

Original Article

Comorbidity of obsessive- compulsive disorder in early and late onset manic depressive disorder

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Abstract

Introduction: The aim of this study was to compare obsessive-compulsive disorder (OCD) comorbidity in early and late onset bipolar I disorder and to explore the pattern of obsessive symptoms in these two groups.

Methods: A total of 100 inpatients with early and late bipolar disorder were admitted in the child, adolescent and adult psychiatric ward. They were recruited to the study through convenience sampling. All patients had a current DSM-IV episode based on using K-SADs and SCID. They were evaluated to about obsessive-compulsive disorder comorbidity using Y-BOCS. Clinical data were compared using multivariate test.

Results: Fifty-two percent with early onset versus twenty-eight percent of late onset bipolar cases had a comorbidity of OCD and the difference was significant ($p < 0.05$). Obsessive symptoms in early onset group were more religious, aggressive, sexual and somatic types.

Conclusion: Our study showed high comorbidity rate of OCD among patients with early onset bipolar disorder. Future large-scaled prospective studies are required for better understanding of factors related to bipolar and OCD co-occurrence.

Declaration of Interest: None.

Keywords: OCD, Bipolar disorder, Comorbidity.

Introduction

Bipolar disorder in children and adolescents has recently become the focus of increasing attention. It is now generally accepted that clinical presentation

of mania in childhood may be atypical by adult standard (1). Carlson et al. reported that patients with early onset mania were more likely to have comorbid behavior disorders in childhood and had fewer episodes of remission in a 2-year period than those with adult mania (2). Premorbid psychiatric problems are common in early onset bipolar disorder, especially difficulties with disruptive behavior disorders, irritability and behavioral dyscontrol (3,4,5,6,7,8). Clinical researches found that 24% to 79% of bipolar subjects present at least one anxiety disorder during their lifetime

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(9,10,11). Despite conflicting results in the prevalence rate and frequency orders most common anxiety disorders associated with bipolar disorder are obsessive compulsive disorder, panic disorder and social phobia (12). Epidemiological studies found a prevalence from 14.6% to 21% of OCD in bipolar subjects, a prevalence up to 8.1 times higher was expected for the general population (13,14). Clinical studies diagnosed the association of OCD in about 1.55% to 35.1% with bipolar subjects (15,16). In the Epidemiologic Catchment Area (ECA), the percentage of OCD in bipolar disorder was 16.7% in the absence of panic disorder and 37.1% with its presence (13). In children and adolescents, the association of bipolar disorder and OCD was found in approximately 33% of prepubertal and 12% of adolescents groups (17). In the study of a sample of 43 children and adolescents with bipolar disorder (I or II), 26 (44.2%) of them had comorbid OCD (18). Another study identified OCD in 22 (48.9%) of 45 children with bipolar disorder (I or II) (19). Most studies investigated comorbidity of anxiety disorders with bipolar disorders have notified the lower age at onset of bipolar disorder in cases with comorbidity (20,21). Recent researches suggest that early-onset bipolar disorder can be considered a specific subtype, not only in terms of genetic load, clinical picture and pattern of comorbidity, but also for treatment response (22). Little is known about bipolar disorder in children and adolescents and its relationship with OCD compared to adults. The purpose of this study was to assess the lifetime prevalence of OCD and the pattern of obsessive symptoms in patients with bipolar disorder in two age groups: early onset (age at onset <18 years) compared to late onset (age at onset >18 years).

