

## Nonadherence to Medications among Persons with Bipolar Affective Disorder - A Review

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### ABSTRACT

Treatment nonadherence among persons with bipolar disorder is quite high. An attempt to review studies on nonadherence in bipolar disorder was made. Searched in Google Scholar and snowball search from various sources were made. Finally thirty two studies were considered for review. The results were classified into various themes such as sociodemographic data of persons with nonadherence, reasons for nonadherence, symptoms severity and global improvement, social support, knowledge and attitude about illness in the primary care givers/family members and adherence enhancement interventions. Findings show that there is difficult to define adherence and non adherence, major studies were conducted to understand the reasons for nonadherence and psycho education was the major intervention to enhance adherence. The study implies that the importance of qualitative study to understand the reasons for non adherence, need for an exact definition of adherence and nonadherence and randomized controlled intervention studies to enhance adherence.

**Key words:** adherence, nonadherence, bipolar disorder, medication, treatment.

### INTRODUCTION

Bipolar disorder is a severe mental disorder, it is a recurrent and severe condition [1] and it is one of the leading causes of disease burden. [2] Psychotropic medications are a cornerstone of treatment for individuals with bipolar disorder; however, non adherence with prescribed medication is pervasive and is associated with negative outcomes, such as illness relapse. [3] Medication non adherence is a significant public health problem. [4] Despite new psychopharmacological developments, treatment outcomes still depend upon treatment compliance. [5] In bipolar disorder; even patients receiving optimal medication are likely to have multiple recurrences. [6] Studies found high prevalence of treatment non adherence in bipolar disorder - 10 to

60% [4] and 23 to 68%. [7] Improving treatment adherence of patients with severe mental illness is one of the biggest challenges facing psychiatry today. [8] Many studies have been conducted to understand the problem of “adherence to treatment”, but still non adherence to treatment is a major challenge in mental health. The current review aims to understand the issues on treatment/medication non adherence and related issues in persons with bipolar affective disorder (PwBPAD).

### METHODOLOGY

Objectives of the study are to review the studies related to the treatment non adherence and related issues in persons with BPAD, to identify some of the major gaps

in those studies and to formulate implications for further research.

**Literature selection criteria**

In this work, the adherence related studies operationalized as those studies which related to the prevalence of treatment/medication non adherence, reasons or predictors for treatment non adherence, knowledge and attitude of patient and family members, measurement of treatment non adherence, illness severity and global functioning/improvement, interventions to enhance adherence through psychoeducation, cognitive behavioral therapy, group interventions, family and community interventions.

**Inclusion criteria**

- Articles published from the year January 1993 to March 2014
- Full text or abstracts available in English
- Both qualitative and quantitative studies
- Review studies.

**Exclusion criteria**

- Studies focused only on bipolar disorder (symptom, outcome, course etc.),

psychosocial interventions focusing other than non adherence.

- Treatment adherence enhancement Interventions based on pharmacological/any other physical methods

**Search protocol**

The primary search was carried out in ‘Google scholar’ and snowball search from various sources were made. The search terms were “treatment non adherence in bipolar”, “drug compliance in bipolar”, “medication adherence in bipolar”, “Drug adherence in mood disorders” and “medication adherence in affective disorders”. The search resulted in 1019 titles based on selection criteria. In that 917 were excluded because of other topics related to BPAD and excluded 45 studies because of published before 1993. Later excluded 29 studies because of the focus were not primarily or at least one variable is adherence.

**RESULTS**

**SOCIODEMOGRAPHIC PROFILE**

Sl.	Ref	Aims & objectives	Materials and methods	Results
1.	[9]	To evaluate the prevalence and predictors of non adherence in bipolar disorder	Reviewed 25 papers on medication adherence published between 1979 and 2004.	Single, marital status/living alone one of the main sociodemographic factors for non adherence.
2.	[10]	To compare medication adherence among older vs. younger individuals with bipolar disorder	Adherence was evaluated using the Medication Possession Ratio (MPR) among 26530 patients receiving medication. Mean age of young is (46.9) and older individuals are 69.2.	Younger patients are more non adherent
3.	[11]	To examine adherence with lithium and anticonvulsant medication among patients with bipolar disorder	Bipolar patients (n=44,637) receiving Tab. Lithium. Medication adherence was assessed by using the Medication Possession Ratio (MPR)	Younger, unmarried, non white, or homeless are not adherent
<b>REASONS FOR NON ADHERENCE</b>				
1.	[12]	To Identify risk factors for poor medication adherence	The sample included 41 men and 62 women. Applied Zuckerman Sensation-Seeking Scale, Barratt Impulsivity Scale and Physical Anhedonia Scale	Greater sensation-seeking is associated with poor medication adherence
2.	[4]	To review the prevalence, predictors and methods for improving medication adherence in bipolar affective disorders.	Studies were identified through Medline and PsycLit searches of English language publications between 1976 and 2001. This was supplemented by a hand search and the inclusion of selected descriptive articles on good clinical practice.	Attitudes and beliefs are at least as important as side-effects in predicting adherence
3.	[13]	To explore the prevalence and predictors of non adherence in a cohort of individuals with affective disorders receiving long-term treatment with mood stabilizers	98 subjects with BPAD. Adherence measure using structured interview schedule	Denial of illness, attitudes and behaviours, bothered of having chronic illness

