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Prodromal symptoms and temperamental characteristics in first episode psychotic mania: re-looking the cynosure

Abstract

Background: Prodrome has recently been proposed as target for early intervention but their phenomenology remains obscure and often certain temperamental characteristics are confused with prodromal symptoms leading to the possibility of over-reporting. **Methods**: Fifty-one consecutively admitted patients, between the age group of 18-60 years, fulfilling the ICD-10 criteria for mania with psychotic symptoms were included. They were rated on Young Mania Rating Scale (YMRS) and were started on appropriate medications. After they attained remission (YMRS<12), they were interviewed on the Bipolar Prodrome Symptom Scale- Retrospective version (BPSS-R) and the General Behaviour Inventory (GBI). Twenty-five normal controls were assessed using the same tools. **Results**: Prodromal symptoms were reported by 58.8% of the patients, as compared to eight per cent of controls. Irritability (28.33%) was the most commonly reported prodromal symptom followed by anxiety (13.33%) and sleep disturbance (ten per cent). All the three frequently reported prodromal symptoms were of moderate severity and recurrent in frequency in three-fourth of the patients. The mean number of prodromal symptoms among the patients was 1.14 (SD 1.44), which was significantly higher than the normal controls ($p<0.001$). Hypomanic/depressive temperaments were significantly higher in the patients with prodrome as compared to normal controls ($p<0.01$) as well as patients without prodrome ($p<0.01$). **Discussion**: Significantly higher number of prodromal symptoms was present in the patients and these symptoms were mostly moderate in severity and recurrent in nature. Also, the number of patients who reported prodromal symptoms was much higher than the number of controls. However, when a comparison was made between the reported prodromal symptoms in the patient and control group, a significant difference was noted only in 'irritability'. Further, the proportion of prodromal symptoms reported in our study was lower when compared to previous studies. This could be because most of these studies had looked for these symptoms over the lifetime leading to likelihood of over-reporting. Individually, these symptoms may not have predictive significance but the occurrence of these clinical characteristics in patients who have hypomanic or depressive temperament could be a sign of impending first episode mania.

Keywords: Irritability. Anxiety. Sleep Disturbance. Depressive.

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Introduction

Bipolar disorder is a chronic psychiatric disease often causing disability and significant functional impairment with considerable consequences on the quality of life not only of the patients themselves, but also of their family members and others in their environment.[1] The disorder represents a major public health problem; it frequently requires hospitalisation and is associated with significant mortality due to suicide, the rate of which (15-20%) is higher than that in the general population and other psychiatric or medical patient populations.[2-4] It has been ranked fifth for people between 15 and 44 years of age.[5] The prevalence rate of bipolar spectrum disorders may rise to five per cent or higher with sensitive detection of hypomania.[6,7]

Since descriptions by Falret[8] and Kraepelin,[9] we have recognised bipolar disorder as an illness defined by its changing course. Both described the disorder as an episodic illness, alternating between periods of high and low mood. The view of bipolar disorder, however, generally has continued to be one of the alternations of extremes, in a "burst" pattern,[10] followed by periods of general quiescence. Less attention has been paid to what occurs between episodes of mania and major depression.

However, literature of more recent times provide newer details of the natural course of bipolar disorder, highlighting the importance of subsyndromal symptoms which were overlooked before. Subsyndromal symptoms outside an episode are common in bipolar disorder.[11] These are symptoms that may not reach the severity of an episode but cause significant disruption in patients' lives.

Several studies have found that over half of bipolar patients suffered from significant subsyndromal symptoms.[12-14] These subsyndromal symptoms may progress into prodromal symptoms, which may further progress to a syndromal manic episode. Therefore, such subsyndromal symptoms, apart from causing distress and social functional impairments, may make patients vulnerable to relapses during their illness course.

Prodrome in mania and its significance

In recent years, much clinical and research interest has been directed at the early and prepsychotic phases of psychotic disorders.[15] Unfortunately, the focus has been put almost exclusively on non-affective disorders to such an extent that early psychosis has almost become synonymous to early schizophrenia.[16] As a result, research into the early phase of affective psychoses, such as bipolar affective disorder (BPAD), has been a relatively neglected area[17] and warrants further study as it is likely that the key principles of early intervention in psychosis, apply equally well to bipolar disorder, specially with regards to:

- Early diagnosis and management of affective disorders.
- Early diagnosis of relapse.
- Development of neurobiological and phenomenological theories of psychosis.
- Prognostic significance.

Thus, similar to work with psychotic populations, it is likely that an approach aiming at the identification of impending first-episode mania with psychotic symptoms is currently a realistic and manageable strategy to promote earlier treatment.

