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Original Article

Prevalence and predictors of metabolic syndrome in drug naïve bipolar patients

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1. Introduction

What is metabolic syndrome? Metabolic syndrome is an entity of various clinical abnormalities ranging from hypertension, insulin resistance, dyslipidemia, obesity, impaired glucose regulation, and microalbuminuria [1,2]. Metabolic syndrome contributes to an increased risk of diabetes and myocardial infarction. The International Diabetes Federation criteria for metabolic syndrome include:

1. Central obesity, i.e., waist circumference ≥90 cm in males and ≥80 cm in females (Asian Origin) plus two or more of the following:
2. Two of the following:
   i. Systolic blood pressure (SBP) ≥130 mmHg and/or diastolic BP (DBP) ≥85 mmHg (or on treatment for hypertension)
   ii. Triglyceride (TG) levels ≥150 mg/dl (or on specific treatment for this abnormality)
   ii. High-density lipoprotein (HDL) cholesterol levels ≥40 mg/dl for males and ≥50 mg/dl for females (or on specific treatment for this abnormality)
   iv. Fasting blood glucose (FBG) ≥100 mg/dl (or on specific treatment for diabetes mellitus).

Metabolic syndrome is growing exponentially, especially in India where it has a prevalence of 19–41%, and 19–22% in North India [3]. Bipolar affective disorder (BPAD) ranked 25th most disabling illness globally, and metabolic disturbances rank highly as causes of mortality and morbidity in these patients [4,5]. Studies show that patients with BPAD are at double the risk of developing metabolic syndrome as compared to the general population [6,7]. Consequently, psychiatrists have had to adapt their management protocols for these patients [8].

There are multiple causes which lead to metabolic disturbances: poor dietary habits; substance use, such as alcohol and smoking especially in the acute phase of mania; unhealthy lifestyle and lack of exercise [9]. Treatment typically involves mood stabilizers and antipsychotics [10–3].

There is evidence of HPA axis derangement which is endogenous to bipolar patients [14–6]. There are multiple studies on metabolic syndrome with treatment in BPAD, but there is scant data on metabolic syndrome in drug naïve bipolar patients, which can affect the management of these patients. Current research is focusing on physical well-being as one of the key factors for enhancing and rebuilding mental health. Thus, the aim of this study is to determine the prevalence and predictors of metabolic syndrome in BPAD patients in the northern region in the vicinity of our institute, so that preventive measures can be taken to reduce the amount of burden on our economy by reducing morbidity and mortality in BPAD with current episode mania or depression patients. This study will also provide a base for the holistic approach of BPAD patients that the mental, as well as the physical well-being, needs to be secured so that they can perform well in all aspects of life.

2. Materials and methods

Our study is a cross-sectional study which was conducted in patients with the diagnosis of BPAD with current episode mania or depression as per ICD 10, who were admitted in the psychiatry ward of MMIMSR. We conducted this study after taking ethical committee approval (Reference No. MMU/IEC/2017/595). Patients were enrolled for the study after obtaining written informed consent.

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2.1. Instruments and tools used

1. ICD 10 diagnostic criteria for establishing the BPAD
2. Socio-demographic performa for anthropometric measurement used in our department.
3. Weight, waist circumference, and BP assessment were done by using the standard protocol
4. FBG, TGs, HDL cholesterol, low-density lipoprotein (LDL) cholesterol was measured by taking venous sample under aseptic conditions

2.2. Inclusion criteria

· Patients who were admitted to the psychiatry ward of MMIMSR
  ☐Patients who have voluntary consent for the study
  ☐Patients in the age group of 25–80 years (both males and females).
  ☐Patients with a diagnosits of bipolar mania or depression as per ICD 10.
  ☐Drug native patients, i.e., patients who either never received any antipsychotics or mood stabilizers for more than two weeks and not so in last three months; which was ascertained by information gathered from patients and their caregiver and wherever available, the reveiw of treatments records.