Methods

For this cross-sectional study data were gathered from 100 patients with bipolar disorder admitted in the child, adolescent and adult psychiatric service between 2004-2006 at the Imam Hossein hospital, Tehran, Iran. In the consecutive case ascertainment, every new admitted patient who was diagnosed by his/her clinician to have bipolar disorder was evaluated by semistructured interviews. Inclusion criteria were males and females above six years old with current bipolar disorder based on using Kiddi-Schedule for Affective Disorder and Schizophrenia (K-SADS) for children and adolescents, and Structured Clinical Interview for DSM-IV (SCID) for adults (23,24,25,26,27). Exclusion criteria were IQ < 70, previous developmental disorders, epilepsy or other major medical or neurological disorders. The rationale for these inclusion and exclusion criteria included the following: subjects needed to have bipolar I disorder to avoid diagnosing mania only by symptoms that overlapped with those for ADHD specially in early onset group. They need to have an IQ of at least 70 to cooperate in interview and to recall obsessive symptoms in the past. The participants were divided into two groups, corresponding to age at onset of bipolar disorder. Early onset was considered when the main symptoms of the bipolar disorder began before age of 18 and late onset of 18 or above. It was supposed to recruit equal numbers in each group. Informed consent was obtained from each patient's parent or guardian and the subjects above 18 were consented themselves before participation in the study. The diagnosis of bipolar disorder which had been made clinically by general psychiatrist (in adult group) and child and adolescent psychiatrist (in children and adolescents group) was confirmed using semistructured instruments (K-SADS and

SCID). A range of demographic and clinical variables were analyzed. Age, gender, age at onset (AAO) of bipolar disorder and age at onset of OCD were obtained from medical record and interview with the patient and one family member. AAO of bipolar disorder was considered the age at the first admission in hospital. Age at onset of OCD was defined the age at the first identified episode meeting criteria for OCD. Diagnosis of lifetime OCD and its subtypes was made using K-SADS and the Yale-Brown scale (children and adults version) (28,29). They were assessed following recovery from the acute affective phase and within one week before discharge to increase reliability. Obsessions and compulsions were grouped according to four categories described by factor analysis studies (30,31,32). In our study, patients were included in a specific symptoms dimension only when severity and impairment of symptoms was clinically significant according to the researcher's judgement. Data analysis used SPSS 10.0 R software for windows. Clinical data were compared using the Fisher Exact Test, chi square, independent sample t-test and multivariate tests. The statistical significance level was defined as $p < 0.05$.

Results

One hundred patients were enrolled in the study. Subjects were divided into early onset (50 patients) and late onset (50 patients) groups.

Subjects in early onset group had a mean age of 15.6 ± 1.62 and in late onset group, the mean age was 32.90 ± 0.52 . Mean AAO of bipolar disorder were 14.30 ± 2.02 in early onset and 25.40 ± 7.67 in late onset group. Table 1 shows sex ratio, OCD comorbidity and subtypes of OCD in both groups. There was no statistical difference between two groups in relation to gender variable. However, there

was a significant difference in terms of the presence or absence of comorbid OCD in the two groups. There was no significant difference in comorbidity rate based on gender factor. Table 1 displays the types of obsessions and compulsions in two groups.

Table 1. Clinical variables in early and late onset bipolar disorder

	Early onset n (%)	Late onset n (%)	P
Sex			
Male	27(54)	26 (52)	
Female	23 (46)	24 (48)	
Age at onset of BD (Mean $\pm$ SD)	1430 $\pm$ 2.02	25.40 $\pm$ 7.6 7	
Comorbidity with OCD	26 (52)	14 (28)	0.024
Obsessive symptoms			
-Contamination	11 (22)	9 (18)	0.655
- Symmetry & ordering	4 (8)	2 (4)	0.414
-Religious, aggression and sexual	11 (22)	6 (14)	0.033
-Hoarding	0	0	

Contamination obsessions and cleanliness and washing compulsions were reported in 22% of young and 18% of adults without significant difference between two groups. Symmetry obsessions and ordering, counting and repeating compulsions were reported in 8% of young and 4% of adults without significant difference. Aggressive, sexual, religious and somatic obsessions and checking compulsions were obtained in 22% of the young and 6% of the adults and the difference is statistically significant ($p < 0.05$). In both groups, no one displayed hoarding symptom. There was no significant differences between mean and standard deviations of obsession, compulsions and total scores between two groups.

The average age at onset of OCD in early onset group who were comorbid with OCD was $12.69 \pm$

2.44. It shows the priority of the AAO of OCD compared to the AAO of bipolar disorder in children and adolescents ($p < 0.05$). There was no significant correlation between age and YBOC scores in the cases with comorbidity in both groups (Spearman's $\rho = 0.048$, $p = 0.772$).