Evidence in support of manic prodrome

Existing literature suggests that some patients who will develop a first manic episode present a set of attenuated symptoms that can be identified. However, the findings are not consistent. In a review by Howes *et al*.,[18] 318 studies on BPAD prodrome were identified, out of which only 14 studies had addressed the issue of clinical features preceding the onset of the first manic or hypomanic episode. Out of these, some of retrospective studies used a variety of methodologies to collect data from bipolar individuals and/or their carers about clinical features that pre-dated the onset of the disorder.[19-25] The most commonly reported putatively prodromal features were mood lability/swings, depressive mood, sleep disturbance, and irritability; however, even these putative symptoms have not been reported uniformly across all the reviewed studies.

Opinions regarding the number and severity of the prodromal symptoms reported are conflicting. While some studies report them in upto 70-100% of their patients,[20,23-26] others[19,20] have reported in lesser proportion of their patients.

Aim, objective, and hypothesis

Our aim and objective was to identify a set of underlying symptoms that exist before the onset of first episode psychotic mania and to provide a description of the symptoms charactering the 12-month period preceding the occurrence of such an episode, and to explore the temperamental characteristics in such patients and comparing it with normal healthy control group. We hypothesised that there would be no prodrome or temperamental characteristics occurring during the 12 months preceding the onset of mania when compared with healthy controls.

Methodology

The study was carried out at the Central Institute of Psychiatry, Ranchi, Jharkhand, India. The study was cleared by the ethical committee of the institute. For the purpose of the study, all the consecutively admitted patients between the age group of 18-60 years, fulfilling the ICD-10 criteria for mania with psychotic symptoms were selected for the study period of one year. A total of fifty one patients were included in the study after obtaining a written informed consent. Socio-demographic and clinical data at the time of admission was recorded for each patient. At the time of admission, the key informant was identified as a parent, sibling, or a relative who has stayed with the patient at least for the last one year and who could provide adequate information regarding the patient's condition. The same informant was asked to be present during the discharge. Patients were rated on the Young Mania Rating Scale (YMRS) [27] to assess the severity of illness at first contact.

The patients were started on appropriate medications by the treating team and after they attained remission (YMRS<12) and during the discharge, they were interviewed on the Bipolar Prodrome Symptom Scale- Retrospective version (BPSS-R)[23] with the help of the key informant. The BPSS-R assesses systematically the pattern of onset, duration, severity, and frequency of 38 symptoms and signs that are noticed prior to the first major depressive and/or first manic episode. It encompasses all the DSM-IV symptoms of depression and mania, and provides specific details for a more precise rating. Prodromal symptom severity is rated on an ordinal scale from zero to three and frequency is rated from zero to four respectively. It is a holistic tool because in addition to symptoms present during the mania prodrome, the BPSS also assesses presence of the same symptoms during the first manic episode. In addition, the BPSS-R was developed after an extensive review of literature on risk factors and early symptoms of bipolar disorder, published assessment tools for prodrome in psychosis, and interviews of youths with bipolar disorder and their primary caregivers regarding initial subthreshold symptoms prior to the onset of a mood episode.

The General Behaviour Inventory (GBI)[28] was applied to assess trait-based symptom measure of unipolar and bipolar affective conditions. GBI is a self-report inventory. The items are related to affective symptoms, including depressive, hypomanic, and biphasic symptoms. GBI is composed of two subscales, the Depressive scale and the Hypomanic-Biphasic scale. These

scales were derived on the basis of a two-dimensional model of these symptoms. GBI has 73 items and the reporter is asked to rate unipolar depression, hypomania, and biphasic symptoms over the past week. Responses are recorded on a four-point Likert scale, with a score of zero signifying never or hardly ever and score of three suggesting very often or almost constantly. Thus, high scores represent greater psychopathology.

As recommended by Depue,[28] items can be scored using a dichotomous model, dividing a population into cases and noncases, where those individuals responding zero or one to an item receive zero points and those responding two or three to an item receive one point. Scoring can also be done in Likert manner by adding up the subject's responses. We adopted the Likert method because this manner of scoring provides more information. The observed scores also show more variations in Likert method. According to the scoring method recommended by Depue,[29] Depression scale is based on 45 items and Hypomanic-Biphasic scale is based on 28 items (item 44 is included on both scales). In this study, the score above the minimum possible score on manic, i.e. 28 and the minimum possible score on depressive, i.e. 45 was taken. The Depressive and Hypomanic-Biphasic scales have shown good reliability and validity in adult populations.[27,30,31]

The BPSS-R was also applied on twenty five normal subjects who were matched for age, sex, and education, and after they obtained a score of less than three on GHQ-12.[32]

Statistical analysis

Data was analysed using descriptive statistics with the help of SPSS version 16.0 for windows. Quantative data are presented as mean (±SD). For categorical variables Chi-square test was used to analyse difference between the groups and Fisher's Exact test was used where the sample (N) was less than 20. Quantitative data that were normally distributed were analysed using independent sample t- test. We used two-tailed statistics set at a significant p value at <0.05.