2.3. Exclusion criteria

☐Patients with a comorbid psychiatric illness.
☐Patients with comorid mental reterdation.
☐Patients with a comorbid physical illness that can influence the metabolic profile like diabetes mellitus, hypertention, thyroid disorder,etc.
☐Pragnant females.

2.4. Statistics

Findings were analyzed by using chi-square and *t*-test.

3. Results

3.1. Socio-demographic profile (Table 1)

A total of 30 patients (18 females and 12 males); 16 belonged to bipolar mania (53.3%); 14 (46.67%) to bipolar depression. Most were unskilled professionals (28; 93.3%), educated up to higher standards (10), were married (18), were Hindu (20).

3.2. Metabolic profile

Only 2 patients had SBP >130 mmHg, 18 had DBP >85 mmHg, 3 had FBG >100 mg%, 8 had TGs >150 mg%, 23 had HDL <50 mg%, 16 females and 7 males had waist circumference >80 and > 90 cm respectively. Most of the patients were diagnosed with bipolar depression (Table 1). The mean of all the parameters is shown in Table 2. All findings were statistically insignificant.

3.3. Predictors of metabolic syndrome

A total of 10 patients (33.33%) had metabolic syndrome. Seven (70%) belonged to bipolar depression although it was statistically insignificant (Table 3). BP and HDL cholesterol were significant determinants of metabolic syndrome in BPAD mean of SBP/DBP 1 and 2 of 123.21/87.11 and 122.22/85.33 mmHg respectively, and for HDL 35.77 mg%, this was statistically significant at p-value <0.05 (Table 4). It was found that all patients with metabolic syndrome had a high waist circumference and low HDL cholesterol. Six patients had high DBP, 5 had high TGs, three high FBG and only 2 had high SBP (Table 5).

Mean SBP1/DBP1 of $126 \pm 5.29/90 \pm 3.26$, SBP2/DBP2 of $125.33 \pm 3.77/88 \pm 1.63$, HDL 35 ± 2.4 in bipolar manic patients (Table 6). SBP1/DBP1 $119.42 \pm 12.89/84.57 \pm 10.37$, SBP2/DBP2 of $117.42 \pm 11.78/83.42 \pm 8.77$, HDL 37.14 ± 6.36 in bipolar depression (Table 6).

4. Discussion

4.1. Demographic parameters

Certain components of metabolic syndrome are modifiable risk factors, so if we modify them at an early age, we can revert the train of metabolic syndrome which is leading towards dangerous situations like cardiovascular problems, cardiovascular accidents, diabetes mellitus, and ultimately death. Previous studies have focused upon metabolic syndrome in bipolar patients who were on treatment with antipsychotics or mood stabilizers, and insufficier-esearch work is available on metabolic syndrome in drug-free bipolar patients. Moreover, we could not find any study which has compared the risk of metabolic syndrome in bipolar mania versus bipolar depression, so we conducted it.

Our study consisted of a predominantly female (male: female 12:18) which is going with a study done by Weissman [17] showing female predominance in BPAD. While there was a study showing the predominant male picture, which can be explained by the fact that particular research was done in military veterans.

Most of the patients belonged to Hindu community as the study was conducted in Haryana where majority population belongs to Hindu community as shown in 2011 census [18].

We have seen that in our study most of the patients were married which is contrary to the finding of a study done by Weismann et al. [17]. Showing that BPAD is more common in the unmarried population. This inconsistency can be explained by the fact that this study was done in the USA where marriage is not an issue of prime importance, while in India, marriage is considered as panacea [19] for mental illness; thus Indian people tend to marry their children with the belief that marriage will relieve their illness.

Our study shows that most of the patients belonged to unskilled professionals and more than half of the patients belonged to bipolar mania which is consistent with a study which showed that unskilled profession was predominant in bipolar patients [20].

