

# Recurrent Unipolar Mania: Does it Warrant a Separate Nosological Status?

Thippeswamy Harish, Sandeep Grover and Debasish Basu

Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Corresponding author: Dr Debasish Basu, Additional Professor, Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India; E-mail: [db\\_sm2002@yahoo.com](mailto:db_sm2002@yahoo.com)

## Abstract

*The concept of unipolar mania, unlike unipolar depression, has received relatively little attention. We review the research available on the validity of it as a separate entity. Studies show that there are few consistent differences in socio-demographic and family history variables in unipolar mania compared to other bipolar disorders, but there are a few differences regarding clinical picture, neuroimaging and response to lithium. Many studies have come from nonwestern countries or settings, probably indicating an influence of culture on the disorder. The debate on the nosological status of unipolar recurrent mania seems premature in view of the lack of consensus on the very definition of the condition and the difficulties inherent in constructing such a definition. There appears, however, sufficient evidence to indicate that the issue merits further study, because there are a sizeable number of patients, reported from several countries and cultures, who demonstrate a recurrent unipolar manic course. As a way out of this dilemma, we propose that a course specifier be added to the diagnosis of bipolar disorder indicating the course of unipolar recurrent mania. This will currently obviate the need to debate whether unipolar recurrent mania is a distinct 'disorder'; rather, the focus will be on the course of the broad rubric of bipolar disorder. This will also generate systematic data, which then can be subjected to a more formal analysis. Tentative operational criteria for the course specifier categories are proposed (German J Psychiatry 2005;8(1):8-15).*

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## Introduction

Mood disorders have been known for more than 2,500 years (Angst & Marneros, 2001). The concept of unipolar mania has been raised, rejected, and resurrected by a number of authors (Leonhard, 1957; Angst & Perris, 1968; Makanjuola, 1985; Khanna et al., 1992; Yazici et al., 2002). Although the position of unipolar mania in the current psychiatric nosology is still controversial, but the concept of unipolar recurrent mania, like the proverbial phoenix, still refuses to die and again comes out from its ashes. Relatively few studies are available on the topic, and there are methodological issues involved. In this article we will review the literature available on the topic and see what tentative conclusions can be drawn from the same.

The search strategies for this update included both search of electronic databases as well as manual search of relevant publications or cross references. Electronic search included both PUBMED searches and searches using other search engines and databases such as EMBASE and PSYCLIT. Cross-searches of key references (both electronic and hand-search) often yielded other relevant material. The search terms used (in various combinations) were: recurrent mania, unipolar mania, recurrent unipolar mania, periodic mania, pure mania, bipolar others; history, nosology, validity, definitions, course, outcome, management, and treatment. In this article an attempt has been made to provide an update within the constraints of search strategies employed.

## Historical Aspects

The historical aspects of bipolar disorder and the bipolar-unipolar controversy have been comprehensively described by Angst and Marneros (2001). The concept of affective disorders is historically very old. Descriptions of the depressive (melancholia) and manic states can be found in the pre-Hippocrates era, but it was Hippocrates who first systematically described mania and depression. Aretaeus was the first person to explicitly link mania and melancholia. He considered melancholia and mania as two different images of one single disease having same aetiology. The seventeenth and eighteenth century maintained Aretaeus' view. However, it was Falret (1851), a follower of Esquirol, who for the first time drew the conclusion that bipolar disease is an entity of its own. He described an entity named "folie circulaire" characterized by a continuous cycle of depression, mania and free intervals of varying length. Three years later Baillarger (1854) described "folie a double forme", the concept of which was similar to that of Falret, except that he did not consider the interval between the episodes to be of any importance. The above concepts found enthusiastic supporters, but also had critical opponents, like Meyer (1874), who labeled it as meaningless.

Later it was Emil Kraepelin (1893, 1896) who dichotomised endogenous psychoses into 'manic-depressive insanity' and 'dementia praecox'. He stressed the close relationship between the syndromes of depression and mania and contributed enormously to the understanding, diagnosis and prognosis of manic-depressive illness. However, he also described cases of manic irritability with no features of depression, which he termed as "periodic mania".