Results

Table 1 shows the mean age of patients as 24.62 (SD 8.0) years and that of the controls as 24.20 (SD 3.99) years. Majority of the patients were males, Hindu, unskilled workers, from lower socioeconomic status, and belonging to rural domicile. The gender distribution was even between the two groups. There was no significant difference between the patients and controls with regards to any of the socio-demographic

Table 1: Comparison of sociodemographic characteristics between patient (N=51) and control groups (N=25)

Variables	Mean±SD, n (%)		χ^2/t	df	p
	Patients	Controls			
Age (in years)	24.62 (8.00)	24.20 (3.99)	0.25	74	0.80
Prodromal symptoms	1.14 (1.44)	0.08 (0.27)	3.62	74	0.001*
Sex					
Male	39 (76.5)	12 (72.0)	0.179	1	0.779
Female	12 (23.5)	7 (28.0)			
Marital status					
Married	26 (51)	17 (68)	1.97	1	0.219
Unmarried	25 (49)	8 (32)			
Religion					
Hindu	40 (78.4)	21 (84)	0.328	1	0.761
Others	11 (21.6)	4 (16)			
Education					
Illiterate to up to 5th	19 (37.3)	13 (52)	2.488	2	0.289
5th to 10th	19 (37.3)	5 (20)			
Above 10th	13 (25.5)	7 (28)			
Occupation					
Unskilled	26 (51)	16 (64)	1.775**	2	0.495
Semiskilled	22 (43.1)	7 (28)			
Skilled	3 (5.9)	2 (8)			
Socioeconomic status					
Lower	35 (68.6)	16 (64)	0.163	1	0.796
Middle	16 (31.4)	9 (36)			
Domicile					
Rural	47 (92.2)	22 (88)	0.334**	1	0.678
Urban	4 (7.8)	3 (12)			

*Significant p<0.01 (two-tailed), **Fisher's Exact test, df=Degree of freedom

characteristics. However, a significant difference (p=0.001) was noted in the number of prodromal symptoms reported by the patients (1.14; SD 1.44) when compared to the controls (0.08; SD 0.27) (p=0.001) (Table 1). Among the 38 items on the BPSS-R, it was noted that irritability was the most commonly occurring prodromal symptom (28.33%), followed by anxiety (13.33%) and insomnia (6.66%) in the patients (Table 2).

Further exploration of the reported prodromal symptoms revealed that irritability was of moderate severity in 82.3%, recurrent in 88.3% patients, and substance use was reported in 35% of the patients who reported it as a prodromal symptom. Anxiety was reported in 15.7% of the patients. It was of moderate severity in 75%, recurrent in 37.5%, and substance use was reported in 50% of the patients. Insomnia being reported only in 7.8% of the patients was of moderate severity and recurrent frequency in 75% patients with substance use of more than one month before the onset in 25% of them (Table 3).

Table 2: Frequency of prodromal symptoms reported in the patients

S. No.	Prodromal symptom	Frequency n (%)
1	Irritability	17 (28.33)
2	Anxiety	8 (13.33)
3	Insomnia	4 (6.66)
4	Frequent mood swings	3 (5)
5	Trouble controlling anger	3 (5)
6	Social isolation	3 (5)
7	Overly talkative	2 (3.33)
8	Decreased need for sleep	2 (3.33)
9	Overly self-confident	2 (3.33)
10	Trouble concentrating things	2 (3.33)
11	Suspiciousness	2 (3.33)
12	Tiredness	2 (3.33)
13	Increased creativity	1 (1.66)
14	Oppositionality	1 (1.66)
15	Drop in functioning at school/work	1 (1.66)
16	Self-injurious behaviour	1 (1.66)
17	Physical slowdown	1 (1.66)
18	Decreased interest in things	1 (1.66)
19	Depressed mood	1 (1.66)
20	Physically agitated	1 (1.66)
21	Extremely active	1 (1.66)
22	Overly cheerful	1 (1.66)

When a comparison was done among the reported prodromal symptoms between the two groups, it was seen that irritability was present in a significant number of patients (p=0.001) whereas other commonly reported prodromal symptoms in the patients such as anxiety (15.7%) and insomnia (7.8%) showed no significant difference when compared to the controls (Table 4).

Further, the comparison of temperamental characteristics indicated that hypomanic behaviour (p=0.001) and depressive behaviour (p=0.002), as assessed on GBI were significantly higher in the patients compared to the controls (Table 5).