In our study, we have seen that most of the patients were educated up to higher standards which is similar to a study [21] showing the same finding that bipolar is more common in the education of 10 t h class. This can be explained by the fact that educated people prefer more to have medical services for their illness than less educated people.

In our study, we have seen that the mean age is 32 years which was 31.67 ± 8.44 years in manic patients while it was 32.28 ± 8.72 years in bipolar depressives. There was a study [22] done showing the age of onset in bipolar patients was 26 years. This inconsistency can be explained by the fact that our study included only drug naïve bipolar irrespective of the duration of illness or number of past episodes while the other study included first reporting of symptoms of the illness thus they are younger.

Moreover, our study is conducted in India and that too in the northern region where there is little awareness of mental illness, due to stigma. Before visiting a psychiatrist, many people visit faith

Table 1
Socio-demographic profile of the sample.

				ICD -10		Total	Chi-square value	P-value
				Bipolar mania	Bipolar depression			
Socio-demographic Profile	Sex		FEMALE	8	10	18	1.42	0.232
			MALE	8	4	12		
	Occupation		UNSKILLED	15	13	28	0.0095	0.26
			SEMI SKILLED	1	1	2		
			SKILLED	0	0	0		
	Education		UNEDUCATED	2	2	4	5.42	0.24
			PRIMARY	2	6	8		
			SECONDARY	3	3	6		
			HIGHER	8	2	10		
			GRADUATE	1	1	02		
	Marital Status		MARRIED	9	9	18	0.20	0.65
			SINGLE	7	5	12		
	Religion		HINDU	12	8	20	1.07	0.30
			MUSLIM	4	6	10		
			SIKH	0	0	0		
Blood Pressure and individual Metabolic Parameters	SBP		≤130 mm Hg	16	12	28	2.44	0.11
			≥130 mm Hg	0	2	02		
	DBP		≤85 mmHg	13	9	22	1.09	0.29
			≥85 mmHg	3	5	8		
	FBS		≤100 mg/dl	15	12	27	0.53	0.46
			≥100 mg/dl	1	2	03		
	TG		≤150 mg/dl	14	8	22	2.06	0.15
			≥150 mg/dl	2	6	8		
	HDL		≥50 mg/dl	5	2	7	1.20	0.27
			≤50 mg/dl	11	12	23		
	Waist Circumference	F	≥80 cm	7	9	16	0.02	0.86
			≤80 cm	1	1	2		
		M	≥90 cm	5	2	7	0.17	0.67
			≤90 cm	3	2	5		

Table 2
Metabolic profile.

Mean	Sample	Bipolar Mania		Bipolar Depression		P-VALUE
	Mean ± SD	Mean	SD	Mean	SD	
Age	31.9 ± 8.36	31.67	8.44	32.28	8.72	0.97
Height	159.2 ± 9.4	161.81	10.92	156.14	11.2	0.28
Weight	89.4 ± 10.6	88.68	11.89	90.142	12.89	0.82
Waist circumference	91.3 ± 9.	90.75	8.93	91.85	9.22	0.73
SBP -1	116.73 ± 9.22	115.50	6.63	118.14	11.62	0.72
DBP − 1	81.13 ± 8.33	80.00	8.70	82.35	8.47	0.41
SBP - 2	116.00 ± 8.85	115.00	6.61	117.14	11.03	0.74
DBP - 2	80.66 ± 7.71	79.37	7.75	82.00	7.68	0.53
FBS	92.20 ± 16.63	89.87	19.13	94.85	13.44	0.12
Triglycerides	126.81 ± 56.99	119.87	55.32	134.71	59.9	0.53
HDL	41.60 ± 9.18	43.25	10.25	39.71	7.73	0.50
Cholesterol	155.13 ± 52.35	141.25	26.90	171.00	69.06	0.47
LDL	92.13 ± 37.28	78.25	18.35	108.00	46.94	0.10
VLDL	24.83 ± 14.18	23.06	12.64	26.85	16.00	0.92

Table 3
Prevalence of metabolic syndrome in BPAD.

