban locality and higher BMI. Among the various components of metabolic syndrome, high waist circumference had the highest predictive value, followed by abnormal triglyceride levels, raised blood pressure, high fasting glucose levels and low high density lipoproteins levels had the least predictive value.

Discussion

To our knowledge, this is the first study from India which has evaluated the prevalence of metabolic syndrome in patients of depressive disorders. It is important to understand the relationship between depression and risk for the metabolic syndrome because a history of depression predicts future risk for heart disease.[7] The sociodemographic profile of patients included in the present study is fairly representative of depressed patients seen in our set up[25,27] and other parts of India.[28] The lipid

Table 2: Metabolic parameters

Variable	Total sample (n=166)	Males (n=79)	Females (n=87)	Chi-square value (p)
Systolic BP ≥ 130 mm Hg	76 (45.8%)	43 (54.4%)	33 (37.9%)	4.54* (p=0.033)
Diastolic BP ≥ 85 mm Hg	63 (38.0%)	40 (50.6%)	23 (26.4%)	10.29*** (p=0.001)
Abnormal BP (≥130//≥85) or diagnosed as having hypertension	85 (51.2%)	50 (63.3%)	35 (40.2%)	8.81** (p=0.003)
TG levels ≥ 150 mg or on lipid lowering agents	68 (41.0%)	39 (49.4%)	29 (33.3%)	4.40* (p=0.036)
Lower HDL (<40 mg M, <50 mg F) or on lipid lowering agents	76 (45.8%)	26 (32.9%)	50 (57.5%)	10.06** (p=0.002)
FBG levels ≥100 mg % or diagnosed as DM	48 (28.9%)	26 (32.9%)	22 (25.3%)	1.17 (p=0.27)
Abnormal Waist circumference (>90 cm for males and >80 cm for females)	115 (69.3%)	48 (60.8%)	67 (77.0%)	5.13* (p=0.02)
MetS as per IDF	69 (41.6%)	31 (39.2%)	38 (43.7%)	0.33 (p=0.55)
MetS as per modified NCEP ATP-III (with FBS >100 mg %)	73 (44.0%)	34 (43.0%)	39 (44.8%)	0.05 (p=0.81)

BP – Blood pressure; DM – Diabetes mellitus; FBG – Fasting blood glucose; HDL – High density lipoprotein; HTN – Hypertension; MetS – Metabolic syndrome; TG – Triglycerides; WC – Waist circumference

Table-3: Mean values of various anthropometric measures, blood pressure, lipid profile and fasting blood glucose levels

Variable	Mean ±SD
Body Weight (kg)	68.48 ±17.52
Height (cm)	163.67 ±8.71
Body mass index	25.50 ±6.32)
Waist circumference (cm)	91.11 ±15.01
Systolic Blood pressure (mm Hg)	122.87 ±13.97
Diastolic blood pressure (mm Hg)	80.57±9.35
Triglyceride levels (mg/dl)	155.32±70.42
High density lipoprotein (HDL) levels (mg/dl)	46.28 ±9.41
Low density lipoprotein levels (mg/dl)	110.90±33.50
Total Cholesterol levels (mg/dl)	185.49±42.95
Fasting blood Glucose levels (mg/dl)	97.83 ±32.21

profile of the patients included in the present study is also comparable to the lipid profile reported for depressed patients in one of the previous studies from our centre.[25]

The prevalence of metabolic syndrome in the present study was found to be 42-44%. This finding is in the range of prevalence rate reported in previous studies from the West. [6,16,17] When we compare the findings of the present study with a community-based study in our catchment area, the prevalence rates of metabolic syndrome [35.8% (NCEP ATP III), 45.3% (modified NCEP

Table-4: Comparison of patients with and without metabolic syndrome as per modified NCEP-ATP-III

Variable	Subjects with MetS (N=73) Mean ± SD/ Frequency (%)	Subjects without MetS (N=93) Mean±SD/ Frequency (%)	t-test/ Chi-square value
Age in years	48.47 ± 12.17	39.80 ± 13.06	4.51 (p<0.001)
Education in years	11.69 ± 4.46	11.25 ± 4.83	0.64 (p=0.547)
Locality-Urban	56 (76.7)	49 (52.7)	10.15 (p=0.001)
Occupation- Employed/household	69 (94.5)	82 (88.2)	2.00 (p=0.15)
Duration of illness	104.71 ± 95.47	89.36 ± 87.18	0.96 (p=0.33)
Sertraline	7 (9.6)	21 (22.6)	4.92 (p=0.027)
Escitalopram	11 (15.1)	13 (14.0)	0.03 (p=0.84)
Fluoxetine	7 (9.6)	11 (11.8)	0.21 (p=0.64)
Venlafaxine	23 (31.5)	24 (25.8)	0.65 (p=0.41)
Mirtazapine	8 (11.0)	10 (10.8)	0.00 (p=0.96)
Imipramine	7 (9.6)	4 (4.3)	1.84 (p=0.17)
Other antidepressant	12 (16.4)	12 (12.9)	0.41 (0.52)
Antipsychotic –Yes	8 (11.0)	12 (12.9)	0.14 (p=0.70)
Body Mass index	27.62 ± 7.35	23.82 ± 4.76	4.00(p<0.001)
BMI (Asian cutoff)- e” 25	48 (65.8)	30 (32.3)	18.42(p<0.001)

4 subjects received combination of antidepressants (two in each group); Only one subject not fulfilling the criteria for metabolic syndrome had received lithium (no other subject received any other mood stabilizer)