Discussion

Since the time of Kraepelin, the issue concerning prodromal symptoms has not really been the cynosure of all eyes, the details of which have been either shrouded in mystery or conflicting as seen in the studies so far and the initial manic prodrome is no exception. While the characteristics of BPAD spectrum disorders and the variability in polarity of onset exclude a mere transposition of the psychosis- prodrome concept to BPAD, some elements of the literature give support to the similar idea of the occurrence of a period of disturbance of variable duration before the onset of the first manic episode. In particular, findings suggest that patients who later develop BPAD experience attenuated symptoms for up to ten years on average before the acute onset of the illness, but very little research has actually attempted to describe this phase.

In the population studies on bipolar disorder, the mean age of onset of the disorder has varied from 17 to 27 years.[33] The epidemiological catchment area study found a mean age of onset of 21 years[34] and similarly in a large Canadian general population study, 95% of the patients having mania had a mean age of onset of 26 (males) and 25 (females) years.[35] In a more recent study on manic prodrome by Conus *et al*.[25] the mean age was 23.0 (±2.9) years for the study group. The mean age of the patients in our study was 24.62 (±8.0) years, and was consistent with the above mentioned studies. In most of the other studies, age range varied from 13-17 years as they also had included child and adolescent population. Majority of the patients in our study were males (76.5%). Frank and Thase[36] reported that bipolar disorders occur as frequently in female as it does in the males. While more recently, Kennedy *et al*.[37] reported that men had higher incidence rates of first episode mania in the age range of 16-25 years. The higher percentage of male subjects in our study group could be explained by the characteristics of the Indian society where females having mental disorders are often neglected due to social stigma

Table 3: Characteristics of the common prodromal symptoms in patients

S. No.	Symptom			Severity n (%)		Frequency n (%)		Substance use n (%)	
		Present n (%)	Absent n (%)	Mild	Moderate	Infrequent	Recurrent	>1 month before	1 month to 1 day before
1	Irritability	17 (33.3)	34 (66.7)	3 (17.6)	14 (82.3)	2 (11.7)	15 (88.3)	6 (35.3)	-
2	Anxiety	8 (15.7)	43 (84.3)	2 (25)	6 (75)	3 (37.5)	5 (62.5)	4 (50)	-
3	Insomnia	4 (7.8)	47 (92.2)	1 (25)	3 (75)	1 (25)	3 (75)	1 (25)	-

Table 4: Comparison of reported prodromal symptoms between patient (N=51) and control groups (N=25)

S. No.	Variable	n (%)		χ^2 (df=1)	p
		Patient group	Control group		
1	Irritability				
	Present	17 (33.3)	0 (0)	10.73	0.001*
	Absent	34 (66.7)	25 (100)		
2	Anxiety				
	Present	8 (15.7)	1 (4)	2.19	0.26
	Absent	43 (84.3)	24 (96)		
3	Insomnia				
	Present	4 (7.8)	1 (4)	0.40	0.66
	Absent	47 (92.2)	24 (96)		
4	Frequent mood swings				
	Present	3 (5.9)	0 (0)	1.531	0.55
	Absent	48 (94.1)	25 (100)		
5	Trouble controlling anger				
	Present	3 (5.9)	0 (0)	1.531	0.55
	Absent	48 (94.1)	25 (100)		
6	Social isolation				
	Present	3 (5.9)	0 (0)	1.531	0.55
	Absent	48 (94.1)	25 (100)		
7	Overly talkative				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
8	Decreased need for sleep				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
9	Overly self-confident				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
10	Trouble concentrating things				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
11	Suspiciousness				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
12	Tiredness				
	Present	2 (3.9)	0 (0)	1.01	0.55
	Absent	49 (96.1)	25 (100)		
13	Increased creativity				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
14	Oppositionality				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
15	Drop in functioning at school/work				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		

(*Contd...*)

Table 4: (*Continued*)

S. No.	Variable	n (%)		χ^2 (df=1)	p
		Patient group	Control group		
16	Self-injurious behaviour				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
17	Physical slowdown				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
18	Decreased interest in things				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
19	Depressed mood				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
20	Physically agitated				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
21	Extremely active				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		
22	Overly cheerful				
	Present	1 (2)	0 (0)	0.50	1
	Absent	50 (98)	25 (100)		