		Bipolar mania	Bipolar depression	Total	P value
Metabolic syndrome	Absent	13	7	20	0.12
	Present	3	7	10	

healers and physicians, and psychiatrist consultation is a choice only after no response is received from the faith healers/physicians.

4.2. Metabolic parameters

4.2.1. Lipid parameters

In our study, the most common abnormality was low HDL cholesterol, recorded in 23 patients (76.6%). There was a study with inconsistent finding where low HDL cholesterol up to 40%. This disparity can be explained by the fact that this study was conducted in Spain [23], while ours was in India and both country's population has different physiological and biochemical pathways, thus have different biochemical parameters.

It was found that mean HDL in bipolar mania was 43.25 ± 10.25 while it was 39.71 ± 7.73 in bipolar depression. Consistent results [3] were seen where low HDL cholesterol was the most common

Table 4
Predictors of metabolic syndrome.

	WITHOUT MS		WITH MS		P-VALUE
	Mean	SD	Mean	SD	
Age	30.47	8.12	35.42	8.84	0.15
Height	158.76	10.23	160.11	7.54	0.48
Weight	87.14	11.16	94.55	7.50	0.14
Waist circumference	91.14	10.20	91.55	8.23	0.85
SBP -1	114.00	5.22	123.21	13.27	**0.02**
DBP -1	78.85	7.26	87.11	9.27	**0.02**
SBP -2	113.33	5.30	122.22	12.30	**0.02**
DBP -2	78.85	6.87	85.33	7.84	**0.03**
FBS	88.09	7.94	101.77	26.42	0.36
Triglycerides	116.23	48.38	151.44	70.34	0.18
HDL	44.09	9.48	35.77	5.16	**0.02**
Cholesterol	150.23	53.48	166.55	50.73	0.35
LDL	89.09	37.47	99.22	38.01	0.52
VLDL	23.28	13.59	28.44	15.70	0.32

abnormality in patients with metabolic syndrome with a mean of (it is for mean value) 42.7 ± 13.3 [19,24].

High TGs were present in 8 patients (26.6%), and it was 3rd most common finding with mean TG level of 119.87 ± 55.32 in mania and 134.71 ± 59.9 in bipolar depression. Consistent results were seen in a meta-analysis [23–5] showing the TGs in various studies of BPAD patients ranging from 22.7–58.8%. Comparable results [24] were also found for TGs <150 mg% with a mean of 141.3 ± 6.64 mg%. Inconsistent results were seen in a meta-analysis [26] showing that approximately 40% of the patients had hypertriglyceridemia which can be explained by the fact that the meta-analysis included mixed, i.e., both drug-free patients as well as those on bipolar drugs. Also, studies have shown that patients who are on treatment have high TGs as compared to those who are drug-free, which might have raised this percentage up to 40% as compared to our finding of 26.6%.

We have seen in our study that mean cholesterol levels were 155.13 ± 52.35 mg% (141.25 ± 26.90 in mania and 171.00 ± 69.06 in depression). Comparable results were observed in bipolar drug-naïve patients for total cholesterol, with a mean of 163.0 ± 41.9 mg %.[24]There are inconsistent findings [7] for the same with cholesterol level 190.8 ± 45.5 mg%. This inconsistency can be explained by the fact that this study did not exclude patients who had previous hypercholesterolemia; 51% of the patient population had a history of hypercholesterolemia were on treatment for the medical disorder, which also can contribute for these high findings.

There was a study done by Kavoor et al. [27] which reported lipid parameters, such as TG, low VLDL, total cholesterol, low LDL, and almost normal HDL cholesterol, low BMI as compared to healthy controls in manic patients. This inconsistency can be explained by the fact that 1. This study was done in drug-free first episode mania only, whereas we have taken just drug naïve bipolar patients irrespective of the duration of illness and irrespective of the number of episodes; 2. This study was conducted exclusively in males while our study included both genders; thus the picture of biochemical parameters must be different. 3. We have not.