Conclusion

The aim of this study was to compare the comorbidity rate of OCD and the pattern of obsessive symptoms in early and late onset bipolar disorder. The average age at onset of bipolar disorder was 14.30 ± 2.02 and 25.40 ± 7.67 in the first and second group respectively, and it was consistent with two subtypes of early and intermediated onset of (bipolar disorder) BPD in Bellivier's study and early and late onset BPD in Carte's project (33,21). In our sample of BP subjects, those with an earlier onset had a higher frequency of comorbidity with OCD (52%) in comparison with BP subjects with later onset (28%). The frequency of OCD comorbidity in patients with later onset of BPD is similar to the findings of the most clinical and epidemiological studies (13,34,14,35,16).

However, one study reported low frequency of current comorbidity of OCD (7%) (36), which can be due to making diagnosis of lifetime OCD in the present study. Higher frequency of OCD comorbidity among younger group is consistent with two recent and similar studies, which reported OCD comorbidity in 44.2% and 48.9% of children and adolescents with bipolar disorder respectively (47,19). Tillman et al., reported OCD comorbidity in 24.7% of children with bipolar I disorder (38). The discrepancy among studies about comorbidity rate of OCD included differences in setting or methodology such as the phase of BPD during which subjects were assessed for comorbidity, in the use of epidemiologic data versus clinical data from

inpatients or outpatients, in choice of diagnostic interview and in whether lifetime or current diagnoses of OCD were made. In the present study there was no significant difference between all subjects with BPD and OCD regarding to gender, which is comparable to the results of some previous studies (39,13,40). However, we found three studies with different results. Kruger et al. showed all subjects with OCD and BPD were male with bipolar II disorder (36). In contrast to the findings of Tamam (2002), reported subjects with the first episode and male sex had lower rates of anxiety disorders (35). In another study, early age at onset of bipolar disorder was associated with female gender and greater overall comorbidity (51). Our findings regarding to subtypes of obsessions and compulsions showed subjects with earlier age at onset had more aggressive, sexual, religious and somatic obsessions and checking compulsions compared to patients with later onset of BPD (22% compared to 6%). As a whole religious obsessions and checking compulsions are one of the most common obsessions and compulsions in children and adolescents while they are not more frequent in adults. Masi et al. reported more existentialistic, philosophical, bizarre and superstitious obsession in the group with comorbidity of BPD and OCD compared to the group with only OCD (37). Perugi et al. in a study of episodic course in OCD reported significantly higher rates of sexual obsessions and significantly lower rates of order rituals than non-bipolar OCD patients (51). In other studies adolescents' obsessions in cases without bipolar comorbidity typically focus on dirt and germ, fear of an ill fate befalling loved ones, exactness or symmetry and religious scrupulousness (43). Bodily functions, lucky numbers, sexual or aggressive preoccupation and fear of harm to oneself are less common. In adults these remain frequent, but

aggressive and sexual obsessions are more common (44,45,46). In the present study, sexual or aggressive preoccupations were high in early onset bipolar and these results were not in line with what would be expected from developmental perspective. On the other hand, nobody had hoarding symptoms in our finding and this is in contrast to the finding of Mataix-Cols in a pediatric OCD sample. They found a large proportion of children and young people with OCD endorse clinically significant hoarding symptoms (47). Perhaps there is a cultural variation in types of OCD symptoms in different countries or it may be due to bipolar comorbidity. Additional finding was the priority of AAO of OCD to AAO of bipolar in early onset group. It is keeping with the results of the study done by Masi et al., which reported the earlier age at onset of OCD in children with the comorbidity of OCD and bipolar disorder compared to those with only OCD (48,37). However, we did not register the AAO of OCD in late onset group and we cannot compare them according to AAO of OCD. Moreover, this finding supports epidemiologic data suggesting the presence of anxiety disorders may predict the onset of BPD.

