

## Predominant Polarity in Bipolar Affective Disorder: A Scoping Review of Its Relationship with Clinical Variables and Its Implications

Arghya Pal

### ABSTRACT

**Background:** Bipolar affective disorder (BPAD) is an episodic psychiatric disorder that is associated with considerable morbidity. Psychiatrists have found it difficult to treat the disorder owing to the variety of presentation and variety of challenges in clinical decision-making. To guide the clinicians, the concept of predominant polarity (PP) in BPAD has become important. This review was conducted to understand the definition, epidemiology, relationship with sociodemographic and clinical parameters, and implications of PP in BPAD. **Methodology:** The review was conducted after selecting 17 original research studies from PubMed using appropriate search terms. **Results:** There is no consensus definition of PP. Epidemiological data showed varied results, although most common PP demonstrated in most studies was depressive polarity. The relation between sociodemographic and clinical parameters also lacked uniformity, although certain patterns could be identified in their relationships. The implications of PP in diagnostics, treatment, and classificatory system are discussed. **Conclusion:** PP in BPAD conveys clinically important information that aids a clinician in decision-making. Further studies are required so that we can understand the neurobiological underpinning of the concept.

**Key words:** *Bipolar disorder, depression, DSM 5, mania, predominant polarity*

### INTRODUCTION


Bipolar affective disorder (BPAD) is one of the widely prevalent mental disorders, with a lifetime prevalence of 2.4%.<sup>[1]</sup> BPAD usually follows an episodic course with the occurrence of recurrent (at least one) manic, hypomanic, or mixed episode in conjunction with depressive episodes, with varying degrees of interepisodic remission. A significant amount of the

lifetime of patients with BPAD is spent in suffering from affective symptoms,<sup>[2]</sup> with a higher chance of time being spent in depressive episodes. The disorder is also highly associated with suicidality and medical comorbidities. However, data from various Asian centers, including India, tend to differ on this front. Studies<sup>[3,4]</sup> from this region have shown that patients

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Department of Psychiatry, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India

**Address for correspondence:** Dr. Arghya Pal  
Assistant Professor, Department of Psychiatry, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India. E-mail: [drarghyamb@gmail.com](mailto:drarghyamb@gmail.com)

with BPAD tend to have a course predominantly characterized by manic episodes. Such patients with predominant manic episodes, though they tend to have a higher chance of syndromal recovery, also have a higher chance of relapse.<sup>[5]</sup> Thus, it can be said that the course and outcome of BPAD show significant interpatient variation, as a result of which the clinical decision-making in BPAD remains complicated.

For a long time, researchers have been trying to find proxy clinical markers that could reliably predict the future course of BPAD. One such marker was the polarity of the first episode. A retrospective study done on 150 patients with BPAD from India, using the retrospective life chart method, found out that in around 85% of the cases, mania was the first episode and also the most frequent episode.<sup>[4]</sup> The finding was further supported by another study<sup>[6]</sup> which also showed that patients presenting with first-episode mania tended to have more manic episodes subsequently. But soon it became apparent that there is a need for better predictive entities. Various studies thus adopted a longitudinal observation of the course of the illness. The initial studies done on patients with BPAD-I and BPAD-II showed an overwhelming depressive presentation.<sup>[7,8]</sup> But the studies from the tropical regions showed a stark difference and there the manic presentation was more prevalent.<sup>[4]</sup> The developments in psychopharmacology complemented these findings. Newer classification divided drugs as Class A (stabilizers from above), Class B (stabilizer from below), and Class C (stabilizer from euthymia).<sup>[9]</sup> Experts speculated that the trick to effective management of BPAD lies in the fact that if we can obtain clinical information that will enable us to reliably predict the course of the disorder, that will allow us to tailor our prophylactic treatment approaches.<sup>[10]</sup>

The concept of predominant polarity (PP) of BPAD is important in this context. The concept was first described by Angst<sup>[11]</sup> while describing the course of 95 patients with BPAD followed up for more than 16 years. He classified the patients into three classes: “preponderantly manic,” “preponderantly depressed,” and “nuclear.” However, even before that attempt, Leonhard, in his sample of 117 patients with BPAD, had shown that 17.9% had a predominantly manic presentation, 25.6% had a predominant depressive presentation, and 56.4% had an equivocal presentation. Subsequently, the entity of PP in BPAD has generated sufficient interest in the researchers. This review was hence conducted to collect the available evidence regarding PP in BPAD.