The most common abnormality of low HDL can be explained by the fact that Asian-Indians tend towards central obesity. Moreover, our study is a female-predominant picture, and many of them must be around premenopausal and menopausal phase (as estrogen is a protective factor in non-menopausal women) [28–30].

4.2.2. Obesity

WHO [31] has defined obesity on the basis of BMI, as well as by waist circumference, but literature evidences [32] that waist circumference is the best and suitable measure of obesity and thus considered as the best anthropometric measure. High waist circumference remained the second most common finding. There are studies with consistent findings that high waist circumference was amongst the most common results [25,33,34]. This high prevalence of high waist circumference can be explained by the fact that our study was conducted in the north region of India where obesity, in all its types, is more prevalent as compared to the other areas [35].

We have seen that a total of 66.6% patients were fulfilling this criterion of high waist circumference, from them 43.3% females and 23.3% were males. This finding is similar to a systematic review [26] showing that a total of 61% of patients met the criteria of high waist circumference for metabolic syndrome. Comparable results for the mean waist circumference of 88.±11.2 mg% in drug naïve BPAD patients [24].

The mean weight in bipolar patients found to be 89.4 ± 10.6 with mean height 159.2 ± 9.4, consistent values were seen in a study [36] done on drug naïve bipolar patients with the mean weight of 92.7 ± 7 kg, and it was significantly higher than matched controls in that study. Studies have shown that high waist circumference is reported as being the most common abnormality [37].

These higher values of obesity parameters in bipolar patients can be explained [37] by the fact that these patients have physical inactivity, disturbed eating patterns, increased substance consumption for various reasons, and decreased energy consumption all contribute to obesity in acute phases of illness.

4.2.3. Fasting blood glucose

One of the least common findings in our studies was high FBG found in 3 (10%). Consistent results were seen in studies showing that high FBG was the least common finding with frequency up to 12% [3,23-6].

The mean FBG of the study sample was 89.87 ± 19.13 in mania while it was 94.85 ± 13.44 in depression and also it has seen that almost all the patients were bipolar depression. This is consistent with a study which is showing that BPAD patients have three times higher risk [38] of having diabetes mellitus. This fact can be

Table 5
Frequency of individual metabolic parameters in BPAD patients with metabolic syndrome.

	WAIST CIRCUMFERENCE	SYSTOLIC >130 mmHg	DIASTOLIC >85 mmHg	FBS >100 mg/dl	TRG >150 mg/dl	HDL <50 mg/dl
Metabolic present (n = 10)	10	2	6	3	5	10

Table 6
Mean of individual metabolic parameters in BPAD patients with metabolic syndrome.

mean	Mean ± SD SBP1/DBP1	Mean ± SD SBP2/DBP2	Mean ± SD FBS	Mean ± SD TGs	Mean ± SD HDL	Mean ± SD WAIST cms
Bipolar mania	126 ± 5.29/90 ± 3.26	125.33 ± 3.77/88 ± 1.63	109.33 ± 33.62	204.66 ± 70.55	35 ± 2.44	103.33 ± 4.78
Bipolar depression	119.42 ± 12.89/84.57 ± 10.37	117.42 ± 11.78/83.42 ± 8.77	97 ± 18.2	112.57 ± 49.4	37.14 ± 6.36	92 ± 8.30

explained by the research showing that BPAD and diabetes share a common pathophysiological pathway including hypothalamic-pituitary-adrenal and mitochondrial dysfunction, common genetic links, and epigenetic interactions [39]. A consistent finding of mean FBG of 94.6 ± 18.9 in drug naïve bipolar patients [24].