*Significant p<0.01 (two-tailed)

or are usually brought to medical attention very late. For example, in a study from North India by Kulhara *et al*.,[38] that investigated 118 bipolar disorder patients and another by Chakrabarti and Gill,[39] the sample consisting males was 74.58% and 68% respectively. It was seen that the number of patients who were married (51%) and unmarried (49%) was almost equal in the patient group. In study by Khess *et al*.[40] on first episode mania patients, 78% of them were married but the mean age of the study group was higher in their study. Hindus were in majority in the patient group (78.4%). It is just the reflection of the fact that Hinduism is the religion of the majority in India. As far as education is concerned, it was seen that up to 75% of the patients were educated up to tenth or lesser, i.e. less than ten years of formal education. This is in line with the data reported earlier,[41] where 52.6% of the bipolar patients and 78.2% of the schizophrenics could hardly reach high school level. With regards to occupation, it was seen that about half of the patients were unskilled workers. This is more or less a representation of the prevailing employment scenario in the catchment area where the sample was collected. Similarly, lower socioeconomic status prevailed almost uniformly among the patient (68.6%) and the control group (64%) which also is in line with the existing financial condition in this part of the country. Majority of the patients seeking mental health advice at the centre where the data was collected, come from rural background and this was appropriately represented in our data where 92.2% of the patients belonged to rural domicile.

Table 5: Comparison of the temperamental characteristics between the two groups

Variables	Mean±SD		t (df=74)	p
	Patients	Controls		
GBI hypomanic total score	1.70 (2.23)	0.20 (0.58)	3.31	0.001*
GBI depressive total score	1.92 (2.91)	0.00 (0.00)	3.28	0.002*

*Significant p<0.01 (two-tailed), GBI=General behaviour inventory

Thus it can be summarised that our sample had socio-demographic characteristics which was comparable to that of samples of other published studies and that some of the differences that are present could be logically explained.

Characteristics of prodrome

Specifically addressing the issue of prodromal symptoms, 22 out of the 38 prodromal symptoms that were looked for, were reported in our patients. Irritability was most commonly reported (28.33%), followed by anxiety (13.33%) and sleep disturbance (about ten per cent). This is lower than the proportion reported in previous studies,[20,23-25] where these symptoms were reported in up to 60% of the patients.

One of the reasons for this could be the fact that apart from Conus *et al*.,[25] all the other studies had looked for these symptoms over the lifetime of the patients before onset

of the manic episode and considering the low specificity and sensitivity of most of the prodromal symptoms,[18] it is very likely for an individual to have experienced these symptoms and thereby leading to over-reporting. Moreover, none of the above mentioned studies had a control group which was the representative of the general population.

This can be further validated by the fact that when in our study, a comparison was made between the reported prodromal symptoms in the patient and control group, a significant difference was noted only in the irritability. While the studies that included a psychiatric comparator group indicated that many of the putatively bipolar disorder prodromal features may also be seen in other psychiatric disorders.[21,24,42] This is in line with the recent literature that as no single prodromal feature has been identified in all subjects, the bipolar disorder prodrome may be best defined by a cluster of features.[18]

It is interesting to note that though in our study the number of prodromal symptoms reported (mean=1.14, SD=1.44) was less compared to previous studies, when the number of prodromal symptoms reported between the patient and control group was compared it was seen that significantly higher number of symptoms were reported in the patient group. Also, the number of patients who reported prodromal symptom (58.8%) was much higher than the number of controls who reported prodromal symptom (eight per cent) and this difference was statistically significant. In the past almost all the studies have been done only on the patients, without any comparison group or have been compared with a psychiatric control group. Evidence on prodromal symptoms in normal individuals is lacking, so the wide discrepancy in the percentage of patient and normal controls reporting prodrome can be taken as a logical finding and should perhaps serve as a stepping stone for further exploration.

From the analysis of our data it is evident that before the onset of the manic episode the patients experience an alteration from their previous mental state. Thirty out of the 51 patients in our study reported at least one prodromal symptom. This figure is much lower than the previous studies by Correll *et al*.,[23] in which all the 52 patients had reported at least one prodromal symptom. This could be explained on the basis that this study did not particularly address the issue of proximal prodrome and no differentiation was made on the symptoms that could be trait markers rather than the actual prodromal symptom.

Similarly, in the study by Conus *et al*.,[25] all of their 18 patients had reported at least one prodromal symptom and the likely explanation for this could be the fact that though they had addressed the proximal prodromal symptoms, their sample size was much lesser (n=18) and the tool to assess the prodromal symptoms had additional items to those mentioned in the BPSS-R which increases the likelihood of a positive response.

Skjelstad *et al*.,[26] in their review on bipolar prodrome concluded that greater emphasis should be on the delineation of the prodromal phase and in-depth enquiry should be made in the nature and progression of the prodrome. In our study we tried to further describe the prodromal symptoms based on severity, frequency, and associated substance. It was seen that all the three frequently reported prodromal symptoms, i.e. irritability, anxiety, and insomnia were of moderate severity and recurrent in frequency in almost 75% of the patients, which is consistent with the findings by Correll *et al*.,[23] who had reported this in 100% of their patients.

