Concept and Identification of “Soft Bipolarity” in Patients presenting with Depression: Need for Careful Screening by Physicians

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Abstract
The bipolar spectrum is a broader concept, which questions the strict dichotomous categorical division of erstwhile manic-depressive illness into two discrete categories viz. bipolar disorder and major depressive disorder, thereby overlooking a wide ‘spectrum’ of patients which lie ‘in between’ the two extremes. The presence of underlying bipolar ‘spectrum’ or ‘soft bipolarity’ often goes undetected in patients presenting with major depression. This sub-group of patients may not stabilize with indiscriminate use of anti-depressant drugs, and without proper management, it may be associated with continued non-responsive symptoms, increased suicidality and poorer prognosis. There is a need to suspect and identify such cases of soft bipolarity/spectrum by early screening of patients with major depression presenting to medical settings. The review paper covers the current concepts and understanding of bipolar spectrum disorders which is aimed to facilitate early identification, management and referral of cases detected to have soft bipolarity in the general medical settings.

Introduction
Mood disorders are characterized by a fundamental disturbance of mood or affect towards either depressive side or elation, along with the corresponding changes in the activity level, thought etc. In terms of years lived with disability, depression is the second leading cause of global burden.1 By the year 2030, depression is projected to be the leading cause of global disease burden worldwide, highlighting the public health significance of mood disorders. Depression and bipolar disorders together account for around 47% of the DALYs (disability-adjusted life years) contributed by mental and substance use disorders.2

At least 10% of the patients visiting primary care physician may have major depression.3 Physicians working in primary and secondary care settings are often the first point of contact for depressive symptoms. Large scale recent studies have found that the depressive severity was not different, and symptomatic presentations did not differ substantially between primary care and specialty settings.4 Major depressive disorder is more similar than different among patients at primary and specialty settings. Many a times, their treatment is initiated in the general medical settings, especially where psychiatric services are not readily available. Therefore, it becomes imperative that physicians in primary and secondary health care settings are updated and sensitized about the various key aspects of mood disorders in their clinical practice.

One such scenario is the presence of underlying bipolar ‘spectrum disorders’ or ‘soft bipolarity’ which often goes undetected in patients presenting with depression. The review paper covers the current concepts and understanding of ‘spectrum’ and ‘soft bipolarity’ which is aimed to facilitate early identification, management and referral, if necessary.

Relevance for the Physicians
Less than 25% of antidepressants are prescribed by psychiatrists or other mental health specialists. More than 70% of antidepressants are prescribed by the general physicians across most of the world.5 The situation is not different in India in the background of wide mental health gap, with antidepressants being widely prescribed without the consultation of mental health specialists. The figures are alarming considering the propensity of antidepressants

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causing a “switch” to mania in persons with underlying predisposition to bipolarity, leading to significant socio occupational dysfunction.

Hence the concept of soft bipolarity is of greater importance and relevance to the physicians to promote judicious use of antidepressants considering the double whammy of wide mental health gap leading to physicians providing care to depressed patients and vigorous marketing strategies employed by the pharmaceutical companies.

Understanding the Concept of ‘Spectrum’ Disorder (and ‘Soft Bipolarity’)

The spectrum is a term borrowed from physics, where the visible light after passing through the prism appears as a rainbow spectrum of colors. From a medical/psychiatric perspective, the spectrum concept includes the broad areas of psychiatric phenomenology relating to a given ‘classical’ form of disorder, but in addition, also goes on to include:

- **Core, subthreshold and subclinical symptoms** of the classically described disorder
- **Atypical symptoms** related to the prototypic configuration
- **Associated features** including signs, isolated symptoms, symptom clusters & behavioral patterns related to core symptoms
- **Temperamental and/or personality traits**

Spectra of symptoms may be prodromal, precursors of a full disorder or sequelae of a previous full disorder. From a medical perspective, there is a need to pay attention to these spectrum conditions, as this approach for bipolar spectrum disorders may help us in identifying at-risk population, lessen morbidity and providing a rationale for the use of a single group of drugs for a continuum/spectrum of disorders.6,7

The bipolar spectrum is a broader concept, and questions the strict categorical division of erstwhile manic-depressive illness by the third edition of DSM-III into two discrete categories viz. bipolar disorder and major depressive disorder. This strict dichotomy overlooks a wide ‘spectrum’ of patients which lie ‘in between’ the two extremes.