However, Wernicke (1900) opined that manic-depressive illness should only be understood as described by Falret and Baillarger. He maintained that single episodes of mania or melancholia respectively, recurrent depression or recurrent mania without changing into one another was something different from manic-depressive insanity. Kleist too (1928, 1953) differentiated between unipolar and bipolar disorders. Kleist and Neele, by combining Wernicke's syndromic and Kraepelin's prognostic principles, classified phasic psychosis, in which they included pure (monopolar) mania as a separate entity. Neele (1949) in her genetic study was first to suggest a genetic basis for the distinction between monopolar mania and manic-depressive illness. Karl Leonhard classified the 'phasic psychoses' into 'pure phasic psychoses' (such as 'pure melancholia'; 'pure mania' etc.) and 'polymorphous phasic disorder', which included manic-depressive illness & cycloid psychoses (Leonhard, 1957). Neither Kleist nor Leonhard considered monopolar mania to be a component of bipolar disorders in present-day terms. They described monopolar mania separately from manic-depressive disorders.

But the concept of monopolar mania again faded after the influential and independent observations made by Jules Angst and Carlos Perris. Angst concluded that genetic and environmental factors have synergistic role in the aetiology of endogenous depression, gender plays an important role in aetiology of endogenous depression, manic-depressive illness

is nosologically not homogenous (unipolar depression differs significantly from bipolar disorders in many characteristics such as gender, genetics, course and premorbid personality) and late onset depression belongs to unipolar depression (Angst, 1966). Perris (1966) also reached similar conclusions as that of Angst. Both of them further showed that 'unipolar mania' was clinically and genetically very strongly related to bipolar disorders, so that the assumption regarding the separation of the group of unipolar mania was an artifact (Angst & Perris, 1968). After this categorical position statement, over the last nearly forty years only a few studies have appeared on unipolar mania, which are reviewed.

## Nosology

Current internationally accepted classificatory systems such as ICD-10 (World Health Organization, 1992) and DSM-IV-TR (American Psychiatric Association, 2000) do not give separate nosological status to recurrent mania, and include the condition under the realm of bipolar disorders. ICD-9 had a separate category of unipolar mania, which disappeared in ICD-10; patients with two or more episodes of mania are now understood to be bipolar and are included under the category of bipolar others (F31.8). DSM-III, DSM-III-R included all manic episodes under bipolar disorders. The nearest diagnostic category in DSM-IV-TR is 'bipolar disorders not otherwise specified' which includes recurrent hypomanic episodes with no intercurrent depressive features.

However, it is interesting to note that the third edition of the Chinese Classification of Mental Disorders (CCMD-3) published in 2001 has given a separate nosological status to recurrent unipolar mania (Chinese Psychiatric Society, 2001).

## Definitions and Prevalence of Recurrent Unipolar Mania

One of the major limitations to the research in the area of unipolar mania is lack of consensus on the defining criteria. Due to the lack of consensus in defining the same no conclusions can be drawn from the available studies. Different authors have used different criteria for the diagnosis of the recurrent mania with respect to the number of manic episodes, diagnosis of manic episode, and inclusion/exclusion of the depressive symptoms in the intercurrent period. In the studies published in the last decade there appears to be some consensus on the presence of at least 3 manic episodes with no depressive episodes, but there is no consensus on the time frame for the same. For example, recently Aghanwa (2001) defined recurrent mania with 3 previous episodes of mania or hypomania (ICD-10) and the presence of affective illness for at least 4 years. On the other hand, Yazici et al. (2002) defined recurrent mania by occurrence of at least 4 episodes of mania (DSM-IV) and at least 4 years of follow up without any depressive episode. Many clinicians would

agree that these duration limits are also arbitrary as many patients with bipolar disorder have only manic episodes for the initial few years and then go on to develop depressive episodes along with mania. Thus, a vital and critical issue that remains unresolved concerns the maximum number of manic/hypomanic episodes that a person must have in a particular time frame (without any depressive episode) so as to make a confident diagnosis of unipolar recurrent mania. Another related crucial issue in the definition is the necessary absence of depressive episodes. This can become an important practical issue since the diagnosis of recurrent unipolar mania is usually made retrospectively. In making such a retrospective diagnosis based on examination of the patient's life-chart, there always remains the scope of missing a mild depressive episode unless the charting was done very care

fully (Yazici et al., 2002).