Temperamental characteristics

Scores on GBI for both hypomanic and depressive were significantly higher in the patient group who reported prodrome when compared to the patients who did not, suggesting that patients with psychotic mania who undergo a prodromal phase had more evidence of cyclothymic traits. This is consistent with the earliest findings of Kraepelin,[9] who described depressions and excitements of mild intensity and brief duration predating adult manic-depressive psychosis in one out of four adult manic-depressive patients. More recently, in an exploration of developmental pathways to bipolarity, Akiskal[43] suggested that dysthymic, cyclothymic, and hyperthymic temperaments would represent possible pathways to the development of bipolarity. Klein *et al*.[44] have reported that up to 80% of BPAD patients exhibit cyclothymic premorbid personality, and conversely that cyclothymic individuals are at increased risk for development of BPAD.

In seven other studies, cyclothymic features were identified as a precursor of mania.[20,21,24,40,45-48] However, these features were also seen in the well relatives of people with BPAD;[48,49] so, it is not clear whether these features could be a correlate of risk status also seen in some relatives who do not go on to develop bipolar disorder. Furthermore, it remains to be determined whether these features reflect premorbid personality characteristics or are part of a distinct prodrome to BPAD.

In a review of the literature, 19 papers were found which specifically address prodrome in BPAD; of these, only five attempt to describe the symptoms and behaviours characterising the initial prodromal period.[17] Based on these evidences and more recent attempts in separating distal prodromal features (earliest signs and symptoms of BPAD) from proximal prodromal features (symptomatic manifestations during the 12 months preceding the first manic episode),[17] our study focused on characteristics of prodrome during the 12-month period prior to the first psychotic manic episode. The prodrome, by definition, can only be determined in retrospect,[18] as we did in this study and consecutively admitted patients were taken to reduce any bias in the patient selection for the study.

Unlike most of the previous studies which either included only child and adolescent population or made no distinction between childhood-onset bipolar disorder and adult onset bipolar disorder and/or used a broad definition of bipolar disorder, we included only those above 18 years of age with an ICD-10 diagnosis of mania with psychotic symptoms because inferences drawn from studies of childhood-onset bipolar disorder may not be applicable to bipolar disorder patients with adulthood onset.[18] Inclusion of a control group strengthened the possibility of assessing the specificity of the features in the patient population when compared

to the general population. Even if certain symptoms occur in the vast majority of subjects who go on to develop mania, they may also be observed in a general sample of young adults who would later develop other mental disorders, or no disorder at all (i.e. low specificity). Only Rucklidge,[24] Fergus *et al*.,[21], Correll *et al*.,[23] and Conus *et al*.[25] had utilised comparison/control groups in their studies on bipolar prodrome.

Limitations

The retrospective nature of our study is likely to be limited by recollection bias. Though we had conducted our study on a modest sample size, large retrospective studies are needed to confirm these preliminary findings of a prodromal period before the first manic episode. BPSS has not been validated in the Indian population as yet and the lack of blinding while applying the scale could be one of the limitations of the study. Future studies should be an amalgamation of clinical, genetic, and endophenotypic approaches so as to facilitate the timely identification and preventive interventions in individuals at risk for bipolar disorder. While clearly more research needs to be conducted, it is hoped that the specificity of putative bipolar disorder prodromal features needs to be determined with respect to the prodrome of other psychiatric conditions, particularly schizophrenia and recurrent unipolar depression.

Conclusion

This study provides first data regarding characteristics of the first episode manic prodrome on Indian population. Our study supports the fact that before onset of a first episode of psychotic mania, some of the patients go through a phase of change from previous mental state. It is during this prodromal phase that patient's present mood symptoms, sleep disruption, and general functional decline. However, the number and frequency of the prodromal symptoms are less than those reported in recent studies and these symptoms are likely to have low specificity. Our findings also corroborate with existing literature that the existence of childhood traits, such as cyclothymia and also the later development of frank symptoms suggest that there may be 'early' and 'late' prodromal features and these features need to be differentiated from the personality traits of the patient.