<i>Continued table no.1</i>				
4.	<sup>[14]</sup>	To explore the perspective of patients, their family and mental health professionals from their community mental health centre (CMHC) on factors related to treatment adherence.	A total of 52 persons were involved. Qualitative study.	Patients and families had a complex cognitive model, which combined intrinsic vulnerability, psychological suffering during childhood and adolescence, and adverse life events. Denial of the disease and need to test its continuing presence were the main causes of non adherence for patients, while adverse reactions did not play a relevant role. Mental health professionals tended to underestimate non adherence in depressed patients, and did not question their patients about medication adherence. Family members needed more information
5.	<sup>[15]</sup>	To identify factors associated with medication adherence in bipolar disorder (BPD) patients.	2-years, prospective, observational study on the outcomes of BPD patients initiating or changing treatment for a manic/mixed episode. Data were collected at baseline, during the first 12 weeks of treatment (acute phase) and up to 24 months of follow-up (maintenance phase).	Psychotic symptoms, poor insight are major reason
6.	<sup>[16]</sup>	To identify patients' perceptions of medication adherence in bipolar disorder.	An integrated review of the literature published between 1999 and 2010 from Ovid (Medline, CINAHL, Embase, and PsycINFO) and manual searching.	Suggest a need to address adherence from the full range of influencing factors (patient, illness, medication and environmental). Clinicians need to utilise a collaborative approach to working together with patients in order to identify the meaning that patients attribute to the symptoms, diagnosis, prognosis and medication. Understanding patients' perceptions and accepting these may facilitate greater medication adherence and the consequent improved clinical outcomes for patients with bipolar disorder.
7.	<sup>[17]</sup>	To study the prognostic role of perceived criticism, medication adherence and family knowledge in bipolar disorders	Medication adherence was assessed in 33 individuals (TRQ), and expressed emotions assessed with Perceived Criticism (PC) and Perceived Sensitivity (PS) & family members who agreed to completed an assessment of their knowledge and understanding of bipolar disorders	Perceived criticism and medication adherence were significant predictors of admission
8.	<sup>[18]</sup>	Aimed to verify the adherence, knowledge and the difficulties of elderly patients with Bipolar Affective Disorder (BAD)	This is a cross-sectional, descriptive, quail-quantitative study. Used Morisky-Green test	Deficit in knowledge in relation to the medication non adherence
9.	<sup>[19]</sup>	Characterization of reasons for treatment non adherence among individuals known to be poorly adherent with medication treatment.	Illness experience was evaluated with qualitative interview. Quantitative assessments measured symptoms (Hamilton Depression Rating Scale, Young Mania Rating Scale, and Brief Psychiatric Rating Scale), adherence behaviour, and treatment attitudes. Poor adherence was defined as missing 30% or more of medication.	Forgetting to take medication and problems with side effects are primary drivers of non adherence. Lack of medication routines, unsupportive social networks, insufficient illness knowledge, and treatment access problems are contributory
10.	<sup>[20]</sup>	To review studies evaluating factors associated with adherence to treatment in bipolar disorder (BD), as well as the results of interventions developed to enhance adherence in this population	Articles from 1980 to 2012 were included from peer-reviewed publications. Well-conducted observational studies randomized controlled trials (RCT), cross-sectional and case-control studies were considered. Expert consensus reviews were also included.	Patient-related factors (e.g. younger age, male gender, low level of education, alcohol and drugs comorbidity), disorder-related factors (e.g. younger age of onset, severity of BD, insight and lack of awareness of illness) and treatment-related factors (e.g. side effects of medications, effectiveness).
11.	<sup>[21]</sup>	To assess drug treatment adherence in patients with bipolar disorder and to identify factors associated with adherence. The secondary aim was to analyze the impact of suboptimal adherence on clinical and functional outcomes.	A cross-sectional study was conducted in a sample of outpatients receiving an oral antipsychotic drug (31 community-based mental health centres throughout Spain-total 303 patients). Medication adherence was assessed combining the 10-item Drug Attitude Inventory, the Morisky Green Adherence Questionnaire, and the Compliance Rating Scale.	No significant differences were seen in terms of gender, living status, type of bipolar disorder, or disease duration between patients with optimal and suboptimal adherence. However, patients with adherence problems were significantly younger, were more likely to be unemployed, more frequently experienced depressive polarity of the most recent acute episode, and had a greater prevalence of substance abuse/dependence disorder

