Research Paper

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Prevalence of metabolic syndrome in drug naïve bipolar affective disorders- A study from South East Asia (Kashmir)

Medical Science

KEYWORDS : Bipolar affective disorder, Mental illness, Metabolic syndrome, Risk factors

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ABSTRACT

Background: Over the last few decades, there has been a drastic change in life style and behavior, leading to dramatic increase in the metabolic syndrome in general as well as people with mental illness. Metabolic syndrome adds to the burden of disease and affects the treatment course, outcome and rehabilitation. However, no study has been conducted in drug naïve patients in bipolar patients from this part of world.

Objective : To study the prevalence of metabolic syndrome in newly diagnosed drug naïve bipolar affective disorder patients.

Material and methods: Hundred newly diagnosed patients of Bipolar Affective Disorder Type I who were as yet drug naïve were taken up for study. The diagnosis was confirmed by a consultant psychiatrist according to the criterion given in diagnostic and statistical manual of mental disorders 4th text revision (DSM IV TR) . The NCEP ATP-III (National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria for MS diagnosis was used,

Results: The mean age was 27.8 years. Total males and females came to 62% and 38% respectively. Out of the 14 patients with metabolic syndrome 8 were males i.e., 12.9 % had and 6 were females i.e., 15.8 %.

Conclusion : The high prevalence of metabolic abnormalities as well as the hazards posed by their occurrence invites the need for clinicians to carefully screen all bipolar patients for risk factors related to metabolic abnormalities as well as careful clinical scrutiny for incident disturbances in any metabolic parameter.

Introduction:

Metabolic syndrome (MS) is a complex disorder composed by a set of cardiovascular risk factors that are usually related to central depositing of fat and to insulin resistance[1]. Psychiatric disorders have been shown to be associated with metabolic syndrome in a general way even when controlling for the use of the psychopharmacological agents.[2] Patients with bipolar disorders are reported to have an increased frequency of cardiovascular illness and metabolic syndrome compared with general population[3]. The association of bipolar disorders with obesity, diabetes, dyslipidaemias, and hypertension has been reported.[4, 5, 6] Diabetes mellitus and mania have associated disturbances of the hypothalamic–pituitary–adrenal axis, [7,8]. Moreover, the suprachiasmatic nucleolus of the hypothalamus has been implicated both in disturbances of the sleep – wake cycle noted during mania[8] and in the regulation of glucose metabolism[9]. Psychotropic medications, such as valproate and lithium, and antidepressants which themselves leads to weight gain, remain a confounding factor.[9] Since there is significant data available on association of mental disorders with lifestyle diseases like diabetes mellitus, coronary artery disease, obesity, hypertension etc, we hypothesize that forme fruste of manifestations (i.e., components of Metabolic Syndrome) of these lifestyle diseases may originate from disorders of psychological origin. Therefore we plan to study the prevalence of the components of metabolic syndrome in patients suffering from Bipolar Affective Disorders before drug therapy is started in them.

Materials and methods :

The study was conducted in Government Psychiatric Diseases Hospital Srinagar which is an associated hospital of Government Medical College Srinagar. All newly diagnosed patients of Bipolar Affective Disorder who were as yet drug naïve were taken up for study. The diagnosis was confirmed by a consultant psychiatrist according to the criterion given in diagnostic and statistical manual of mental disorders 4th text revision (DSM IV TR) .[10] Informed consent was obtained from each patient; those who were considered incapable of consenting only participated with the consent of their closest family member or custodian. The Modified NCEP ATP-III criterion for MS diagnosis was used, [11] and The results were subjected to appropriate statistical methods.

INCLUSION CRITERION

- All firstly or newly diagnosed drug naive patients.
- Both sexes were included.

EXCLUSION CRITERION

- Presence of pregnancy or a history of pregnancy in the last six months.
- Those who had taken antipsychotics or mood stabilizers previously.
- Presence of any prior psychiatric disorder.
- If diagnosis was not clear.

Results :

Table 1 shows Age distribution

Age group	Number (%)	ATP-III modified NCEP
16-25 years	45 (45%)	Nil
26-35 years	38 (38%)	5(13.15%)
36-45 years	14 (14%)	6 (42.86%)
46+ years	3 (3%)	3 (100%)

45% of the patients were younger than 25 years,38% between 26 to 35 year while only 17% were older than 36 years.