References

1. Angst J, Sellaro R. Historical perspectives and natural history of bipolar disorder. Biol Psychiatry. 2000;48:445-57.
2. Kupfer DJ, Frank E, Grochocinski VJ, Cluss PA, Houck PR, Stapf DA. Demographic and clinical characteristics of individuals in a bipolar disorder case registry. J Clin Psychiatry. 2002;63:120-5.
3. Judd LL, Akiskal HS, Schettler PJ, Endicott J, Maser J, Solomon DA, *et al*. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry. 2002;59:530-7.
4. Chen YW, Dilsaver SC. Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders. Biol Psychiatry. 1996;39:896-9.
5. The World Health Report 2001. Mental health: new understanding, new hope. Geneva: World Health Organization; 2000.
6. Angst J, Cassano G. The mood spectrum: improving the diagnosis of bipolar disorder. Bipolar Disord. 2005;7 Suppl 4:4-12.
7. Angst J. The bipolar spectrum. Br J Psychiatry. 2007;190:189-91.
8. Falret J. Mémoire sur la folie circulaire, forme de maladie mentale caractérisée par la reproduction sucessive et réguliäre de l'état maniqaue, de l'état mélancolique, et d'un intervalle lucide plus or moins prolongé. Bull Acad Natl Med. 1854;19:382-415.
9. Kraepelin E. Manic-depressive insanity and paranoia. Translated by Barclay RM. Edinburgh: E&S Livingstone; 1921.
10. Winokur G. The Iowa 500: heterogeneity and course in manic-depressive illness (bipolar). Compr Psychiatry. 1975;16:125-31.
11. Fava GA. Subclinical symptoms in mood disorders: pathophysiological and therapeutic implications. Psychol Med. 1999;29:47-61.
12. Gitlin MJ, Swendsen J, Heller TL, Hammen C. Relapse and impairment in bipolar disorder. Am J Psychiatry. 1995;152:1635-40.
13. Goldberg JF, Harrow M, Grossman LS. Course and outcome in bipolar affective disorder: a longitudinal follow-up study. Am J Psychiatry. 1995;152:379-84.
14. Keller MB, Lavori PW, Kane JM, Gelenberg AJ, Rosenbaum JF, Walzer EA, *et al*. Subsyndromal symptoms in bipolar disorder. A comparison of standard and low serum levels of lithium. Arch Gen Psychiatry. 1992;49:371-6.
15. Phillips LJ, Leicester SB, O'Dwyer LE, Francey SM, Koutsogiannis J, Abdel-Baki A, *et al*. The PACE Clinic: identification and management of young people at "ultra" high risk of psychosis. J Psychiatr Pract. 2002;8:255-69.
16. Conus P, McGorry PD. First-episode mania: a neglected priority for early intervention. Aust N Z J Psychiatry. 2002;36:158-72.
17. Conus P, Ward J, Hallam KT, Lucas N, Macneil C, McGorry PD, *et al*. The proximal prodrome to first episode mania--a new target for early intervention. Bipolar Disord. 2008;10:555-65.
18. Howes OD, Lim S, Theologos G, Yung AR, Goodwin GM, McGuire P. A comprehensive review and model of putative prodromal features of bipolar affective disorder. Psychol Med. 2011;41:1567-77.
19. Lish JD, Dime-Meenan S, Whybrow PC, Price RA, Hirschfeld RM. The National Depressive and Manic-depressive Association (DMDA) survey of bipolar members. J Affect Disord. 1994;31:281-94.
20. Egeland JA, Hostetter AM, Pauls DL, Sussex JN. Prodromal symptoms before onset of manic-depressive disorder suggested by first hospital admission histories. J Am Acad Child Adolesc Psychiatry. 2000;39:1245-52.
21. Fergus EL, Miller RB, Luckenbaugh DA, Leverich GS, Findling RL, Speer AM, *et al*. Is there progression from irritability/dyscontrol to major depressive and manic symptoms? A retrospective community survey of parents of bipolar children. J Affect Disord. 2003;77:71-8.
22. Berk M, Conus P, Lucas N, Hallam K, Malhi GS, Dodd S, *et al*. Setting the stage: from prodrome to treatment resistance in bipolar disorder. Bipolar Disord. 2007;9:671-8.
23. Correll CU, Penzner JB, Lencz T, Auther A, Smith CW, Malhotra AK, *et al*. Early identification and high-risk strategies for bipolar disorder. Bipolar Disord. 2007;9:324-38.
24. Rucklidge JJ. Retrospective parent report of psychiatric histories: do checklists reveal specific prodromal indicators for postpubertal-onset pediatric bipolar disorder? Bipolar Disord. 2008;10:56-66.
25. Conus P, Ward J, Lucas N, Cotton S, Yung AR, Berk M, *et al*. Characterisation of the prodrome to a first episode of psychotic mania: results of a retrospective study. J Affect Disord. 2010;124:341-5.
26. Skjelstad DV, Malt UF, Holte A. Symptoms and signs of the initial prodrome of bipolar disorder: a systematic review. J Affect Disord. 2010;126:1-13.
27. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry. 1978;133:429-35.
28. Depue RA. General Behavior Inventory (manual). Minneapolis: University of Minnesota; 1987.
29. Depue RA, Krauss S, Spoont MR, Arbisi P. General behavior inventory identification of unipolar and bipolar affective conditions in a nonclinical university population. J Abnorm Psychol. 1989;98:117-26.
30. Klein DN, Dickstein S, Taylor EB, Harding K. Identifying chronic