<i>Continued table no.1</i>				
12.	[22]	Examined the association of patients' perceptions of therapeutic alliance with their psychiatrist, care satisfaction, and medication adherence	3337 participants were included	Patients' perceptions of collaboration, empathy, and accessibility were significantly associated with adherence to treatment in individuals with bipolar disorder completing at least 1 assessment. Patients' perceptions of their psychiatrists' experience, as well as of their degree of discussing medication risks and benefits, were not associated with medication adherence.
13.	[23]	To study the Predictors of adherence to psychopharmacological and psychosocial treatment	Naturalistic prospective 18-month study	Non adherence is more during depressive stage. Non adherence is independently associated with negative <i>attitudes</i> towards mood stabilizers
<b>SYMPTOM SEVERITY AND GLOBAL IMPROVEMENT</b>				
1.	[15]	To identify factors associated with medication adherence in bipolar disorder (BPD) patients	2-year, prospective, observational study on the outcomes of BPD patients initiating or changing treatment for a manic/mixed episode. Data were collected at baseline, during the first 12 weeks of treatment (acute phase) and up to 24 months of follow-up (maintenance phase).	Symptoms was high (hallucinations/delusions) in nonadherents
2.	[24]	To study the efficacy of a psychosocial intervention--customized adherence enhancement (CAE)	Prospective study	BPRS, HAM-D, and YMRS scores all indicated significant improvement at three-month follow-up
3.	[21]	To assess drug treatment adherence in patients with bipolar disorder and to identify factors associated with adherence. The secondary aim was to analyze the impact of suboptimal adherence on clinical and functional outcomes.	A cross-sectional study conducted in 31 community-based mental health centres throughout Spain.	The Young Mania Rating Scale (YMRS) and the Montgomery-Åsberg Depression Rating Scale (MADRS), Modified Clinical Global Impression Bipolar Disorder. Only 37% of patients with suboptimal adherence were euthymic, as compared with 63% in the adherent group. Disease severity and functioning were significantly worse in the suboptimal group than in the adherent group
<b>SOCIAL SUPPORT</b>				
1.	[9]	To evaluate the prevalence and predictors of medication adherence	Reviewed 25 papers on adherence published between 1979 and 2004.	Psychosocial support is major in enhancing adherence
2.	[19]	To study the illness experience of persons with BPAD	A mixed-method (qualitative and quantitative) characterization of reasons for treatment non adherence among individuals known to be poorly adherent with medication treatment.	Lack of social support is contributory for non adherence. 55% of the respondents reported poor social support especially support from family.
3.	[5]	This study aimed to determine the factors affecting treatment compliance during the treatment of bipolar disorder and contribute to current clinical strategies.	78 volunteers , met the remission criteria- depression/mania	Social support was adequate in adherent persons which indicates social support is essential in enhancing the adherence
<b>ADHERENCE ENHANCEMENT INTERVENTIONS</b>				
1.	[25]	To study the effects of psycho education in married bipolar patients.	Randomised control trial among 42 patients	Medication compliance was significantly better among patients receiving the psychoeducational intervention
2.	[26]	To review the effects of CBT in bipolar disorder	Reviewed the literature and case examples.	CBT has significant relevance in enhancing adherence as it has psychoeducational property.
3.	[27]	To review the articles on psychosocial interventions enhance adherence.	Reviewed 12 articles on RCT which mentioned adherence	Interventions that have been shown to be effective include interpersonal group therapy, cognitive-behavioural therapy, group sessions for partners of persons with bipolar disorder, and patient and family psychoeducation.
4.	[28]	To review articles on adherence to treatment in mood disorders.	Reviewed qualitative studies on adherence	The psycho-educational intervention model alone has shown little improvement in adherence. The collaborative managed care model for improving outcomes in depression in primary care is of limited benefit in increasing adherence or indeed outcomes. Psychological approaches have been most successful when concentrating on the patient-clinician alliance when attitudes and experience are explored, recognizing the importance of the patient's opinion in treatment decisions.