**Bipolar spectrum** is thus a broad inclusive term for bipolar disorders (including those beyond classical mania as well). So we can understand bipolar spectrum to encompass sub-threshold, short duration hypomanic symptoms, or depression arising in the background of cyclothymia, hyperthymic temperament, familial bipolarity or hypomania arising due to treatment.7,9 Depressed patients often fail to report past history of subthreshold hypomanic symptoms that are usually associated with intact, or even enhanced functioning.10 The clinical visits are made mainly with prominent depressive symptoms each time, which may pose a hindrance for the diagnosis of bipolar spectrum. In medical settings, since the focus is on treatment of physical illnesses, it may prevent proactive questioning about past hypomanic symptoms. Also, the lack of awareness of spectrum concept amongst physicians may lead to an oversight of important clinical indicators which may point towards bipolar spectrum while treating depression.

Currently the entity of bipolar spectrum is not separately specified under any of the traditional nosological systems such as International Classification of Diseases (ICD) or Diagnostic and Statistical Manual (DSM). The DSM, however, allows and specifies the diagnosis of one of the spectrum disorder viz. bipolar II disorder. For making a diagnosis of Bipolar II, it is necessary to have a current or past hypomania (as opposed to mania in BP-I) lasting at least four days in addition to major depression.11

**Prevalence of ‘Spectrum’/‘Soft’ Bipolarity**

The lifetime prevalence of Bipolar disorder - I (BP-I; defined as presence of depression and atleast one manic episode) is 1% in general population surveys.12 However, when we focus on the entire spectrum of bipolar disorders, the prevalence is much higher. The prevalence for the bipolar disorder II (BP-II; defined as presence of depression and atleast a hypomania) was found to be 1.67% in a large-scale epidemiological survey in U.S.13 The secondary analyses from these landmark studies revealed that if we consider the prevalence of entire bipolar ‘spectrum’ disorders, it was found to be about 6.4% in the community setting implying that the sub threshold cases are atleast five times more common than BP-I and BP-II.14 The findings were further replicated in U.S National Comorbidity Survey- Replication study with the lifetime and 12-month prevalence estimates being 1.0% and 0.6% for BP-I, 1.1% and 0.8% for B P-II, and as high as 2.4% and 1.4% for sub-threshold BPD.15 In terms of clinic prevalence, on applying the broader criteria for ‘spectrum’ bipolarity, it was seen that upto half of the patients with current diagnosis of depression may be bipolar spectrum disorders.10 Timely and accurate diagnosis may facilitate improved management and outcome for these patients.

These alarming figures thereby highlight the importance of focusing not only on the ‘classical’ bipolar disorder, but also a wide variety of difficult-to-recognize / easy-to-overlook bipolar spectrum disorders for its diagnostic relevance, and clinical as well as public health importance.
Box 1: Bipolar spectrum disorders: Akiskal and Pinto (1999)

Bipolar I - Depression and mania
Bipolar II - Depression and discrete hypomania
Bipolar III - Depression and treatment-emergent hypomania
Bipolar IV - Depression (late-life) in context of hyperthymic temperament

*Hypomanic: a milder form of mania usually lasts few days with no marked dysfunction; #Hyperthymic temperament is proposed to be characterized by an excessively positive disposition, along with a set of attributes, similar to, but more stable than, the hypomania.

Box 2: Clinical Signs pointing towards “soft bipolarity”

- Four or more recurrent episodes of major depression
- Psychosis during major depression
- Post partum depression
- First episode of major depression before 25 years of age
- Multiple, brief (less than 3 months) depressive episodes
- Atypical depressive symptoms
- First-degree relative has diagnosis of bipolar disorder
- Hyperthymic personality
- Onset of hypomania after antidepressants
- Loss of response on antidepressant drugs
- 3 or more Antidepressants tried; none worked
- Highly seasonal mood shifts

Key Diagnostic Schema of Bipolar Spectrum/Soft Bipolarity

Key diagnostic schema of BSD were given by researchers, notably Klerman,16 Akiskal& Pinto17 and more recently, by Ghaemi and co-researchers.9 Akiskal and Pinto in their landmark paper on ‘bipolar spectrum disorders’ have described the various subtypes of bipolar disorder from I to IV (Box 1). Additionally, the types I 1/2, II ½ , III1/2 , and VI have been proposed as well.17

More recently, Ghaemiet al9 proposed diagnostic criteria for bipolar spectrum disorders as follows:

A. At least one major depressive episode
B. No spontaneous hypomanic or manic episodes
C. Either of the following, plus 2 items from criterion D, or both of the following
   - A family history of bipolar disorder in a first degree relative
   - Antidepressant-induced mania or hypomania
D. If no items from criterion C are present, 6 of the following 9 criteria are needed.
   - Hyperthymic personality
   - at baseline, non depressed state

Perugi and Akiskal later on have further expanded soft bipolarity encompassing a variety of conditions ranging from mood, anxiety, impulse control, and eating disorders with underlying cyclothymic-anxious-sensitive disposition, mood reactivity and interpersonal sensitivity, though this concept is more of research significance as of now.20

Screening for Soft-Bipolar/Bipolar Spectrum

The screening of patients for depression has been discussed in more detail in a previous review paper in JAPI.21 Asking just a few more questions focusing on any periods (few days to few weeks, even few hours at times) with elated mood, feeling over-energetic, overactive and decreased need for sleep etc may help delineate the subgroup of patients with bipolar spectrum who present to the physicians with current depressive symptoms.