Limitation of our study includes the relatively small sample size of patients with bipolar disorder. Our samples are not representative of bipolar population and are limited to bipolar I disorders and inpatient subjects. Individuals presenting to specialty treatment setting have more severe symptomatology, are more impaired and some from families that feel more burdened by their children's problems, than are individuals with psychiatric disorders who do not present for treatment (49). However, it is important to consider clinical samples for the study of comorbidity, which are very useful when their limitations are appreciated. For example, when the target groups to which one wishes to generalize one's results are other clinical samples. In addition, most

patients with disorders such as bipolar can be expected to present for treatment (50). Another limitation of our study is a likelihood of recall bias on age at onset, and this is the limitation of these retrospective data. The only way to avoid this apparent problem is to measure concurrent and successive comorbidity prospectively in longitudinal studies (50). Future researches might be required to clarify the correlation and etiological factors responsible for this comorbidity. Identifying specific comorbidity in two age groups of bipolar disorder will help refining phenotypic descriptions and subtyping of bipolar disorder. Such studies aim at optimizing treatment strategies.

References

1. Bowering MA, Kovacs M. Difficulties in diagnosis manic disorders among children and adolescents. *Journal of American Academy of Child & Adolescent Psychiatry* 1992; 31:611-614.
2. Carlson GA, Bromet EJ, Sievers S. Phenomenology and outcome of subjects with early and adult onset psychotic mania. *American Journal of Psychiatry* 2000; 157: 213-219.
3. Carlson GA. Child and adolescent maniac. *Journal of Child Psychology & Psychiatry* 1990; 31:331-342.
4. Fergus EL, Miller RB, Luckenbaugh DA, Leverich GS, Findling RL, Speer AM, et al. Is there progression from irritability/ dyscontrol to major depressive and manic symptoms? A retrospective community survey of parents of bipolar children. *Journal of Affect Disorder* 2003; 77:71-78.
5. Geller B, Zimmerman B, Williams M, Delbello MP, Frazier J, Beringer L. Phenomenology of prepubertal and early adolescent bipolar

- disorder: examples of elated mood, grandiose behaviors, decreased need for sleep, racing thoughts and hyper sexuality. *Journal of Child Adolescent Psychopharmacology* 2002; 12:3-9.
6. McClellan J, Breiger D, Mc Curry C, Hlastala S. Premorbid functioning in early onset psychotic disorders, *Journal of American Academy of Child Adolescent & Psychiatry* 2003; 42:666-672.
 7. Werry JS, McClellan J, Chard L. Early-onset schizophrenia, bipolar and schizoaffective disorders: a clinical and follow-up study. *Journal of American Academy of Child and Adolescent Psychiatry* 1991; 30:457-465.
 8. Wozniak J, Biederman J, Kiely K, Ablon JS, Faraone SV, Mundy E, et al. Mania-like symptoms suggestive of childhood-onset bipolar disorder in clinically referred children. *Journal of American Academy of Child and Adolescent Psychiatry* 1995; 34:867-876.
 9. Henry C, Vanden Bulke D, Bellivier F, Etain B, Rouillon F, Leboyer M. Anxiety disorders in 318 bipolar patients: Prevalence and Impact in illness severity and response to mood stabilizer, *Journal of clinic psychiatry* 2003; 69: 331-335.
 10. McElroy SL, Altshuler LL, Suppes T, Keck PE, Frye MA, Denicoff KD, Nolen WA, Kupka RW, Leverich GS, Rochussen JR, Rush AJ, Post RM. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with Bipolar disorder. *American Journal of psychiatry* 2001; 158: 420-426.
 11. Pini S, Cassano GB, Simonini E, Savino M, Russo A, Montgomery SA. Prevalence of anxiety disorders comorbidity in bipolar depression, unipolar depression and dysthymia. *Journal of Affect Disorder* 1997; 42(2-3):145-53.
 12. Issler CK, Sant'Anna MC, Kapezinski F, Lafer B. Anxiety disorders comorbidity in bipolar disorder. *Revista Brasileira de Psiquiatria* 2004; 26: 31-36.
 13. Chen Y W, Dilsaver S C. Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorder. *Psychology research* 1995; 59: 57-64.
 14. Fogarti F, Russel JM, Newman SC, Bland RC. Epidemiologic of psychiatric disorders in Edmonion Mania. *Acta Psychiatrica Scandinavica* 1994; 376: 16-23.
 15. Coryell W. Obsessive - compulsive disorder and primary unipolar depression, Comparisons of Background, Family history, course, and morality. *Journal of Nervous and mental disorder* 1981; 169: 220-224.
 16. Vieta E, Colom F, Corbella B, Martinez-Aran A, Reinares M, Benabarre A, Gasto C. Clinical correlates of psychiatric comorbidity in bipolar Inpatients. *Bipolar disorder* 2001; 3: 253-258.
 17. Weiner JM, Dulcan MK. Textbook of child and adolescent psychiatry 3rd edition. Washington DC: American Psychiatric publishing; 2004.
 18. Masi G, Toni C, Perugi G. Anxiety disorders in children and adolescents with bipolar disorder: a neglected comorbidity. *Canadian Journal of Psychiatry* 2001; 46: 797-802.
 19. Masi G, Toni C, Perugi G. Externalizing disorders in consecutively referred children and adolescents with bipolar disorder. *Comprehensive Psychiatry* 2003; 44:184-189.
 20. Simon NM, Smoller JW, Fava M, Sachs G, Racette SR, Perlis R, Sonawalla SH, Rosenbaum JF. Comparing anxiety disorders