## METHODOLOGY

A search was conducted on PubMed to address the following research questions:

1. What has been the accepted definition of PP in BPAD in the literature?
2. What is the epidemiology of PP in BPAD?
3. What is the relation of PP with sociodemographic and clinical parameters of patients with BPAD?
4. What are the implications of determination of PP in BPAD?

A search was conducted on US National Library of Medicine’s PubMed/MEDLINE using the following search terms: “Bipolar affective disorder,” “Bipolar disorder,” “mood disorder,” “predominant polarity,” “mania,” “hypomania,” “depression.” Appropriate medical subject heading terms (MeSH) were accessed and used. The terms “Bipolar Disorder” [Mesh] AND “predominant polarity” were added to the search builder and articles were accessed. No restriction was placed regarding the time of publication. A secondary search was conducted among the references of the studies, and appropriate studies were accessed.

## Study selection

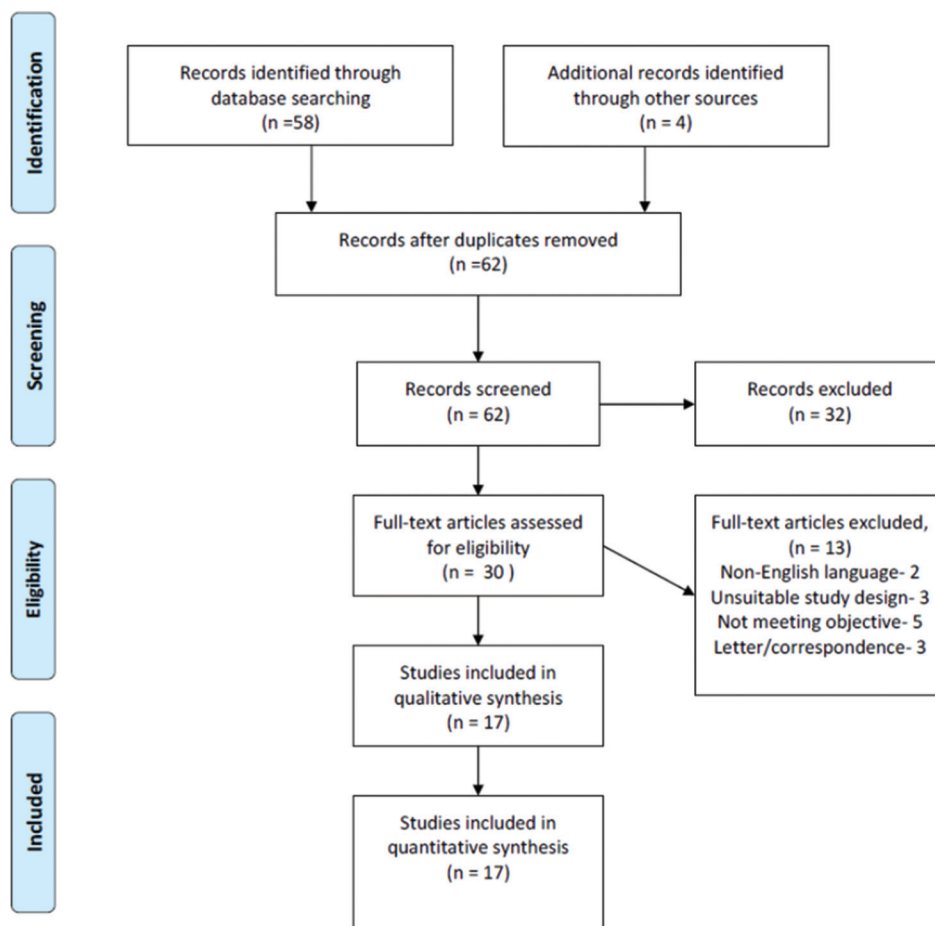
For the purpose of this article, only original articles were included. The abstracts of the studies were initially screened, and full texts of the selected studies were accessed. Only articles whose full text could be accessed and were in English language were included in this review. Overall, 17 article were selected for this review [Figure 1].

## RESULTS

Table 1 describes the studies that have been included in this review. The evidence from the included studies has been hereby arranged so as to address the initial research questions:

## Definition

One of the major points of contention among the studies included the definition used to classify patients according to PP. The most frequently used criteria were those proposed by Colom *et al.*,<sup>[12]</sup> where if two-thirds of the episode is of a particular polarity, the PP of that patient is the corresponding PP. This is also considered as the strict criteria or the Barcelona proposal. On the basis of these criteria, the patients can be classified as manic PP (two-thirds of the episode are manic/hypomanic), depressive PP (two-thirds of the episodes are depressive), or indeterminate PP (neither of the polarity has a two-thirds majority). To clarify, if a patient has had three manic/hypomanic episodes and one depressive episode in the lifetime, then the PP of the patient is manic PP. The other criteria that have also been used, considered the relaxed criteria, are when any one of the polarities of the episodes gain a 51% majority, the PP of the patient is the corresponding



**Figure 1:** Results of literature search

polarity.<sup>[13]</sup> This criterion is also called the Harvard index. Evidently, Harvard index has less diagnostic stability when compared with the Barcelona proposal. But the Barcelona proposal is considered by many as too restrictive, where around 38%–44% of the patients could not be assigned a PP.<sup>[14]</sup> The two sets of criteria were compared in one study<sup>[15]</sup> which showed that the relaxed criteria allowed more patients to be allotted in either manic PP or depressive PP, but that did not significantly change the predictive information gained.

Another source of debate has been the status of the mixed episodes. Many studies had considered the mixed episodes in the calculation in the denominator, but the mixed episodes were assigned to neither polarity for the sake of calculation according to the previously mentioned criteria.<sup>[16]</sup> A few other studies<sup>[15]</sup> had included mixed episodes under the purview of “mania-like episodes” and had calculated accordingly. The Diagnostic and Statistical Manual 5<sup>th</sup> edition (DSM 5)<sup>[17]</sup> has removed the diagnostic entity of bipolar I disorder, mixed episode, which required simultaneously meeting criteria for mania

and depression and has added a specifier instead “with mixed features.” Thus, further discussion in this regard can be considered redundant.

### Epidemiology

The epidemiological studies on PP in BPAD have been largely inconclusive, failing to provide us with any trend. A multicentric study conducted across five centers, namely, Barcelona, Catalonia (Spain); Belmont, Massachusetts (USA); Buenos Aires, (Argentina); Cagliari, Sardinia (Italy); and Bundang, Gyeonggi (Korea), including 928 patients with BPAD-I, found that 199 (21.4%) had manic PP, 290 (31.25%) had depressive PP, and 439 (47.3%) had indeterminate PP.<sup>[15]</sup> An Indian study that included 285 patients with BPAD-I<sup>[18]</sup> showed that the prevalence of manic PP in the sample was 79.3%, whereas the prevalence of depressive PP was only 13.7%. Another study<sup>[16]</sup> conducted in Germany in a sample of 336 patients with BPAD-I and BPAD-II showed that 169 (50.3%) had depressive PP and 46 (13.7%) had manic PP, whereas the rest had indeterminate PP. Another study from Barcelona, Spain,<sup>[12]</sup> conducted on 224 patients with

**Table 1: Summary of the studies included in the review**

Author	Study design and sample size	Definition of PP	Important findings
Azorin <i>et al.</i> (2015)	Cross-sectional ( <i>n</i> =278)	Barcelona proposal and Harvard Index	79.8% could be subtyped according to PP. Adopting the relaxed criteria made little clinical change. MPP showed more psychosis, rapid cycling, stressors at onset, family history of affective illness, and manic FE. DPP showed more chronic depression and comorbid anxiety
Baldessarini <i>et al.</i> (2012)	Cross-sectional ( <i>n</i> =928)	Barcelona proposal	DPP associated with ECT, longer latency of diagnosis, FE depressive or mixed, more suicide attempts, more Axis-II comorbidity, ever having mixed states, ever married, and female sex. MPP associated with FE manic, higher substance use, higher education, and more family history
Belizario <i>et al.</i> (2017)	Cross-sectional ( <i>n</i> =55, HC=31)	Barcelona proposal	MPP demonstrated greater deficit in comparison to DPP, IPP, and HC.
Colom <i>et al.</i> (2006)	Cross-sectional ( <i>n</i> =224)	Barcelona proposal	60.3% had DPP, 39.7% had MPP; DPP associated more with first depressive episode and higher suicidality. MPP mostly treated with atypical antipsychotics and conventional neuroleptics; DPP mostly treated with antidepressants and lamotrigine
de Asis da Silva (2017)	Cross-sectional <i>n</i> =101 [58 euthymic (28 MPP) and 43 in mania (17 MPP)]	Barcelona proposal	BPAD patients in mania had worse insight than those in euthymia, with no effect of dominant polarity. Number of previous manic or depressive episodes did not correlate with insight level
González-Pinto <i>et al.</i> (2010)	Prospective (10 years) ( <i>n</i> =120)	Harvard index	DPP associated with more suicidality, higher family history of affective disorders, and fewer hospitalization. At 10 years, DPP had more episodes, more hospitalization, and more suicidal attempts
Henry <i>et al.</i> (1999)	Cross-sectional ( <i>n</i> =72)	Harvard index	Depressive temperament inversely associated with the number of manic episodes
Janiri <i>et al.</i> (2017)	Cross-sectional ( <i>n</i> =218)	Barcelona proposal	Most common PP in BPAD without SUD was MPP, but the most common in BPAD with AUD and BPD with PSU is DPP
Mazzarini <i>et al.</i> (2009)	Cross-sectional ( <i>n</i> =124)	Barcelona proposal	55% could be classified into PP (DPP two-third, MPP one-third). No difference in affective temperament between MPP and DPP
Nivoli <i>et al.</i> (2011)	Cross-sectional ( <i>n</i> =604)	Barcelona proposal	DPP 23.7%, MPP 18.9%. Females had a higher chance of developing DPP
Nivoli <i>et al.</i> (2013)	Cross-sectional ( <i>n</i> =604)	Barcelona proposal	Treatment of BPAD was in line with PP of the patients
Popovic <i>et al.</i> (2014)	Cross-sectional ( <i>n</i> =604)	Barcelona proposal	MPP associated with more males, younger age, lower age of onset, and more hospitalization. DPP associated with depressive FE, suicidality, and melancholic symptoms. PP of the patients in the sample showed a positive correlation to the PI of the agents being used for the treatment.
Rangappa <i>et al.</i> (2016)	Cross-sectional ( <i>n</i> =604)	Barcelona proposal	MPP associated with manic FE; DPP associated with depressive FE
Rosa <i>et al.</i> (2008)	Cross-sectional ( <i>n</i> =149)	Barcelona proposal	DPP associated with higher latency of diagnosis, depressive FE, lower age of onset, and higher suicidality
Vieta <i>et al.</i> (2009)	Post hoc analysis of published RCT ( <i>n</i> =833)	Barcelona proposal	PP was demonstrable in 46.6% cases (DPP: MPP=2.7:1). Males with MPP showed a better treatment response
Volkert <i>et al.</i> (2014)	Cross-sectional ( <i>n</i> =336)	Barcelona proposal	63.9% had demonstrable PP. DPP and MPP did not significantly vary in terms of PI of the drugs used in its management
Yang <i>et al.</i> (2013)	Cross-sectional ( <i>n</i> =1245 who had more than three admissions)	Admissions of one polarity exceeded the other by two	Patients with predominantly depressive admissions displayed a higher degree of seasonality than patients with predominantly manic admissions

PP – Predominant polarity; MPP – Manic predominant polarity; FE – First episode; DPP – Depressive predominant polarity; ECT – Electroconvulsive therapy; HC – Healthy controls; IPP – Indeterminate predominant polarity; BPAD – Bipolar affective disorder; SUD – Substance use disorder; AUD – Alcohol use disorder; PSU – Poly-substance use; PI – Polarity index

BPAD, showed that 135 (60.3%) had depressive PP and 89 (39.7%) had manic PP.

### Factors associated with predominant polarity

The studies have been able to provide evidence that certain sociodemographic and clinical parameters are associated with PP which are summarized in Table 2.