It must be remembered, however, that these issues are not unique to making a diagnosis of only recurrent unipolar mania; they are equally as important in case of making a diagnosis of recurrent unipolar depression as well. Any further discussion on these conditions, therefore, must be tempered with the definitional caveats as mentioned above.

With these considerations, **Table 1** shows several definitions along with prevalence figures for recurrent unipolar mania. Not surprisingly, it can be seen that the percentage of unipolar mania has been found to be varying very substantively in these studies, from a low of 1.1% (Perris, 1982) to a high of 53% (Makanjuola, 1985). Other than the definitional and diagnostic issues highlighted above, variations in country,

**Table 1. Definition and prevalence of recurrent mania**

Author	Definition	Type of study	Prevalence
Perris (1966)	1 or more manic episode with no depressive episode	Retrospective chart review	4.5% among all bipolar patients
Abrams & Taylor (1974)	"Never had a depressive episode"	Retrospective chart review	28% of manic patients
Abrams et al. (1979)	2 episodes of mania without any depressive episode.	Retrospective chart review	18% of bipolar patients
Nurnberger et al. (1979)	1 or more hospitalizations with no hospitalization or somatic treatment for depression (a history of depressive symptoms or treatment of depression with psychotherapy was not sufficient to exclude a patient from the diagnosis of unipolar mania.	Retrospective chart review & structured interview in one-third cases	15.7% of bipolar I patients
Perris (1982)	1 or more manic episode with no depressive episode	Retrospective chart review	1.1% of all bipolar patients
Pfohl et al. (1982)	1 or more manic episode with no depressive episode	Retrospective chart review	35.2% of bipolar inpatients
Venkoba Rao et al. (1982)	Only mania; no depressive episode during follow-up	Retrospective data from a lithium clinic	2.7% of lithium clinic patients
Venkoba Rao & Madhavan (1983)	Only mania; no depressive episode during follow-up	Retrospective data from a lithium clinic	12% of BPAD patients, when the age of onset was after 60 years
Makanjuola (1985)	At least 2 episodes of manic disorder & none of the depressive disorder. Manic episode defined by Research Diagnostic Criteria (RDC), Spitzer et al. (1978).	Prospective study over 5 years	53% of manic patients
Srinivasan et al. (1985)	3 episodes of mania without any depressive episode.	Retrospective chart review of inpatients	40% of bipolar inpatients
Margoob & Dutta (1988)	Not clear	Retrospective chart review of outpatients	42% of all bipolar patients
Shulman & Tohen (1994)	At least 3 distinct manic episodes without major depression and at least 10 years elapsed from the time of first hospitalization for mania. Manic episode as per DSM-III-R. Comorbid presence of a cerebral organic condition was also included.	Prospective chart review of elderly (>65 yrs) inpatient cohort	12% of elderly manic patients
Khanna et al. (1992)	At least 4 episodes of manic disorder & no depressive episode, as defined by Research Diagnostic Criteria (RDC)	Retrospective chart review of inpatients	44% of bipolar inpatients with 4 or more episodes
Avasthi et al. (1996)	3 or more than manic episodes (ICD-10) without any depressive episode.	Retrospective chart review	6.45% of all affective disorder patients
Aghanwa (2001)	3 previous episodes of mania (ICD-10) or hypomania and the presence of affective illness for at least 4 years.	Retrospective chart review	47.2 % among all bipolar patients
Yazici et al. (2002)	At least 4 episodes of mania (DSM-IV) and at least 4 years of follow up without any depressive episode.	Retrospective chart review	16.3% among all bipolar I patients
Solomon et al. (2003)	Onset with mania/hypomania; no depressive episode thereafter throughout the entire follow-up period	Prospective 15-20 years follow-up study	~26 % had only manic episodes, with no major depressive episodes

settings, type of patients and other unknown factors might have contributed to causing this tremendous variation.

## Validity of Recurrent Mania

To organize the data relevant to the question of validity of recurrent mania the available data can be divided into three classes of potential validators. This schema represents an adaptation and enlargement of the validating criteria for psychiatric illnesses as outlined by Robin and Guze (1970). The potential validators can be divided into antecedent, concurrent and predictive validators.

### Antecedent validators

These include sociodemographic variables, premorbid personality and evidence from family studies. There are a few studies that have described the socio-demographic profile of recurrent mania.

