Bipolar disorder is a common mental illness characterized by recurrent episodes of mania/hypomania and depression. It is ranked among the top 10 causes of global disability among adults by the World Health Organization. Although it is typically described as an illness characterized by remissions and recurrences, a substantial proportion of patients do not completely recover from mood episodes and continue to experience residual mood symptoms along with significant impairment in all areas of individual’s functioning. Bipolar disorder is also associated with high rates of suicide. It is because of the severity of illness and associated morbidity and mortality that identifying and treating bipolar disorder effectively is of paramount importance and of great public health relevance. There are two major factors that contribute to burden of disease. One, a substantial delay between the first experience of symptoms and the initiation of appropriate treatment, which can be as long as 8 to 9 years. Second, inability or rather lack of adequate knowledge among patients and relatives in identifying early symptoms of relapse/recurrence in those with established bipolar disorder. In essence, there are two types of prodromes, one of bipolar disorder and the other of recurrence of mood episodes in those with established bipolar disorder. The study by Sahoo and colleagues in this issue is a study on prodrome of relapses in bipolar disorder.

The prodrome constitutes a period of disturbance characterized by distinct features/symptoms leading to the development of the full-blown disorder. Although prodrome is often determined in retrospect, it can however, be used to identify individuals at risk of developing an illness or a recurrence of illness prospectively provided the prodrome is of satisfactory specificity and sensitivity. In the context of bipolar disorder, there can be separate prodromes of depressive and manic/mixed recurrences. A recent systematic review set out to identify two key questions: is there a bipolar prodrome and if there is, what its characteristic features are. Study reviewed seven retrospective and seven prospective studies including two community studies and concluded that mood lability/swings and depressed mood were the most common putative prodromal features followed by racing thoughts, anger/irritability, physical agitation and anxiety. It is evident that some are attenuated forms of bipolar symptoms, some are symptoms common to many mental disorders and a few are potential personality traits, particularly cyclothymia. Typically most studies reviewed did not provide specificity and sensitivity data. Based on two studies, the review concluded that specificity of several features, particularly those of elevated/irritable/depressed mood, lability of mood, and hearing voices was high (>90%) but sensitivity was generally low (all <80%).

The study by Sahoo et al is a welcome addition to the growing but somewhat sparse literature on prodrome of recurrences in established bipolar disorder. The study is unique because it examines the ability of the relatives and not just patients to identify prodrome. Most studies examine whether patients can recognize prodrome by themselves. This is no less important, but in the Indian context where most patients live with their family and where families play a major role in not just treatment seeking but also in subsequent follow up and treatment adherence, studying the ability of immediate relatives in recognizing prodrome plays a vital role in the planning of overall management, specifically in prevention of full-blown mood episodes. The main finding of the study was that the relatives’ ability to detect prodrome of mania was significantly greater than that of patients (97 vs. 70%) in bipolar disorder and that in unipolar depression this difference was not obvious. In addition, prodrome of mania was much shorter than that of depression of unipolar depression.
The study also identified symptoms of prodrome of mania and idiosyncratic prodromal symptoms called ‘relapse signatures’.

The study has important clinical implications. Most importantly, it emphasizes the need to educate relatives of prodromal symptoms since they are better in recognition of prodrome than patients. This is particularly vital because run up to full-blown episodes seems to be rather swift for mania. A relapse to a full-blown episode to mania may prove to be extremely dangerous, often ending in prolonged inpatient care and resultant burden to the patient and family. Since most Indian patients stay with their families, educating family members may play a vital role in averting a full-blown relapse. The study findings also emphasize the need to include education about prodrome in psychosocial interventions.

It is also believed that prodromes of mania are longer and easier to identify than those of bipolar depression. On the contrary, the findings of this study suggest otherwise. However, such a conclusion may be fallacious, considering an important methodological limitation of this study. That is, the study investigates only a prodrome of manic relapses in bipolar disorder and not depressive relapses. This is possibly due to the fact that the study includes those who have remitted recently from a manic episode. A comparison with depressive prodrome of unipolar depression does not serve the purpose of determining if prodromes of mania and bipolar depression are of similar or of differing duration.

After applying the Bonferroni correction for multiple comparisons, hostility, ideas of grandiosity, distractibility, being uncooperative, and ideas of persecution were reported significantly more frequently among patients with mania than in depression. Of a long list of symptoms, 30 symptoms were common for both depression and mania prodromes. The ‘idiosyncratic’ prodromal symptoms included increased religiosity, taking decisions easily, reddening of eyes, being abusive, being uncooperative, listening to loud music, recalling past events, and ideas of reference. Common prodromal symptoms closely approximated the symptoms of the disorder itself. Surprisingly, sleep and mood disturbances do not appear to be useful prodromal symptoms of mania whereas it is widely recognized that changes in sleep patterns (mainly insomnia) followed by mood changes (expansive mood, volatility, hopelessness), changes in sexual behaviour, financial indiscretion, involvement in excessive number of projects and impaired judgment are considered characteristic features of impending mood episodes. Similarity of the prodromal symptoms of the disorder and that of the disorder itself may be related to the fact that it may have run up to full-blown residual and sub-syndromal symptoms form the prodrome. In addition, assessment of prodrome was made within 2 wk of remission from mania and this may have biased recollection of symptoms. Considering the fact that a substantial proportion of patients with bipolar disorder may not recover completely from index episodes and may continue to have residual symptoms in between the episodes, the findings of this study seem to be generalizable only to patients who run a typical remitting and relapsing course with almost complete recovery from episodes.

In studies of putative prodrome of bipolar disorder, it was not possible to determine if symptoms represented a distinct prodrome of bipolar disorder. In patients with an established course of bipolar disorder, it may be possible to identify a distinct prodrome to recurrences of depressive and manic episodes. Specificity and sensitivity of prodromal features have to be established. High specificity is desirable considering the fact that prodrome indicative of an impending relapse may warrant a pharmacological intervention. At the same time, the prodrome needs to have acceptable sensitivity. This may be achieved if patients with bipolar disorder are followed up prospectively in longitudinal studies with closer monitoring of changing clinical profile over the course of illness. Although retrospective studies are easy to execute, these may not yield reliable findings. Future studies should also examine prodromes of various phases of bipolar disorder and of bipolar II subtype. There is limited literature on the prodrome of bipolar II disorder.

Studies of prodromal features in bipolar disorder have important clinical implications. In this context, the study by Sahoo et al emphasizes the need to educate patients and relatives of prodrome of recurrence and has potential implications for effective long-term management of patients with bipolar disorder.

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