A two-question screen for mood lability may help identify bipolar II disorder patients if there is positive response to at least one question indicating mood lability.22 The questions are as follows:

“Are you a person who frequently experiences ups and downs in mood over life?”

“Do these mood swings occur without cause?”

Along with these presence of atypical symptoms, reversed vegetative symptoms like hyperphagia and hypersomnia during depression instead of loss of appetite and sleep, past history of elevated mood and increased activity, family history of bipolarity or treatment induced mood symptoms should be enquired about, using questions such as: “Have you had periods of feeling so happy or energetic that your friends told you were talking too fast or that you were too ‘hyper’ than your usual self?”
Mood Disorder Questionnaire is one of the most commonly used screening tool. It has 17 questions pertaining to hypomanic symptoms, presence of several of these symptoms in the same time duration and the impact of these symptoms. When structured diagnostic interviews were applied to patients on antidepressant treatment attending family physicians 30% of the patients were found to be having bipolar disorder.

The Bipolar Index is another assessment tool which evaluates across five domains namely signs and symptoms, age of onset, course of illness, response to treatment, and family history and researchers have found that a score ≥50 had good sensitivity and specificity for identifying bipolar disorders.

Screening using the relevant clinical questions or instruments should be done in all patients presenting with major depressive episode in a busy outpatient setting.

Treatment Principles and need for Referral

Some general principles for managing the suspected cases of soft bipolar or bipolar spectrum disorders are as follows:

- **Family members should be psychoeducated about identification and delineation of the early symptoms of hypomania** (decreased need for sleep, increased energy, euphoria etc)
- **In case of a definite ‘switch’ from depression to hypomania, the dose of antidepressant drugs must be immediately reduced or stopped.**
- **In cases with Bipolar II or III, the decision may have to be made to initiate the long-term treatment with mood stabilizer (such as lithium, valproate etc) or an atypical antipsychotic drug, in order to prevent future affective episodes.**
- **In known bipolar I patients, antidepressants should be prescribed very judiciously and for short-term under the cover of mood-stabilizing medication, especially if depressive symptoms are mild.**
- **Use of tricyclic antidepressants in patients with suspected “pseudo-unipolar” depression should be avoided as they carry a higher risk for a ‘switch’ than the Selective Serotonin Reuptake Inhibitors (SSRIs) and Bupropion.**
- **Ensure a regular sleep-wake cycle to all patients with ‘soft bipolarity’, as sleep-deprivation can precipitate mania/hypomania in predisposed individuals.**
- **The cases with suspected clinical pointers of spectrum/soft bipolarity should be identified and sent for an expert opinion. These should be referred to a psychiatrist for further evaluation and management.**

Implications for Under-Recognition and Under-Treatment

As the diagnosis may be more easily clinched on cross-sectional presentation of patient rather than the longitudinal history, therefore the hypomanic or subthreshold symptoms are often missed. Patients are often left in the “shadow” due to the current nosological status of bipolar spectrum not being particularly emphasized. The role of a thorough history to rule out past history of any hypomania or elated mood state cannot be overemphasized.

Misdiagnosing bipolar spectrum as pure depression has its own share of risks as majority of these patients get treated with antidepressants alone. There exists a risk of incomplete or inadequate remission, anti-depressant-induced switch, anti-depressant induced rapid cycling and mixed state, and destabilization of mood. Injudicious use of antidepressants in cases with underlying bipolarity may also lead to continued subthreshold symptoms, and increased risk of suicidality, poor prognosis and adverse psychosocial outcomes.

While majority of the patients remain under diagnosed, there is a definite risk of over diagnosis and unnecessary exposure to mood stabilizers and antipsychotic medication. Caution is also needed regarding the potential risks of over diagnosis, which is also detrimental.

Conclusion

To conclude, the concept of spectrum and soft bipolarity is of increasing importance to the general physicians in the recent times owing to their clinical and public health burden. The patients with bipolar spectrum often fall prey to unscrupulous prescribing of antidepressants which may lead to devastating consequences. Hence, there is a definite need for the physicians to be wary of the clinical profile of full spectrum of bipolarity.

Some of the “soft pointers” towards bipolar spectrum should be kept in mind while assessing depressed patients. Though screening instruments are available, the feasibility of screening instruments in the busy outpatient setting is again a matter of concern. In case of switch, the antidepressant must be stopped immediately. Patients with signs of soft bipolarity may be referred to mental health professional conforming to the principle of medical ethics of non-maleficence—“Primum non nocere”.

References

1. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden


