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Research paper

# Exploration of comorbid obsessive-compulsive disorder in patients with bipolar disorder: The clinic-based prevalence rate, symptoms nature and clinical correlates

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ABSTRACT

*Background:* Comorbidity of bipolar disorder (BD) and obsessive-compulsive disorder (OCD) has received clinical attention. However, the detailed nature and nolosogic validity of the comorbidity have not been fully explored. This study investigated the comorbidity rate, clinical nature, and correlates of OCD in patients with BD.
*Methods:* Patients (n = 314) with BD were recruited and lifetime clinical characteristics were evaluated comprehensively. The comorbid OCD ('OCD-BD') group and the 'non-OC BD' group were compared in terms of the clinical variables of BD.
*Results:* OCD was found in 15.9% of patients. Earlier age at onset, more frequent pharmacological (hypo)manic switch and a higher rate of comorbid panic disorder were associated with comorbid OCD. In two-thirds (65.4%) of the OCD-BD subjects, obsessive-compulsive symptoms worsened or were confined to depressive episodes. Contamination obsession and checking compulsion were the most common types of obsessive-compulsive symptoms. Drug-induced (hypo)manic switch was observed in more than 60% of the OCD-BD subjects who were previously exposed to antidepressants. None of the OCD-BD subjects were taking antidepressants for OCD in the current specialty clinics.
*Limitations:* Subject recruitment from specialty clinics, retrospective and cross-sectional evaluation, and difficulties in clarifying the causal relationships.
*Conclusions:* The comorbidity rate of OCD in Korean BD patients was comparable to that of Caucasian patients. Even though OCD seems to be more often linked to depressive episodes, a heterogeneous nosologic relationship including a possibility of drug-mediated induction is suggested.

## 1. Introduction

It has become apparent that anxiety disorders are frequently comorbid with bipolar disorder (BD) (Simon et al., 2004). Obsessive-compulsive disorder (OCD), which has been separated from the category of anxiety disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric Association, 2013), had a higher comorbidity rate than did other anxiety disorders in a clinic-based survey of Korean BD patients (Baek et al., 2014a). According to a recent systematic review, the prevalence of OCD in BD patients was 11–21% in population-based studies (Amerio et al., 2014a). This is much higher than the prevalence of OCD, 2–3% in the general population (Sadock et al., 2014) and exceeds the estimated rate of 12–13% in schizophrenia patients (Schwartz, 1986; Schirmbeck and Zink, 2013).

Obsessive-compulsive symptoms manifest in BD patients in several different ways. They may emerge before the onset of BD as a frank comorbid OCD or appear *de novo* during the course of BD. In both cases, they could be associated with mood episodes or specific mood symptoms. According to a review by Amerio et al. (2014a), the majority of comorbid OCD cases appear to be secondary to depressive episodes. Considering the increasing use of second-generation antipsychotics (SGA) as mood stabilizers in BD patients (Ghaemi et al., 2006; Hayes et al., 2011; Baek et al., 2014b), the triggering or exacerbation of

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obsessive-compulsive symptoms by these drugs are also expected in BD patients, as has been clearly identified in schizophrenia patients (Lim et al., 2007; Hong, 2015). There is heterogeneity in terms of symptom origin and clinical meaning; the prevalence of comorbid OCD in BD in different hospital-based studies ranges widely, i.e., from 1.8% to 35.1% (Amerio et al., 2014a).

According to a recent systematic review (Amerio et al., 2015), the comorbidity rate of OCD in BDs seems to be higher in children and adolescents than in adults, and in bipolar I disorder (BD-I) than in the other subtypes of BD. The pooled prevalence among Asian studies was lower than that in North America (10.6% vs. 16.4%) (Amerio et al., 2015). Among disease-related variables, a greater number of previous depressive episodes and more antidepressant-induced manic/hypomanic state were associated with a higher rate of OCD comorbidity (Vieta and Bernardo, 1992; Issler et al., 2010; Tondo et al., 2010; Goes et al., 2012). Rapid cycling course (Simon et al., 2004; Magalhaes et al., 2010), a history of suicide attempts, and co-occurrence of substance and alcohol use were also reported as related clinical factors (Kruger et al., 2000; Magalhaes et al., 2010; Goes et al., 2012). In most of previous studies, however, a limited number of clinical characteristics were evaluated based on the varied research focus and designs of the different studies. Therefore, many findings were inconsistent and it is difficult to compare data between studies.

In a recent clinic-based study conducted in Turkey (Ozdemiroglu et al., 2015), a depressive episode as the first mood episode, a greater number of previous hypomanic episodes, seasonality, bipolar-II disorder (BD-II), and earlier age of BD onset were newly reported to be associated with comorbidity with OCD. More recently, a larger-scale hospital-based study was performed in BD-I patients in which clinical variables were comprehensively evaluated (Shashidhara et al., 2015). In that study, patients with OCD (7.6% of a total of 396 patients) showed poorer global functioning, a higher unemployment rate, less psychotic symptoms, and higher rates of comorbid social anxiety and avoidant personality. The number of mood episodes and the age of onset were not associated with the comorbidity.