- and anxiety- related traits in bipolar disorder and unipolar depression. *Journal of psychiatric research* 2003; 37: 187-192.
21. Carter T D, Mundo E, Parikh S V, Kennedy J L. Early age at onset as a risk factor for poor outcome of bipolar. *Journal of psychiatry Research* 2003; 37: 296-303.
 22. Schurhoff F, Bellivier F, Jouvent R. Early and late-onset bipolar disorders: Two different forms of manic depressive illness? *Journal of Affect Disorder* 2000; 58: 215-221.
 23. First M, Spitzer R, Gibbon M, Williams JB. Users guide for the Structured Clinical Interview for DSM-IV Axis I disorders: SCID-I clinician version. Washington DC: American Psychiatric Association 1996.
 24. First M, Spitzer R, Gibbon M, Williams JB. Users guide for the Structured Clinical Interview for DSM-IV Axis I disorders (clinician version): SCID administration booklet. Washington Dc: American Psychiatric Association; 1997.
 25. Ghanizadeh A, Mohammadi MR, Yazdanshenas A. Psychometric proper-ties of the Farsi translation of the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version. *BMC Psychiatry* 2006; 6(1):10.
 26. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for school age children-present and Lifetime version (K-SADSPL): Initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry* 1997; 36(7):980-988.
 27. Sharifi V, Assadi SM, Mohammadi MR, Amini H, Kaviani, Semnani Y, Shabani A, Shahrivar Z, Davari-Ashtiani R, Hakim Shooshtai M, Seddigh A, Jalili M. A Persian translation of the Structured Clinical Interview for Diagnostic and statistical manual of Mental Disorders, Fourth edition, Psychometric properties, *Comprehensive psychiatry* 2009; 50(1): 86-91.
 28. Rajezi Esfahani S, Motaghipour Y, Kamkari K, Zahiredin A, Janbozorgi M. Reliability and Validity of the Persian Version of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). *Iranian Journal of Psychiatry and Clinical Psychology (IJPCP)* 2012; 17 (4) 17 (4) :297-303.
 29. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleishmann RL, Hill CL, Heninger GR and Charney D S. The Yale-brown obsessive compulsive scale. *Archives of general psychiatry* 1989; 45: 1006-1011.
 30. Baer L. Factor analysis of symptom subtypes of obsessive compulsive disorder and their relation to personality and tic disorder. *Journal of clinical Psychiatry* 1994; 55: 18-23.
 31. Leckman JF, Grice DE, Boardman J, Zhang H, Vitalr A, BondiC,et al. Symptoms of obsessive-compulsive disorder. *American Journal of Psychiatry* 1997; 154: 911-917.
 32. Summerfeldt LJ, Richter MA, Antony MM, Swinson RP. Symptoms structure in obsessive-compulsive disorder: a confirmatory factor-analytic study. *Behavior Research and Therapy* 1999; 37(4): 297-311.
 33. Bellivier F, Golmard JL, Rietschel M, Schul T G, Malafss A, Preisig M, McKeon P, Mynett-Johnson, L Henry C, Leboyer M. Age at onset in bipolar I affective disorder: further evidence for three subgroups. *American Journal of Psychiatry* 2003; 160: 999-1001.
 34. Coryell W, Endicott J, Andreasen N, Keller M. Bipolar I, bipolar II and non-bipolar major