4.2.4. Blood pressure

One of the least common findings in our studies was high SBP/DBP. On reviewing our research, we have seen inconsistent conclusion where it was observed that high BP was one of the most common findings. Moreover, we have seen that mean SBP/DBP was 116.00 ± 8.85/80.66 ± 7.71, with consistent results of the mean of 119 ± 31/78 ± 18 mmHg in drug naïve bipolar patients [24].

Our BP finding of 126.0 ± 15.7/75.5 ± 10.3 mmHg is inconsistent with previous studies.[7,25]This may be explained by the fact that in that study hypertension was prevalent in 47% of patients, while our exclusion criteria included hypertensive patients or any other medical comorbidity. Also, it is not mentioned whether the patients were excluded who were taking antihypertensive or not which is not the case in our study as we have not accepted patients with medical comorbidity.

Our study showed that BP is the least common abnormality, which is comparable with other studies.[24]We reported elevated SBP in 7% of patients and elevated DBP in 26% of patients. A study in drug naïve bipolar patients showed high BP is the least common abnormality in up to 13% of patients.

4.2.5. Predictors of metabolic syndrome

In our study, there were ten patients (33.3%) with metabolic syndrome. This is consistent with other studies which show results with the prevalence of metabolic syndrome up to 35% in BPAD [35,40,41].

In our study, we have seen the determinants of metabolic syndrome in BPAD. It shows that patients who had metabolic syndrome were older, taller (160.11 ± 7.54 cm), obese (94.55 ± 7.50 kgs), had higher BP (122.22 ± 12.30/85.33 ± 7.84), with more FBG (101.77 ± 26.42), higher TGs 151.44 ± 70.34, higher cholesterol and all its types, i.e., 166.55 ± 50.73 total cholesterol, lower HDL 35.77 ± 5.16, higher LDL 99.22 ± 38.01, and higher VLDL cholesterol 28.44 ± 15.70. Comparable results [25] were seen in a study done in BPAD patients with metabolic syndrome.

From our study, we have observed that BP and HDL cholesterol are risk factors for developing metabolic syndrome in BPAD which is in concordance with studies done in the past [3,42].

We found from our research that there were ten patients out of 30 who had metabolic syndrome. Out of these 10, 7 (70%) belonged to bipolar depression while 3 (30%) belonged to bipolar mania. On reviewing the literature, we could not find any study comparing bipolar mania versus bipolar depression. Also, on further exploring, we found that the patients with bipolar mania had BP, have increased FBG, higher TG levels, and larger waist circumference as compared to bipolar depression. It was only HDL cholesterol which was lesser in bipolar mania as compared to bipolar depression.

As we have seen that BPAD patients have the innate tendency to develop metabolic syndrome and it can further exaggerate with treatment with mood stabilizers, antipsychotics, and antidepressants. Thus, every bipolar patient should be screened, monitored for metabolic parameters, and therefore treatment for such patients needs to be individualized.

5. Conclusion

From our study, we found that high BP low HDL and are the risk factors in drug naïve bipolar patients. Thus, all bipolar patients whether freshly diagnosed or already on treatment must be screened and monitored in for all these parameters and accordingly treatment should be individualized.

5.1. Salient points

The Metabolic syndrome is an alarming condition in today's world, which has a high association with the severe mental illness like bipolar illness.

- Past research has focused on metabolic syndrome in treatment-seeking bipolar patients; high prevalence of metabolic syndrome is reported in such patients.
- Very scanty data are available regarding the prevalence of metabolic syndrome in drug naïve bipolar.
  - ☐In our research, we observed that metabolic syndrome has a prevalence of metabolic syndrome up to 33.33% in bipolar patients.
  - ☐Deranged parameters (statically insignificant) but low HDL cholesterol and high Blood pressure are the significant risk factors in such patients
  - ☐It has been observed that all the metabolic parameter derangements is more bipolar depression as compared to biploar mania.
  - ☐Thus all the biploar patients should be screened and monitored for matabolic syndrome irrespective of treatment status (i.e., whether treatment native or on treatment) especially blood pressure and HDL cholestrol.

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