### Age of onset

Taylor & Abrams (1973) reported that late onset mania (30+yrs) run a course of unipolar mania in half of the patients whereas early onset mania (< 30 years) tend to run a typical bipolar course. In a subsequent study Abrams et al. (1974), while comparing unipolar mania with bipolar mania, found that the mean age of onset in unipolar mania was 37 years in contrast to 25 years for bipolar disorders; this difference was statistically significant. However, on further analysis when they excluded all the patients with age at onset less than 30 years (early onset) to test whether the difference in age of onset was associated with polarity of illness alone, no difference for mean age of onset was found between bipolar and unipolar mania. Nurnberger et al. (1979), Pfohl et al. (1982), Makanjuola (1985), Srinivasan et al. (1985), Khanna et al. (1992), and Aghanwa (2001) reported no statistical difference in age of onset between unipolar and bipolar mania. Interestingly, a few recent studies have shown age of onset of unipolar mania to be significantly *less* than that of bipolar mania. In a study of elderly manic patients Shulman & Tohen (1994) reported that the age of onset was significantly lower in unipolar manics (41.2 years) compared to a mean of 64.7 years for bipolar elderly manics. Yazici et al. (2002) reported that unipolar manics had significantly earlier age of onset (23 years) compared to bipolar patients (26 years). The remaining studies have not reported any significant differences regarding age at onset.

### Age when first seen at clinic

Nurnberger et al. (1979) found no difference between unipolar and bipolar I patients regarding age when first seen at clinic. Pfohl et al. (1982), however, reported a significantly lower age at index hospitalization for unipolar mania than that for bipolar mania.

### Sex Ratio

Abrams & Taylor (1979), Nurnberger et al. (1979), Pfohl et al. (1982), Makanjuola (1985), Kubacki (1986), and Khanna et al. (1992) observed that unipolar mania was slightly more or equally prevalent in males. Again, recent studies by Aghanwa (2001), Yazici et al. (2002), and Solomon et al. (2003) reported unipolar mania to be more common in females. Of these, Solomon et al.'s (2003) study was a prospective study with follow up period of 15-20 years but it did not have any comparison with bipolar I group

### Marital Status

Aghanwa (2001) and Yazici et al. (2002) found no significant difference between unipolar mania and bipolar patients. In the study by Solomon et al. (2003), out of 7 patients 3 were separated/divorced, 3 were never married and 1 patient lived together. No comparison was made with bipolar I group. Other available studies have not commented upon this variable.

### Educational Status

Makanjuola (1985), Starkstein et al. (1991), and Yazici et al. (2002) did not find any significant difference regarding level of education amongst unipolar mania, bipolar and single manic episode patients.

### Occupational status

No significant difference between occupational status of unipolar mania and bipolar patients was found by Aghanwa (2001), though unemployed were more common amongst unipolar mania.

### Culture

Many of the studies of unipolar mania have come from nonwestern cultures such as Nigeria (Makanjuola, 1982, 1985), Hong Kong (Lee & Yu, 1994), India (Khanna et al., 1992; Avasthi et al., 1996), Fiji Islands (Aghanwa, 2001), and Turkey (Yazici et al., 2002). Authors from Nigeria have stated that unipolar mania is the 'rule there rather than an exception' (Makanjuola, 1985). Of the few studies reported from USA, the study of Pfohl et al. (1982) was conducted on patients from Iowa. Even in the 20-year follow up study by Solomon et al. (2003) from U.S.A. five of the seven subjects with unipolar mania came from Iowa site. The authors explained this difference between the prevalence among various sites on the basis of Iowa being predominantly a rural setting (probably a less developed 'nonwestern' setup) in contrast to the urban setting of the other four sites studied. Due to limitation of studies of unipolar mania in nonwestern cultures it needs to be seen whether culture has any role in its prevalence, and, if so, in what way.

### Ethnicity

The only study that compared the prevalence of unipolar mania amongst different races in the same setting in the Fiji

Islands (Aghanwa, 2001) did not find any significant difference.