Table 2 : Showing mean age and SD

	Case	Control
Mean age	27.8	25
SD	9	8

Table 3 : Prevalence of metabolic syndrome in Male case vs. control

Males	Cases	Control	
Metabolic syndrome	8 (12.90%)	2(2.9%)	Chi-Square= 4.636, P= 0.046 (Sig)
No Metabolic syndrome	54 (87%)	67(97.1)	

Females	Cases	Control	Chi Square= 0.56, P=.50 (Non sig)
Metabolic syndrome	6(15.8%)	3(9.68%)	
No Metabolic syndrome	32(84.2%)	28(90.32%)	
Metabolic syndrome (Male + Female)	14(14%)	5(5%)	

Table 4 : Prevalence of metabolic syndrome in case vs control

Metabolic syndrome	Cases	Control	Chisquare =11.206 P=0.004
No Metabolic syndrome	57 (57%)	75 (75%)	
Some Metabolic syndrome	29(29%)	20 (20%)	
Metabolic syndrome	14 (14%)	3 (5 %)	

Distribution of patients (NCEP ATP-III modified for Asians)

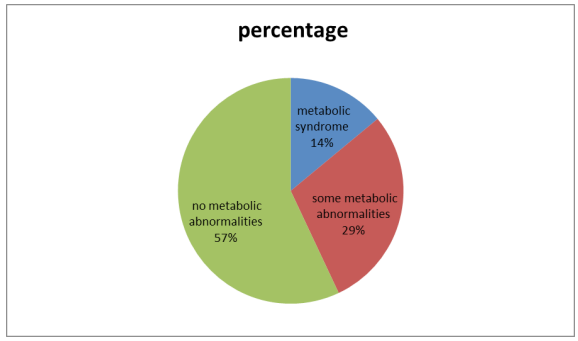
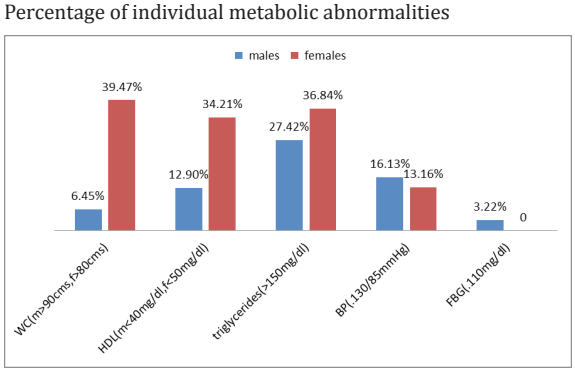


Table 5 : Prevalence of metabolic abnormalities in bipolar patients

Metabolic parameters		Total number of patient with abnormalities	Males (%)	Females (%)
Waist circumference	Males>102cms, females >88cms	4 (4%)	nil	4 (10.52%)
	Males>90cms, females>80cms (modified)	19(19%)	4(6.45%)	15(39.47%)
High density cholesterol (<40mg/dl males,<50mg/dl females)		21 (21%)	8 (12.90%)	13 (34.21%)
Triglycerides(>150mg/dl)		31 (31%)	17 (27.42%)	14 (36.84%)
Blood pressure ≥ 130/85 mmHg		15 (15%)	10 (16.13%)	5 (13.16%)
Fasting plasma glucose ≥ (110 mg/dl)		2 (2%)	2 (3.22%)	Nil

31% patients had increased levels of triglycerides,21% had decreased HDL levels, 15% had high blood pressure, 2% had hyperglycemia, while 4% had abdominal obesity using NCEP-ATPIII criterion. But 19% had abdominal obesity using modified criterion.