The general trend shown by the studies was that patients with a predominant depressive polarity usually had a higher chance of being female,<sup>[15,18,19]</sup> though certain other studies<sup>[12,13,20,21]</sup> could not replicate this finding. These patients usually had a depressive episode as their first episode<sup>[15,21,22]</sup>

and a longer latent period before the disorder is diagnosed. The course of illness in these patients is usually characterized by melancholic symptoms,<sup>[12,22]</sup> mixed episodes,<sup>[12,15]</sup> and a seasonal pattern.<sup>[12]</sup> These patients were likely to have a history of suicidal acts<sup>[12,13,15,18,20,22]</sup> and receiving electroconvulsive therapy.<sup>[15]</sup>

The patients with a manic PP tended to have an earlier age of onset<sup>[13,15,22]</sup> and male gender.<sup>[22]</sup> However, many other studies failed to show male gender preponderance in manic PP.<sup>[12,15,23]</sup> These patients also usually had a manic episode as their first episode<sup>[15,18,22]</sup> and a higher prevalence of substance use.<sup>[12,22]</sup>

**Table 2: Relationship of predominant polarity of bipolar disorder with sociodemographic and clinical parameters**

Clinical parameter	Citation
Depressive polarity of first episode	7, 13, 14
Suicidal acts	4, 5, 7, 10, 12, 14
Married	5, 7
Female gender	7, 10, 11
History of electroconvulsive therapy	7
Diagnostic latency	7, 13
Melancholic symptoms	4, 14
Mixed episodes	4, 7
Seasonal pattern	4, 16
Manic predominant polarity	
Younger age of onset	5, 7, 14
Manic polarity of first episode	7, 10, 14
Male gender	14
Substance use	4, 14
Parameters which were noncontributory	
Current age	4, 5, 12, 13, 15
Total duration of illness	4, 5, 12, 13, 15
Episodes/year	4, 5, 12, 13

### The relationship between seasonal pattern and predominant polarity

It has already been mentioned in the previous section that patients with depressive PP tended to show a seasonal pattern when compared with patients with manic PP.<sup>[12,24]</sup> One of the studies which explained this result had followed up an inpatient cohort of 9619 patients with BPAD.<sup>[24]</sup> The study also showed that other than PP, the polarity of the first episode can also predict the development of seasonal pattern in these patients. A mixed polarity followed by a depressive polarity of the first episode was associated more with the seasonal pattern when compared with a manic index episode.

### The relationship between temperament and predominant polarity

A few studies tried to examine the relationship between PP and affective temperament. In their study, Henry *et al.*<sup>[25]</sup> provided some rudimentary evidence that hyperthymic temperament was positively correlated with a higher number of manic episodes and depressive temperament was correlated with a higher number of depressive episodes. However, the study was not conducted using the concept of PP. Subsequently, Mazarini *et al.*<sup>[20]</sup> compared the temperament between patients with BPAD [depressive PP ( $n = 22$ ) vs manic PP ( $n = 47$ )] and unipolar depressive disorders ( $n = 19$ ). They found that patients with depressive PP or manic PP did not have any significant differences in terms of temperament. One possible reason behind this could be the fact that the study did not have a large enough sample size to garner enough power. But patients with BPAD had significantly less depressive temperament

and higher cyclothymic and hyperthymic temperament. Finally, Azorin *et al.*,<sup>[26]</sup> in their study conducted among 278 patients with BPAD (79.8% depressive PP and 20.2% manic PP), were able to show that patients with manic PP had higher cyclothymic and hyperthymic temperament.

### The relationship between substance use and predominant polarity

Substance use disorders and PP have been shown to bear a complicated relationship. A few studies have been able to show that if substance use precedes the first affective episode in BPAD, the possibility of manic PP is higher.<sup>[12,22]</sup> However, these studies failed to show any relationship between current substance use and PP. In a long-term follow-up study<sup>[13]</sup> of up to 10 years, the authors demonstrated no significant differences in alcohol and other substance use at baseline. But in patients with manic PP, the frequency of alcohol and other substance abuse decreased significantly when compared with depressive PP. This result was further supported by another study<sup>[27]</sup> which compared the PP among BPAD patients without substance use ( $n = 86$ ), BPAD patients with alcohol use ( $n = 69$ ), and BPAD patients with polysubstance use ( $n = 63$ ). The authors found that patients with BPAD without substance use tended to have a manic PP, whereas those with alcohol use or polysubstance use tended to have a depressive PP.