- depression among the relatives of affectively ill probands. *American Journal of psychiatry* 1985; 142: 817-821.
35. Tamam L, Ozpoyraz N. Comorbidity of anxiety disorder among patients with bipolar I disorder in remission. *Advance Therapy* 2002; 19(1): 17-26, 35, 203-209.
 36. Kruger S, Braunig P, Cooke RG. Comorbidity of obsessive compulsive disorder in recovered in patients with Bipolar disorder. *Psychopathology* 2000; 2: 71-74.
 37. Masi G, Perugi G, Millepiedi S, Toni C, Mucci M, Pfanner C, Berloffia S, Pari C, Akiskal HS. Bipolar co-morbidity in pediatric obsessive-compulsive disorder: Clinical and Treatment implications. *Journal of Child Adolescent Psychopharmacol* 2007; 17 (4): 475-86.
 38. Tillman R, geller B, Bolhofner K. Ages of onset and rates of syndromal and subsyndromal comorbid DSM-IV diagnoses in a prepubertaland early adolescent bipolar disorder phenotype. *Journal of American Academy of Child and Adolescent Psychiatry* 2003; 42: 1486-1493.
 39. Kruger S, Cooke RG, Hasey GM, Jorna T, Persad E. Comorbidity of obsessive – compulsive disorder in bipolar disorder. *Journal of Affective disorder* 1995; 34: 117-20.
 40. Perugi G, Akiskal HS, Pfanner, Presta S, Gemignani A, Millanfranchi A, Lensi P, Ravagli S, Cassano GB. The clinical impact of bipolar and unipolar affective (Comorbidity in obsessive-compulsive disorder). *Journal of Affective disorder* 1997; 46: 15-23.
 41. Perugi g, AkiskalHS, Cemignani. Episodic course in obsessive compulsive disorder. *European Archives of psychiatry and clinical neurosciences* 1998; 248:240-244.
 42. Swedo SE, Rapoport JL, Leonar dH, Lenane M, Cheslow D. Obsessive compulsive disorder in children and adolescents: clinical phenomenology of 70 consecutive cases, *Arch Gen Psychiatry* 1989; 46(4): 335-341.
 43. Angold A, CostelloJ, Erkanli A. Comorbidity. *Journal of Child Psychology, Psychiatry& allied disciplines* 1999; 40(1):57-87.
 44. Angold A, Messer SC, Stangl D, Farmer EMZ, Costello EJ, Burns BJ. Perceived adolescent psychiatric disorders. *American journal of public health* 1998; 8: 75-80.
 45. Angst J. The emerging epidemiology of hypomania and bipolar II disorder. *Journal of Affect disorder* 1998; 50: 143-151.
 46. Dowson JH. The phenomenology of severe obsessive compulsive neurosis. *British Journal of Psychiatry* 1977; 131:75-78.
 47. Klein DN, Depue RA, Slater JF. Inventory identification of cyclothymiacs. IX. Validation in offspring of bipolar I patients. *Arch General psychiatry* 1989; 43: 441-445.
 48. Kutcher S. Practical child and adolescent psychopharmacology. Cambridge University Press; 2002.
 49. Lewis M. *Child and Adolescent psychiatry* 3rd edition, Philadelphia: Williams and Wilkins; 2002.
 50. Masi G, Millepiedi S, Mucci M, Bertini N, Milantoni L, Arcangeli F. A naturalistic study of referred children and adolescents with obsessive-compulsive disorder. *Journal of American Academy of Child and Adolescent Psychiatry* 2005; 44: 673-681.