Percentage of individual metabolic abnormalities



Discussion

Psychiatric disorders are among the leading causes of global morbidity.[12] Patients with bipolar disorders are reported to have an increased frequency of cardiovascular illness compared with general population.[3] The bulk of the research on metabolic syndrome shows that the use of the psychopharmacological agents, especially the newer ones, is associated with metabolic side effects such as weight gain, and deranged glucose tolerance and lipid profiles[13]

In our study we tried to eliminate the effects of psychotropic drugs as they are known to cause weight gain and alteration of other metabolic parameters. We found prevalence of metabolic syndrome as 14% with modified NCEP ATP-III criterion. Taylor et al[14] studied 24 newly diagnosed bipolar patients which drug naive and found that 11.2% of patients met the diagnostic criteria for metabolic syndrome at baseline. This was in accordance to our study. Sircas et al[15] found 24.7% metabolic syndrome (NCEP ATP-III) in a group of 178 patients who were on treatment. The mean age was 45.5 yrs. As mean age of our sample was 27.8 years and our population was not on medications which can explain the higher prevalence in the study by Sircas[15] et al. Atypical antipsychotics and mood stabilizers may result in additional risk for obesity and associated metabolic abnormalities in bipolar patients.[16]

Winkel et al (2008) [17] studied 60 bipolar patients for and found prevalence of metabolic syndrome of 16.7% . This suggests that factors other than treatment itself may be responsible for excessive weight in persons with bipolar affective disorder.[18] CEP ATP-III, 18.3% with adapted NCEP ATP-III (fasting blood glucose >100mg/dl). Our study showed similar trends with prevalence of 14% with NCEP ATP-III modified for Asians even when the patients in the sample taken by Winkel et al were taking mood stabilizers, antipsychotics and antidepressants. As atypical antipsychotics have been reported to be associated with a high prevalence of metabolic abnormalities.[19,20]

Garcia-Portilla[3] found prevalence of metabolic syndrome as 22.4% in a sample of 194 patients using NCEP ATP-III criterion. These patients were taking an average of three psychotropic drugs and the mean age of this sample was 46.6 years, while patients in our sample were not taking drugs and were younger with mean age of 27.8 years. Psychotropic drugs are known to cause weight gain and metabolic syndrome and also as the age increases there is increase in the rate of MS. Chang et al[21], found a prevalence of 33.9% by using IDF 2005 criterion for metabolic syndrome in 117 bipolar patients most of whom were taking lithium and valporate. As some of these patients were taking psychotropic drugs which can also leads to metabolic syndrome and also IDF criteria take fasting blood sugar >100 mg/dl as cut off, while NCEP ATP-III takes fasting blood sugar >110 mg/dl as cut off which we were using. This can explain high prevalence in the study by Chang et al[21]. Fagiolini et al[22] found prevalence of metabolic syndrome of 30% in a sample of 171 bipolar patients using NCEP ATP-III criterion. As these patients were not drug naïve, they showed high prevalence of MS. This suggests that factors other than treatment itself may be responsible for excessive weight in persons with bipolar affective disorder.

Individual components of metabolic syndrome

Waist circumference

On applying modified NCEP criterion, 19% patients had abdominal obesity (W.C. >90 cms in males and >80 cms in females) which consisted of 6.45% of males and 39.47% of females. Garcia-Portilla et al[3], reported prevalence of 54% abdominal

obesity (modified NCEP ATP-III) in 194 bipolar patients on medications. Fagiollini et al[22], reported prevalence of 49% for abdominal obesity (unmodified NCEP ATP-III) in 171 bipolar patients on treatment. Chang et al [21] found 61% prevalence of large waist circumference (IDF 2005) in 117 bipolar patients on lithium or valproate. Winkel et al 17 found 30% abdominal obesity with more obesity in females. The patients in these three studies were already taking psychotropic drugs. The use of psychopharmacological drugs leads to weight gain.[13] Other reasons may be the more sedentary lifestyle of people in these developed countries as compared to our population. Women had more prevalence of abdominal obesity in our study. This in accordance with study by Fleet et al[23] and winkel et al[17] who found higher abdominal obesity in females.

HDL levels

In our study on applying NCEP ATP-III criterion, 21% of patients met the criterion for low HDL levels(less than 50 mg/dl for females and less than 40 mg/dl for males). 12.9% males and 34.21% females met this criterion. Fagiollini et al[22], reported 23% met criterion for low HDL (NCEP ATP-III) in 171 bipolar patients on treatment which is in accordance with our study. Similarly Winkel et al[17] found 21.7% with low HDL levels using ATP-III. Garcia-Portilla et al[3], reported 38.2% met criterion for low HDL (NCEP ATP-III) in 194 bipolar patients on medications. Chang et al[21] found 53% prevalence of low HDL (IDF 2005)in 117 bipolar patients on lithium or valporate and Sircas et al[15] found 54.5% prevalence of low HDL. Patients in these studies were taking mood stabilizers and other antipsychotics which also lead to abnormalities in lipid profile.[24]