### The relationship between insight, cognitive functions and predominant polarity

In a study<sup>[28]</sup> involving 55 euthymic patients with BPAD distinguished in terms of their PP (manic PP 17, depressive PP 22, indeterminate PP 16) and 31 healthy controls, the authors used a neuropsychological battery testing for attention, verbal fluency, planning, and memory. The study showed that patients with manic PP were significantly poor performers in alternating attention, verbal fluency, and delayed memory when compared with all other groups. Patients with depressive PP showed no deficit in any of the tests when compared with manic PP or indeterminate PP. The authors even speculated that the cognitive deficits in BPAD might be related to the polarity of the episodes rather than the number of episodes. Another study,<sup>[29]</sup> involving 101 patients with BPAD [58 euthymic (28 MPP) and 43 in mania (17 MPP)] showed that PP does not have any bearing on the level of insight.

### Polarity index

The concept of PP has led to the advent of the concept of polarity index (PI). PI as a construct is a number that denotes the ability of a drug used in the management of BPAD to prevent episodes of either polarity. It is defined as the ratio of the number needed to treat (NNT) for prevention of a depressive episode to the NNT

for prevention of a manic episode. A PI of more than 1 denotes a superior antimanic property, whereas a PI of less than 1 denotes a superior antidepressive property. Popovic *et al.*,<sup>[22]</sup> in a sample of 604 patients with BPAD, showed that patients who had manic PP were cumulatively treated with drugs with a higher PI when compared with patients with depressive PP. A similar attempt<sup>[16]</sup> on a sample of German patients ( $n = 336$ ) found that the concept fitted poorly to their sample as there was no significant difference in the PI of the regime used in the management of patients with manic PP or depressive PP. The authors speculated that one of the major reasons behind the negative result could have been the fact that many of the drugs which were a part of the study could not be analyzed as there was no PI assigned to them (e.g., antidepressants). In spite of such results, PI remains a useful construct and should be a focus of further research.

### The implications of predominant polarity

The expression of PP in a patient with BPAD conveys a substantial amount of information about the patient. Table 2 has already stated the important sociodemographic and clinical parameters that can be associated with certain PP. Colom *et al.*<sup>[12]</sup> were able to demonstrate that different PPs are associated with very different management goals in BPAD-I and BPAD-II. In BPAD-II, the most common PP is the depressive PP, and the most important target should be to prevent a depressive episode, whereas in BPAD-I, prevention of both manic and depressive episodes is important.

The elaboration of PP in BPAD can also imply a lot of information regarding the treatment choices made for the patients. A naturalistic study<sup>[30]</sup> has been able to demonstrate that the treatment strategies predominantly used in a cohort of patients with BPAD are in line with their PP. The authors conducted a principal component analysis of a sample of 604 patients with BPAD. The three main prescription patterns that arose were “antimanic stabilization package” for “predominantly manic-psychotic BPAD-I patients,” “antidepressive stabilization package” for patients with depressive PP, and “antibipolar II package” including antidepressant monotherapy for patients with BPAD II with depressive PP. The antimanic stabilization package consisted of mood stabilizers (lithium, valproate, and carbamazepine), three atypical antipsychotics (clozapine, risperidone, and olanzapine), and electroconvulsive therapy. The antidepressive stabilization package consisted of lamotrigine and atypical antipsychotics such as quetiapine. The antibipolar II package, on the other hand, comprised the use of antidepressants such as tricyclic antidepressants, monoamine oxidase inhibitors, serotonin selective reuptake inhibitors, and

serotonin/noradrenaline reuptake inhibitors. In another sample of 788 patients with bipolar depression,<sup>[23]</sup> it was found that PP could be established in 367 patients, the majority of whom had depressive PP. Males in this sample with predominant depressive polarity showed a worse outcome to treatment when compared with males with manic PP. This pattern could not, however, be seen among the females in the sample.