### Family Studies

Taylor & Abrams (1973) observed that unipolar manics had fewer relatives with affective illness, drug abuse and characterological pathology compared for bipolar patients. In a re-analysis, Abrams & Taylor (1974) further confirmed the above results of unipolar manics having fewer relatives with affective illness and alcoholism. However, when age of onset was controlled there were no significant differences regarding genetic variables. In a subsequent study Abrams et al. (1979) observed relatives of unipolar mania patients had a significantly increased morbid risk of unipolar depression, whereas a number of studies have reported the morbid risk of psychiatric illnesses in first-degree relatives to be similar to bipolar group (Nurnberger et al., 1979; Pfohl et al., 1982; Srinivasan et al., 1985; Shulman & Tohen, 1992; Aghanwa, 2001). Yazici et al. (2002) found that the relatives of unipolar mania had lesser morbid risk of unipolar depression and absence of family history of suicide in unipolar group. However, differences failed to reach a significant level. Solomon et al. (2003) reported that out of their 7 patients, 4 patients had a family history of major depression, mania, schizoaffective depression/ mania, but they did not compare with bipolar I group.

## Concurrent validators

### Clinical features

Abrams & Taylor (1974) compared unipolar and bipolar patients on various clinical parameters and found that unipolar mania patients more commonly exhibited euphoria and expansive mood, lability, persecutory delusions, confusion and less commonly flight of ideas, incomplete auditory hallucinations, visual hallucinations, head decoration and catatonia, but this difference was not significant statistically. Other clinical features that have been reported to be present significantly more in unipolar mania compared to bipolar mania are grandiosity (Abrams et al. 1979; Pfohl et al., 1982), more total illness episodes (Khanna et al., 1992), significantly higher psychotic symptoms, especially delusions (Pfohl et al., 1982; Yazici et al., 2002), non-alcohol substance abuse such as marijuana and amphetamine (Pfohl et al., 1982), and pre-morbid hyperthymia (Yazici et al., 2002). On the other hand, the clinical features less commonly reported in unipolar mania compared to bipolar mania are lesser suicidal rates and rapid cycling (Nurnberger et al. 1979; Yazici et al., 2002). Studies have also reported no difference in phenomenology and other clinical features between unipolar and bipolar patients (Srinivasan et al., 1985), number of episodes (Aghanwa, 2001; Yazici et al., 2002), and duration of episodes (Yazici et al., 2002). In a study of 50 recurrent manic patients Avasthi et al. (1996) noted that 11 fulfilled the Rosenthal criteria of seasonal affective disorder. On comparison, recurrent manic patients with seasonal pattern had significantly more psychotic symptoms (delusions and hallu-

cinations) and significantly higher number of episodes with onset in autumn.

### Neuroimaging

Mukherjee et al. (1992) reported that both third ventricular widths as well as parieto-occipital cortical sulcal ratings were significantly less in unipolar mania patients (DSM-III-R) than in bipolar mania patients. The third ventricular width, but not the parieto-occipital cortical sulcal ratings, remained significantly different between the groups even after controlling for the variance due to age and sex. In another study of bipolar and unipolar mania in patients following brain injury by Starkstein et al. (1991) demonstrated significant difference in location and size of brain lesions. Unipolar manic patients sustained significantly large cortical lesions, primarily in right orbitofrontal and right basotemporal cortices and less of subcortical lesions.

### Laboratory Study

In a study of lithium clinic patients Lee et al. (1992) found thyroid autoimmunity in a proportion of bipolar patients, and it was absent in unipolar patients. Pfohl et al. (1982) found significantly more 'abnormal blood count or chemistry' in bipolar mania, but the details of these tests are not mentioned.

### Neuropsychology

Starkstein et al. (1991) in a study of bipolar and unipolar mania in patients following brain injury found patients with unipolar course had significantly higher mini-mental status examination score compared to bipolar manics.

## Predictive Validators

### Treatment Response

There are only 4 studies that examined the effect of treatment in recurrent unipolar mania. Abrams et al. (1974) did not find any significant differences in treatment response between the unipolar and bipolar manics. Nurnberger et al. (1979) found the efficacy of lithium prophylaxis to be similar in unipolar manics and in bipolar patients hospitalized for depression, and this efficacy was superior to those in bipolar patients not hospitalized for depression. The above finding suggested that depressive predominance in bipolar patients was associated with better response to lithium prophylaxis.