affective disorders in outpatients: validation of the General Behavior Inventory. J Consult Clin Psychol. 1989;57:106-11.
31. Mallon JC, Klein DN, Bornstein RF, Slater JF. Discriminant validity of the General Behavior Inventory: an outpatient study. J Pers Assess. 1986;50:568-77.
32. Goldberg DP, William P. A user's guide to the General Health Questionnaire. Windsor: NFER-Nelson; 1998.
33. Joyce PR. Epidemiology of mood disorders. In: Gelder MG, Andreasen NC, Lopez-Ibor JJ Jr, Geddes JR, editors. New oxford textbook of psychiatry. 2nd ed. Oxford: Oxford University Press; 2009:645-50.
34. Smith AL, Weissman MM. Epidemiology. In: Paykel ES, editor. Handbook of affective disorders. 2nd ed. Edinburg: Churchill Livingstone; 1992:111-29.
35. Bland RC, Newman SC, Orn H. Age of onset of psychiatric disorders. Acta Psychiatr Scand Suppl. 1988;338:43-9.
36. Frank E, Thase ME. Natural history and preventative treatment of recurrent mood disorders. Annu Rev Med. 1999;50:453-68.
37. Kennedy N, Boydell J, Kalidindi S, Fearon P, Jones PB, van Os J, *et al*. Gender differences in incidence and age at onset of mania and bipolar disorder over a 35-year period in Camberwell, England. Am J Psychiatry. 2005;162:257-62.
38. Kulhara P, Basu D, Mattoo SK, Sharan P, Chopra R. Lithium prophylaxis of recurrent bipolar affective disorder: long-term outcome and its psychosocial correlates. J Affect Disord. 1999;54:87-96.
39. Chakrabarti S, Gill S. Coping and its correlates among caregivers of patients with bipolar disorder: a preliminary study. Bipolar Disord. 2002;4:50-60.
40. Khess CR, Das J, Akhtar S. Four year follow-up of first episode manic patients. Indian J Psychiatry. 1997;39:160-5.
41. Nardi AE, Nascimento I, Freire RC, de-Melo-Neto VL, Valença AM, Dib M, *et al*. Demographic and clinical features of schizoaffective (schizobipolar) disorder--a 5-year retrospective study. Support for a bipolar spectrum disorder. J Affect Disord. 2005;89:201-6.
42. Angst J, Gamma A, Endrass J. Risk factors for the bipolar and depression spectra. Acta Psychiatr Scand Suppl. 2003;(418):15-9.
43. Akiskal HS. Developmental pathways to bipolarity: are juvenile-onset depressions pre-bipolar? J Am Acad Child Adolesc Psychiatry. 1995;34:754-63.
44. Klein DN, Depue RA, Slater JF. Inventory identification of cyclothymia. IX. Validation in offspring of bipolar I patients. Arch Gen Psychiatry. 1986;43:441-5.
45. Akiskal HS, Downs J, Jordan P, Watson S, Daugherty D, Pruitt DB. Affective disorders in referred children and younger siblings of manic-depressives. Mode of onset and prospective course. Arch Gen Psychiatry. 1985;42:996-1003.
46. Kochman FJ, Hantouche EG, Ferrari P, Lancrenon S, Bayart D, Akiskal HS. Cyclothymic temperament as a prospective predictor of bipolarity and suicidality in children and adolescents with major depressive disorder. J Affect Disord. 2005;85:181-9.
47. Berk M, Dodd S, Callaly P, Berk L, Fitzgerald P, de Castella AR, *et al*. History of illness prior to a diagnosis of bipolar disorder or schizoaffective disorder. J Affect Disord. 2007;103:181-6.
48. Findling RL, Youngstrom EA, McNamara NK, Stansbrey RJ, Demeter CA, Bedoya D, *et al*. Early symptoms of mania and the role of parental risk. Bipolar Disord. 2005;7:623-34.
49. Jones SH, Tai S, Evershed K, Knowles R, Bentall R. Early detection of bipolar disorder: a pilot familial high-risk study of parents with bipolar disorder and their adolescent children. Bipolar Disord. 2006;8:362-72.

Motichand S, Ram D, Sarkhel S, Mehta VS, Praharaj SK. Prodromal symptoms and temperamental characteristics in first episode psychotic mania: re-looking the cynosure. Open J Psychiatry Allied Sci. 2017;9:41-9. doi: 10.5958/2394-2061.2018.00009.5. Epub 2017 Aug 17.

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