Triglycerides level

Similar is the case with hypertriglyceridemia where we have comparable results, even though our patients were drug naive. In our study on applying NCEP ATP-III criterion, 31% of the patients met the criterion for hypertriglyceridemia out of which 27.42% males and 36.84% females met criterion for hypertriglyceridemia (TG >150 mg/dl). Sircas[15] found 23% of the patients with high triglyceride levels in a sample of 178 BPAD patients which was almost same as in our study.Winkel et al found 26% patients with high triglycerides level (ATP-III) in a sample of 60 BPAD patients.[17] Garcia-Portilla et al[3], reported 36.1% met criterion for hypertriglyceridemia (TG >150 mg/dl) as per NCEP ATP-III in 194 bipolar patients on medications. Chang et al found 36.8% prevalence of hypertriglyceridemia (IDF 2005)in 117 bipolar patients on lithium or valporate. Fagiollini et al[22], reported that 48% met criterion for hypertriglyceridemia (NCEP ATP-III) in 171 bipolar patients who were on psychotropic drugs.

Hypertension

In our study on applying NCEP ATP-III criterion, 15% patients met criterion for hypertension (>130/85 mm of Hg). 16.13% males and 13.16% females met criterion for hypertension. This is in accordance with Chang et al[21] who found 18.6% prevalence of hypertension (IDF 2005) in 117 bipolar patients on lithium or valporate. Garcia-Portilla et al[3], reported 20.9% out of 194 bipolar patients on medications met criterion for hypertension (NCEP ATP-III). Fagiollini et al[22], reported 39% out of 171 bipolar patients on treatment met criterion for hypertension (NCEP ATP-III). The reason for high prevalence of hypertension in this study may be the effect of drugs and also the mean age of the sample in this study by Fagiolini was 46.9 years while mean age of our sample was 27.8 years. Increased age is also associated with a significant increase in the prevalence of hypertension and especially of systolic hypertension after age 60 years.[25]

Fasting blood glucose

In our study on applying NCEP ATP-III criterion, 2% patients met criterion for fasting glucose (>110 mg/dl) or taking ant diabetic medications. All of them were males. Garcia-Portilla et al[3], reported 12.2% for high fasting glucose (NCEP ATP-III) in 194 bipolar patients on medications. Fagiollini et al[22], reported 8% met the criterion for high fasting glucose or antidiabetic medication use among 171 bipolar patients on treatment (NCEP ATP-III). Chang et al[21] found 13.7% prevalence of hyperglycemia (IDF 2005) in 117 bipolar patients on lithium or valporate. This discrepancy may be because in all three studies patients were on drugs and antipsychotics may increase the risk for the development of type 2 diabetes in patients with mood disorders.[26] and in study by Chang et al[21] IDF criterion takes fasting blood glucose as >100mg/dl while NCEP ATP-III takes fasting blood glucose as >110mg/dl as cut off for diagnosis of MS.

Conclusion :

Though prevalence of metabolic syndrome was only 14% modified criterion but the individual metabolic abnormalities were even higher in bipolar individuals even before the time of initiating pharmacological treatment. There may be some inherent risk factors for metabolic syndrome in BPAD patients and the effects of medication may further compound that risk. The high prevalence of metabolic abnormalities as well as the hazards posed by their occurrence invites the need for clinicians to carefully screen all bipolar patients for risk factors related to metabolic abnormalities as well as careful clinical scrutiny for incident disturbances in any metabolic parameter. The incorporation of psychosocial treatment strategies that emphasize educational aspects (diet and exercise counseling) related to metabolic risk and medical co morbidity holds promise to reduce the burden of illness and improve outcomes in bipolar disorder.

Limitations : There were a few limitations in our study.

1. First limitation was the cross-sectional design of our study which precludes us from establishing causal relationships among variables.
2. Second, we did not collect detailed information on health habits, such as smoking, use of drugs and alcohol, excessive caloric and cholesterol intake, and physical inactivity, all of which may contribute to the metabolic abnormalities observed.
3. Third limitation is that our study did not include other metabolic parameters, such as insulin levels and BMI which are important constituents of metabolic syndrome.

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