Yazici et al. (2002) assessed the response to lithium in 202 patients, of which 42 were unipolar manics and rest were bipolar patients. There was no significant difference in mean duration of treatment (5.9 years for bipolar, 5.5 years for unipolar) in both the groups. They defined treatment response in three categories, i.e. good response, moderate response and poor response. Good response was defined as presence of definite improvement with no major or minor mood swings or only with minimal mood changes not requiring additional treatment, expect for a short duration of

benzodiazepine administration during lithium prophylaxis. Poor response was defined as no improvement in episode frequency, duration, and severity during prophylaxis; moderate response was taken in cases whose response was intermediate between the two groups. In the bipolar group 44% were in good response category, 36% in moderate response category and 20% were in the poor response category whereas in the unipolar group 28% were in good response category, 36% in moderate response category and 36% were in the poor response category. The difference in the two groups was not significant but the ratio of poor response seemed higher in the unipolar manic patients. However, the difference was statistically significant when good and moderate response categories were clubbed together and compared. Husain et al. (1993) reported good response to maintenance ECT in a case of an elderly female with recurrent unipolar mania (Bipolar disorder, manic as per DSM-III-R) who was resistant to antipsychotics and mood stabilizers, lithium intolerant, treated with 81 ECTs over a period of 2 years.

From the limited data available it appears that recurrent unipolar mania patients may be relatively less responsive to lithium.

**Follow-up data**

A number of studies provide useful data on the course and change in polarity of initially diagnosed unipolar mania. These are shown in **Table 2**, which shows the course of unipolar recurrent mania.

As seen in **Table 2**, although most of the data that are available are retrospective in nature, but it is informative to a large extent. The duration of illness assessed in various studies has varied from 5.9 years to 27.7 years, over which pa-

tients had only manic episodes indicating that the illness may be running a true unipolar manic course in certain patients. However, studies that have prospectively assessed the patients over few months to years have shown that many patients are reclassified. In the study by Nurnberger et al. (1979) 29% of cases were reclassified as true bipolars when assessed properly over the period of three months. In the recent prospective study from USA where patients with manic episodes were followed up prospectively for 15-20 years (Solomon et al., 2003), 7 out of 27 patients (26%) did not develop depression over follow-up. This, according to the authors, lends clear support to the validity of unipolar mania. However, 2 of these 7 patients had no recurrence of mania either (after their index episode). Thus, unipolar mania as described by Solomon et al. (2003) is not necessarily recurrent mania.

A few points limit the informative nature of the data. As reviewed (table 2), most of the studies done are retrospective in nature and have looked for the number of episodes as documented or recollected. This may be fallacious because of the fact of inaccuracy of data or poor recall by the patients and relatives. Further, lack of proper assessment may lead to fallacious findings, for example, Nurnberger et al. (1979) in their study on unipolar mania found that on detailed assessment with structured interviews, many patients with unipolar mania do have some depressive symptoms. Twenty nine percent of the patients initially thought to have unipolar mania based on the clinical history were reclassified because they showed signs of depression that required treatment. Another limitation of the data can be because of the lack of observation for appropriate duration in prospective studies; for example, Perris (1982) in his study found that in majority of the cases, change in polarity from mania to depression occurred by the 3<sup>rd</sup> episode after the onset of the

**Table 2. Course of recurrent mania**

Author	Type of study	Duration of follow-up in years	Mean number of episodes/ change in polarity
Abrams et al. (1974)	Retrospective chart review	10.86	0.61 per year
Abrams et al. (1979)	Retrospective chart review	11.7	1.2 episodes per year
Nurnberger et al. (1979)	Retrospective chart review & structured interview in one-third cases		29 % of patients were reclassified as true bipolar over 4 months period of assessment
Perris (1982)	Retrospective chart review		Change in polarity from mania to depression occurred by the 3 <sup>rd</sup> episode after the onset of the illness, but 10 out of his 45 cases had their first episode of depression after the third episode, rarely after the 8 <sup>th</sup> episode
Makanjuola (1985)	Prospective study over 5 years	5.9*	4.5
Srinivasan et al. (1985)	Retrospective chart review and interview with key informant	12	5
Shulman & Tohen (1994)	Prospective chart review of elderly (>65 yrs) inpatient cohort	27.7	No change in polarity in any patient
Khanna et al., 1992	Retrospective chart review of inpatients	9.5	7.2 years
Avasthi et al. (1996)	Retrospective chart review	7	4 episodes in non-seasonal and 9 in seasonal variants
Aghanwa (2001)	Retrospective chart review	16.6	0.76 per year
Yazici et al. (2002)	Retrospective chart review	12	1.27 per year
Solomon et al. (2003)	Prospective 15-20 years follow-up study	20	7 out of 27 continued to have the diagnosis of unipolar mania

\*Duration between the first episode and last follow up

illness but 10 out of his 45 cases had their first episode of depression after the third episode, rarely it may occur even after the 8<sup>th</sup> episode. So it is quite possible that many patients have been labeled as unipolar manics simply because the time for a depressive episode has not yet arrived.