Table-5: Comparison of patients with and without metabolic syndrome

Variable	Subjects with MetS Mean ± SD/	Subjects without MetS Mean ± SD	Mann-Whitney U test
Serteraline	**N=7**	**N=21**	
Duration of serteraline use	22.00 ± 19.98	28.20 ± 31.94	0.00 (p=1.0)
Dose of serteraline	114.29 ± 24.39	125.0 ± 45.16	– 0.760 (p=0.447)
Cumulative dose of serteraline	2842.90 ± 3096.16	3455.00 ± 4064.99	– 0.083 (p=0.934)
Escitalopram	**N=10**	**N=12**	
Duration of escitalopram use	30.90 ± 19.90	25.17 ± 17.14	– 0.618 (p=0.537)
Dose of escitalopram	14.01 ± 6.91	15.42 ± 4.50	– 1.03 (p=0.305)
Cumulative dose of escitalopram	479.09 ± 439.94	416.67 ± 319.30	– 0.154 (p=0.878)
Venlafaxine	**N=22**	**N=21**	
Duration of venlafaxine use	21.23 ± 32.09	15.71 ± 21.66	– 0.171 (p=0.864)
Dose of venlafaxine	175.52 ± 42.33	142.83 ± 56.44	– 1.878 (p=0.060)
Cumulative dose of venlafaxine	3607.6 ± 5238.97	2033.1 ± 2969.34	– 0.791 (p=0.429)

ATP III) and 39.5% (IDF criteria)] is more or less equal to the findings of the general population. [29] However, it must be remembered that in this study patients were not screened for depression and it is possible that some of these patients may be having depression and other psychiatric disorders which would have remained undiagnosed and would have influenced the prevalence of metabolic syndrome.

Increased waist circumference was the most common abnormality seen in the present study,

Table-6: Simple binary logistic regression analysis showing predictors of metabolic syndrome as per NCEP-ATP III criteria

	B	SE	df	Wald	Odds Ratio	p	Confidence interval
Age	0.05	0.01	1	16.63	1.058	< 0.001	1.030-1.087
Locality	1.08	0.34	1	9.81	2.958	0.002	1.501-5.830
Age of onset	0.04	0.01	1	8.71	1.045	0.003	1.015-1.075
Body mass index	0.15	0.04	1	14.03	1.165	< 0.001	1.076-1.262
Body mass index e" 25	-1.39	0.33	1	17.66	4.032	< 0.001	0.129-0.475
Abnormal Waist circumference (> 90 cm for males & >80 cm for females)	2.86	0.55	1	26.77	17.62	< 0.001	5.94-52.25
Abnormal BP (≥130//≥85) or diagnosed as having hypertension	1.98	0.35	1	31.03	7.27	< 0.001	3.61-14.60
TG levels ≥150 mg or on lipid lowering agents	2.07	0.35	1	33.52	7.95	< 0.001	3.94-16.04
Lower HDL (<40 mg M, <50 mg F) or on lipid lowering agents	1.60	0.33	1	22.61	4.99	< 0.001	2.57-9.68
FBG levels ≥100 mg % or diagnosed as DM	1.88	0.38	1	23.54	6.56	< 0.001	3.07-14.04

this was followed by higher blood pressure. This is in keeping with previous studies which have shown that depression is most commonly associated with abdominal obesity, [4,6] hypertension.[11,12]

In the present study, certain differences were seen in the prevalence of various subcomponents of metabolic syndrome among males and female. Male patients had significantly higher prevalence of raised blood pressure and raised triglyceride levels, whereas female patients had significantly higher prevalence of raised waist circumference and lower high density lipoprotein levels. Higher prevalence of increased waist circumference in female depressed patients is supported by the findings from the West[30]. Studies from the West also support the finding of higher prevalence of lower high density lipoprotein levels in depressed women,[4,6,18] but the findings of higher prevalence of raised blood pressure and triglyceride levels in males is in contradiction to some of studies from the West.

Taken together findings of the present study and literature suggest that it is important to study the influence of gender on various sub components of metabolic syndrome.

In the present study, besides the sub-components of metabolic syndrome, BMI more than 25 was the strongest predictor of metabolic syndrome and similar association has also been reported earlier.[31]Thus, it is logical to assume that weight gain contributes most to the development of MS.

Among the various sociodemographic variables, urban locality emerged as a significant predictor of metabolic syndrome. This finding is line with that reported by Ravikiran et al, [29] which evaluated the prevalence of metabolic syndrome in Indian setting. This could be due to the life style and dietary factors. Studies from the West suggest that metabolic syndrome is more prevalent in depressed women, but findings of the present study do not support the same.[30,32,33]

When we examined the predictive value of

individual subcomponents of metabolic syndrome, it was seen that increased waist circumference had the highest predictive value. The predictive value of abnormal triglyceride levels and high blood pressure was nearly same.

Although the number of patients on each antidepressant medications was small, findings of the present study suggest that antidepressants have no influence on the prevalence of various subcomponents of metabolic syndrome or metabolic syndrome per se. This is in agreement with the exsiting literature. [34,35]

We are aware of the limitations of the present study namely a cross-sectional design and lack of healthy control group. Although we did not exclude patients with various comorbidities, the data were not recorded for comorbidities. Similarly, data for drug abuse were not recorded. The relationship between the severity of illness, residual symptoms, treatment refractoriness and life style and prevalence of MS was also not studied. Future studies should try to overcome these limitations.

To conclude, the present study reveals that about 42-44% of patients with unipolar depressive disorder have metabolic syndrome. Metabolic syndrome in unipolar depression is predicted by urban locality and higher BMI. Higher body mass index had the highest odds ratio of predicting MS. With respect to components of MS, higher waist circumference and high blood pressure were present more frequently than other components and high predictive value for full metabolic syndrome. These findings imply that monitoring body mass index, waist circumference and blood pressure can be useful in monitoring the development of possible metabolic syndrome in unipolar depression patients.

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