<i>Continued table no.1</i>				
5.	[29]	To present the rationale, development, and pilot study of a medication adherence skills training (MAST-BD) intervention for older adults with bipolar disorder (BPD).	Quasi-experimental clinical trial among 21 patients.	Improvements in self-reported medication adherence, medication management ability, depressive symptoms.
6.	[30]	To evaluate the efficacy of psychoeducation in the treatment of bipolar disorder according to specific therapeutic targets such as treatment compliance, patients' and families' knowledge of the illness and its treatments	A systematic review of the literature published on psychoeducation up to July 2006 was carried out using the main electronic data bases (Medline, PubMed). The key words employed included bipolar disorder, psychoeducation, depression, mania, relapse prevention and treatment compliance	Psychoeducational components improve compliance, both to lithium and to other mood stabilizing treatments and to improve the patient's knowledge and attitude towards the illness and its treatments. Also increases family member's knowledge of the illness, its treatments
7.	[31]	To examine the challenges involved in improving medication adherence in bipolar disorder, and to extract some suggestions for future directions from the core psychosocial studies that have targeted adherence as a primary or secondary outcome.	Publications from 1996 to 2008 using Medline, Web of Science, CINAHL PLUS, and PsychINFO. The following key words were used: adherence, compliance, alliance, adherence assessment, adherence measurement, risk factors, psychosocial interventions, and psycho-education.	Needs large scale randomised control studies to define adherence, measurement and interventions.
8.	[32]	To study the feasibility of CAE in adherence	Uncontrolled trial evaluating the feasibility, acceptability, and preliminary efficacy of CAE in 43 poorly adherent BD patients. A study report after 3 months	Showed improvement in adherence and in symptoms.
9.	[24]	To study the feasibility of CAE in adherence	Uncontrolled trial evaluating the feasibility, acceptability, and preliminary efficacy of CAE in 43 poorly adherent BD patients. A study report after 6 months	Showed improvement in adherence and in symptoms.
10.	[33]	To study the effectiveness of a simple individual psycho-education program on quality of life, rate of relapse and medication adherence in bipolar disorder patients	RCT among 86 patients with BPAD, for a period of 18 months follow up.	Significant in improving knowledge and adherence.
11.	[34]	test the effect of motivational interviewing (MI) on medication adherence in patients with bipolar disorder (BD) in an outpatient setting.	Pre test–post test design was used. The 3-week MI intervention consisted of one face-to-face session and two follow-up telephone interventions	Overall, the participants' self-efficacy and motivation to change improved over time
<b>FAMILY MEMBERS' KNOWLEDGE AND ATTITUDE</b>				
1.	[30]	To evaluate the efficacy of psychoeducation in the treatment of bipolar disorder according to specific therapeutic targets such as treatment compliance, patients' and families' knowledge of the illness and its treatments, relapse prevention, symptomatic (depressive or (hypo)manic) phases of the illness or social and occupational functioning.	A systematic review of the literature published on psychoeducation up to July 2006 was carried out using the main electronic data bases (Medline, PubMed). The key words employed included bipolar disorder, psychoeducation, depression, mania, relapse prevention and treatment compliance.	Psychoeducation increases family member's knowledge of the illness, its treatments resulted in better adherence
2.	[17]	To study the prognostic role of perceived criticism, medication adherence and family knowledge in bipolar disorders	Conducted in 81 patients and 13 family members	Poorer knowledge or understanding of several aspects of the BPAD in family members have contributed in adherence

Totally twenty eight studies were considered for the current review process.

The study findings variables grouped into

- Sociodemographic details of PwBPAD
- Reasons for non adherence

- Symptoms severity and global improvement
- Social support
- Knowledge and attitude about illness in the primary care givers/family members

- Adherence enhancement interventions for PwBPAD

The details of the studies are briefly explained below.

## DISCUSSION

The current study reviewed 28 studies. Objectives of the study were to review studies related to the treatment non adherence and related issues in persons with BPAD, to identify some of the major gaps in those studies and to formulate implications for further research. The major gaps found are; there is no clear definition for ‘adherence’ and ‘non adherence’ and hence the measurement of adherence is difficult. These findings are go along with finding in other review studies <sup>(7,31,35)</sup> also. Many studies depended on subjective reporting of adherence. The findings indicate that; it needs to frame the exact definition for “non adherence” and “adherence”. And it needs studies to develop gold standard tools to measure in bipolar disorder.

Majority of the studies concentrated to understand the reasons for “non adherence” than adherence enhancement interventions. Reasons for nonandherence are multi factorial. Marital status (being single), young, lack of social support, poor knowledge and attitude in family members and homelessness etc. play major role in poor adherence. Similar findings have been noted in another study. <sup>[36]</sup> Require more qualitative researches to understand the reasons for non adherence from patients’ and families’ perspective. Psycho education was the main interventions or the strategy used to enhance adherence. These findings match with the findings in another review study. <sup>[30]</sup> In most of the studies; the duration for post assessments after interventions are very short; mostly three to six months and most of the studies are with small sample size and there is lesser the number of studies with randomization. It is need of the hour to have randomized control trials (RCTs) of interventions in enhancing the adherence. Similar suggestion was found

in another study <sup>[31]</sup> that in adherence research it needs more RCTs. As the follow up is shorter, future studies should be with long term follow up. Psychoeducation is the most used strategy to address the non adherence at present. Require RCT studies on other strategies to enhance adherence.

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