## Conclusion and a Proposal

From the above review of literature it can be concluded that unipolar mania have received very less attention compared to unipolar depression and bipolar disorders and only a handful of literature is available, that too mostly from non-western countries. The available studies show that there is no major difference in the age of onset (although a few recent studies indicate an earlier age of onset for unipolar mania) and other sociodemographic variables compared to other bipolar disorders. In clinical presentation, compared to bipolar mania, unipolar mania more frequently has grandiosity, more total illness episodes, significantly higher psychotic symptoms, premonitory hyperthymia and less frequently exhibit rapid cycling and have lesser suicidal rates. Neuroimaging findings of subjects with unipolar mania show significantly less third ventricular size than in bipolar mania patients and have significantly large cortical lesions, primarily in right orbitofrontal and right basotemporal cortices and less subcortical lesions. Regarding treatment response, subjects with unipolar mania seem to respond poorly to lithium compared to bipolar subjects. Most of the data come from retrospective studies, which limit the understanding of the course, but a few studies that have followed the patients suggest that some subjects require a change in diagnosis. The influence of culture on this particular diagnosis has received very little attention although studies have mostly proliferated from non-western countries.

One of the major limitations of the available research is lack of consensus on the definition on recurrent mania. Future studies with consensus on the definition, focus on cross-cultural issues and larger sample sizes with prospective follow-up are required to reach to any firm conclusion regarding this particular entity.

For the time being, there does not seem to be enough consistent and strong evidence to justify a nosological separation of unipolar mania from bipolar disorder. Although some differences in clinical and/or psychopathological features have been noted as summarized above, these are unfortunately not consistent across studies, nor do they seem to be bold enough to act as possible 'markers' or indicators of one particular type of illness. At the same time, however, there does seem to be sufficient evidence to indicate that the issue merits further study, because there are a sizeable number of patients, reported from several countries and cultures, who demonstrate a recurrent manic course without any depressive episode throughout.

Thus, we propose that a course specifier should be added to the diagnosis of bipolar disorder indicating the course of unipolar recurrent mania. This will help in attracting the attention of the clinician as well as the research community

to this particular course of the illness, without any premature debate on its nosological place. This will also generate systematic data, which then can be subjected to a more formal analysis. More importantly, there will be always a provision for a change in the course specifier from 'unipolar' to 'true bipolar' whenever such a change is warranted due to a depressive episode occurring in the follow-up period. This will obviate the current need to debate whether unipolar recurrent mania is a distinct 'disorder' (i.e., the nosological debate); rather, the focus will be on the course of the broad rubric of bipolar disorder.

We propose the following operational criteria for the course specifier categories of bipolar disorder:

**Definite bipolar course:** presence of at least one clear depressive episode in addition to manic or hypomanic episodes (diagnosed as per relevant criteria of the particular nosological system in question) during the course of the illness.

**Possible unipolar recurrent manic course:** presence of at least 2 manic or hypomanic episodes but no diagnosable depressive episode. (This criterion reflects the 'loose' or 'broad' definitional approach adopted by many of the earlier authors, e.g., Abrams et al., 1979; Makanjuola, 1985.)

**Probable unipolar recurrent manic course:** presence of at least 4 manic or hypomanic episodes and a total duration of affective illness for more than 4 years. (This criterion reflects the relatively more 'tight' or 'narrow' definitional approach adopted by the recent authors, e.g., Aghanwa et al., 2001; Yazici et al., 2002.)

There can be no definite unipolar recurrent manic course specifier, simply because any future depressive episode would immediately nullify it!

With these proposals, we hope that the study of this important area will get a research impetus that it deserves. It must be remembered that these are only tentative criteria to guide systematic research presently, and these can be modified in the light of fresh data.

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