In addition, a population-based longitudinal and multigenerational family study using the Swedish Patient Register (Cederlof et al., 2015) found that BD was significantly more common in the relatives of OCD probands than in those of matched control subjects. This finding suggests a shared genetic etiology between OCD and BD. Other factors, including medication effects and brain pathologies, that occur during the disease process might also result in comorbid conditions (Amerio et al., 2015; Cederlof et al., 2015; Hong, 2015).

To understand the shared mechanism of BD and OCD, and to approach difficult issues in pharmacotherapy, e.g., antidepressant-induced (hypo)mania and SGA-induced obsessive-compulsive symptoms, we need more data from studies covering different clinical stages, treatment settings, and ethnic backgrounds. The aim of this study was (1) to estimate the clinic-based prevalence of OCD in BD in the Korean population, (2) to identify the clinical correlates of OCD comorbidity by comparing those with and without OCD, and (3) to examine the course and symptom natures of OCD in those with BD.

## 2. Methods

### 2.1. Subjects

Subjects were recruited between March 2012 and October 2016 from two specialty clinics at university-affiliated hospitals in the Seoul metropolitan area (Samsung Medical Center and Seoul National University Bundang Hospital). Adult patients ranging in age from 18 to 65 who received a primary diagnosis of BD-I, BD-II, or bipolar disorder not otherwise specified (BD-NOS) according to the diagnostic criteria of the DSM-IV (American Psychiatric Association, 1994) were included. We excluded individuals who had mental retardation or any organic mental problems that could have confounded the diagnosis or rendered the assessment procedures difficult. Patients who were clinically unstable, i.e. who scored 4 or higher on the Clinical Global Impression (CGI) severity scale (Guy, 1976), were also excluded. Written informed consent was obtained from all participants after a complete explanation of the study. This study was approved by the Institutional Review Boards of Samsung Medical Center and Seoul National University Bundang Hospital.

### 2.2. Assessment

A semi-structured clinical interview was performed for each patient. Additional information was collected through interviews with caregivers and/or physicians who treated the patient, as well as a review of each patient's medical records. The detailed clinical features of BD and axis I comorbid conditions including OCD were assessed by the criteria set forth in the DSM-IV using either the Korean version of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (Hahn et al., 2000) or the Diagnostic Interview for Genetic Studies (DIGS) (Joo et al., 2004).

Among the subjects with comorbid OCD (n = 50), 26 subjects who were recruited since 2015 were assessed using the Korean version of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (Kim et al., 2012) and the Korean version of the Obsessive–Compulsive Inventory-Revised (OCI-R-K) (Lim et al., 2008). Onset of OCD during the use of antipsychotics, the longitudinal course of OCD, and its association with mood episodes were also evaluated. We defined the onset of OCD as emergence of subjectively distressing obsessive-compulsive symptoms that eventually developed to meet the DSM-IV criteria for OCD. Symptom frequencies for each category of the Y-BOCS symptom checklist (Y-BOCS-SC) were calculated, except for 'miscellaneous obsession' and 'miscellaneous compulsion.'

All assessments were performed by trained psychiatrists and clinical psychologists working at SMC and SNUBH who had at least one year of research experience. All of the raters had participated in regular training sessions for reliable assessments. For each patient, the decision of the rater was compared with that of the treating psychiatrist (SJ, JHB, SYY, SWA, KH or KSH for most of the patients). Disagreement between them was resolved by a researcher meeting for consensus diagnosis.

### 2.3. Statistical analyses

Comparisons of socio-demographic and clinical variables between the patients with comorbid OCD ('OCD-BD group') and the patients without OCD ('non-OC BD group') were performed, using the chi-square test, Fisher's exact test, or *t*-test. We observed the distribution of the symptom categories on the Y-BOCS-SC (Fig. 1) and compared the frequency of each category with that of Korean OCD patients (n = 130) presented in a previous study by Ha et al. (2004) by calculating the intra-class correlation coefficient (ICC).

A probability (p) value less than 0.05 was considered statistically significant. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 23.0 software.

## 3. Results

### 3.1. Subjects characteristics and comorbidity rate of OCD

A total of 314 patients with a primary diagnosis of BD were enrolled in the study (219 subjects from Samsung Medical Center and 95 from Seoul National University Bundang Hospital). The participants were predominantly female (65.3%) and their mean age was 34.9 ± 11.6 years. The mean age at onset of BD was 23.4 ± 9.2 years, while the mean duration of illness was 12.3 ± 8.4 years. Of the 314 patients, 203 (64.6%) had BD-I and 107 (34.1%) had BD-II. The others were diagnosed as BD-NOS. Most recent episode was major depressive episode in