## DISCUSSION

This review was able to find two sets of definitions for PP. Arguably, the Barcelona proposal has been the more widely used definition so far, but the relevance of the Harvard index remains when the research design does not endorse a diagnostic orphan or “indeterminate polarity.” However, the scope for further research to achieve a unifying definition remains. The diagnostic status of the mixed episodes also was a source of ambiguity, much of which has been made redundant following the publication of DSM 5<sup>[17]</sup> and the anticipated changes according to the beta version of International Classification of Disease 11<sup>th</sup> edition.<sup>[31]</sup>

No major trend arose from the epidemiological studies. But certain trends have been speculated in the literature, where authors have found a manic preponderance in tropical areas and a depressive preponderance from the temperate regions.<sup>[3]</sup> Studies that included patients with BPAD-I also showed a higher prevalence of manic PP.<sup>[15]</sup> However, that could not be replicated in patients with BPAD-II. Hence, we should potentially invest some efforts to find out any trends, if they exist, and the reason behind that.

The studies reviewed have been able to associate various clinical features with certain PPs. But many of the findings could not be replicated across research. One important reason could be that all the studies did not have the methodological rigor to negate the effect of confounding factors adequately. Another reason could be a recall bias against the non-PP of the clinical course. However, in spite of that, the associated parameters convey important information that could aid decision-making. It is important to recall at this stage that evidence suggests that there is a very close association of PP with the polarity of the first episode. Manic PP has been closely linked with substance use and male gender. Depressive PP is associated with female gender, suicidality, and higher diagnostic latency. Studies also demonstrated that patients with manic PP tended to have higher cognitive deficits when compared with those with a depressive PP. The existing literature also supports the fact that cognitive impairment in BPAD is not just state-dependent and that probably certain cognitive deficits also persist in remission.<sup>[32]</sup>

The concept of PP and PI also seems to complement each other. Patients with manic PP were usually treated with drugs with higher PI (denoting superior antimanic property) when compared with depressive PP and vice versa. This review points out that we should be guided by the PI of the drugs while choosing appropriate stabilizing medication. However, certain deficiencies need to be corrected. For example, the PI of certain drugs cannot be calculated. The PI of paliperidone cannot be calculated because the NNT for depressive episodes is negative. Again, due to the definition of PI, an agent which is very good in both antimanic and anti-depressive properties cannot be differentiated from an agent which is weak in both antimanic and antidepressive properties. More research is also required to further substantiate the evidence that the prophylactic serum levels of lithium may vary according to the PP of the patients.<sup>[33,34]</sup> The prophylactic serum level is less for prevention of a depressive episode when compared for a manic episode.

A lot of enthusiasm was there regarding the possibility of PP to be a specifier in the DSM 5 criteria,<sup>[35]</sup> which has subsided after its publication. Although it has not been accepted as a specifier, the facts that mixed episode has ceased to be an independent polarity and that there has to be a polarity attributed to any episode even with mixed features reiterate the importance of PP. The current belief is indeed that PP remains an important clinical variable in the management of BPAD.<sup>[36]</sup>

## LIMITATIONS

The available literature has not been able to reach a single definition of consensus. As a result, it has been difficult to compare the results of the studies. Although some efforts have been made to find out the differential effects of this variety, further research is required to arrive at a consensus. In the same vein, we need to think about how we should interpret the substantial information that we have been able to accumulate about the so-called “indeterminate polarity.” Does it actually represent a distinct group of patients with BPAD? Or is it just a victim of a categorical conceptualization of a construct?

In spite of the concept not being very new, there has been a dearth of large-scale prospective data. It should also be noted that the studies that were conducted are from a few centers. As a result, there is ample scope and requirement of replicating the findings across other centers.

## CONCLUSION

In the aftermath of the release of DSM 5, where the concept of PP was disregarded and not accepted as a

course specifier, the enthusiasm seems to have died down. This is reflected by the fact that the number of studies subsequent to its release has been sparse. But there is no denying the fact that PP remains a useful construct in our clinical practice. One of the putative reasons behind this apparent disregard may be the fact that we are trying to move toward a psychiatric classification that is less dependent on phenomenology and more on neurobiology. Hence, our further efforts should be focused on developing neurobiological correlates of PP. Further studies should be conducted on genetics, neurobiology, and neuropsychology and to find biomarkers of PP in BPAD.

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## Conflicts of interest

There are no conflicts of interest.

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