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Research paper

# Is parity status associated with bipolar disorder clinical features, severity or evolution?

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ABSTRACT

*Objective:* To assess prospectively the association of the number of past pregnancies on the evolution of bipolar disorder (BD).
*Methods:* Data were drawn from the 2 waves of the National Epidemiologic Study of Alcohol and Related Conditions (NESARC), a representative sample of the US population of 34,653 participants. All women diagnosed with BD were included. The number of children and BD's characteristics, i.e. BD type, age of onset, hospitalization and suicide attempt, and lifetime psychiatrics comorbidity were assessed at wave 1. Mood episode and BD's characteristics were also assessed at wave 2.
*Results:* In the sample of 1190 women with BD, 27% had no child, 17% had one, 25% had two 31% had three children or more. Women with at least two children were more likely to have BD I, to report hypomania and suicide attempt during the follow-up than women without child. Parity was not associated with other characteristics of BD, nor with the severity and course of the illness.
*Limitations:* Not provide information on pregnancies not ending to a delivery.
*Conclusion:* Parity is associated with a higher incidence of hypomania and suicide attempt during a 3-years follow-up in women with BD.

## 1. Introduction

Bipolar disorder (BD) is a severe and chronic affective disorder which affects both women and men, with an early age of onset. BD is the seventh leading cause of disability and premature mortality in women of childbearing age (The World Health Organization, 2001).

Peripartum period, which includes pregnancy and the first year following delivery, is known to be at risk for psychiatric disorders in general, and more specifically for BD (Tebeka et al., 2016). Peripartum is associated with a higher risk of either first episode or recurrence of BD (Laursen, 2012; Sharma and Pope, 2012; Jones et al., 2014; Parial, 2015; Pope et al., 2014). More than 50% of the women with BD will present peripartum depression during their lifetime (Maina et al., 2014; Viguera et al., 2011). Hypomanic, manic or mixed episodes can also occur in the postpartum period (Maina et al., 2014; Viguera et al., 2011; Doyle et al., 2012) and usually with an earlier onset during postpartum than postpartum depression (Di Florio et al., 2013).

Perinatal mood episodes can be complicated by a poor quality of early maternal-child relationship, inadequate neonatal care, and may affect child's development (Kingston et al., 2012; Johnson et al., 2014). Perinatal mood episodes in BD are more likely to be longer, treatment-resistant and more likely to be with associated addictive comorbidities than mood episodes occurring during non-perinatal periods (Battle et al., 2014). During the post-partum period, women with BD are more likely to be hospitalized than women with other psychiatric disease (Munk-Olsen et al., 2009). Post-partum is also marked by a higher rate of hospitalization in patients with BD compared to non-post-partum periods (Munk-Olsen et al., 2009).

Occurrences of mood episode in the peripartum period are a risk factor for recurrences during subsequent pregnancies (Freeman et al., 2002; Pope et al., 2014).

Having in mind the negative impact of pregnancy and post-partum on bipolar disorder course, it is somehow counterintuitive that, in numerous cross-sectional studies, the number of past-pregnancies (e.g parity) is associated with a lower rate of mental disorders in the general population (Viguera et al., 2011), and with a lower burden of disease in BD (Munk-Olsen et al., 2006) (Munk-Olsen et al., 2014). Indeed, multiparity is associated with lower prevalence of manic and psychotic

*Abbreviations:* AOR, adjusted odd ratio; BD, bipolar disorder; CI, confidence interval; MDE, major depressive disorder; NESARC, National Epidemiologic Study of Alcohol and Related Conditions; OR, odd ratio; SA, Suicide attempt

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episodes, but not with a lower prevalence of depressive episodes (Di Florio et al., 2014).

To our knowledge, no study assessed prospectively the association of the number of past pregnancies on the evolution of BD. Using a large US epidemiological survey, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the aim of our work was to determine if parity status was associated with clinical features, severity or recurrences of BD.

## 2. Methods

### 2.1. Sample

The NESARC is a nationally representative sample of the US civilian population. It includes 34,653 civilian non-institutionalized people, over 18 years, evaluated two times: at first between 2001 and 2002 (Wave 1) and a second evaluation between 2004 and 2005 (Wave 2). We used participants witch completed both waves of interviews, which results in a cumulative response rate of 70.2% for both waves 1 and 2. Members of the US Census Bureau conducted face-to-face interviews. The research protocol, including informed consent procedures, received ethical approval from the US Census Bureau and the Office of Management and Budget.

For this study, the sample consisted of all women who were diagnosed with BD, defined by a history of mania or hypomania, according to the Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV (AUDADIS-IV).

More details on sampling and weighting procedures can be found elsewhere (National Institute on Alcohol Abuse and Alcoholism, 2005).

### 2.2. Measures

#### 2.2.1. Number of children

Number of children was assessed at wave 1 with one direct question. Number of children was categorized into: no child, one child, two children and more than two children.

### 2.3. Sociodemographic measures

Race/ethnicity was separate into 5 groups (White, Black, American Indian /Alaska native, Hispanic/Latino, and others). Age at interview was classified into 4 groups (18–24, 30–44, 44–64 and more than 65 years old). Marital status was classified into 3 groups (married, never married and widowed/separated/divorced). Educational level was categorized in 3 groups (less than high school, high school and some college or higher). Familial income was divided in 4 groups ($0–19,999, $20,000–34,999, $35,000–59,999, and $60,000 or greater). Urbanicity was categorized into rural or urban. Region of residence was separate into 4 groups (Northeast, Midwest, South, and West). Health insurance coverage was separate into 3 groups (private, public, and none).

### 2.4. Diagnostic of bipolar disorder and its characteristics

The AUDADIS-IV is a valid and reliable structured diagnostic interview, used to assess lifetime mania, hypomania and major depressive episode (MDE) at wave 1, according to DSM-IV criteria. BD type 1 (BD1) was defined as lifetime mania. BD type 2 (BD2) is defined as lifetime hypomania in the absence of lifetime mania. BD was defined as BD1 or BD2.

The age of onset of BD was defined as the age at earliest episode. The number of each kind of mood episode is evaluated with a single question for each.

Hospitalization for MDE or mania was assessed with one question for each.

Suicide was assessed if respondents endorsed a period of depressed mood and/or anhedonia for at least 2 weeks. Participants were asked whether they ever “attempt suicide” or “think about committing suicide?”. Participants were considered as having lifetime history of respectively “suicidal attempt” or “suicidal ideation” if they respond yes. Psychiatric diagnoses were also measured using the AUDADIS-IV. We considered three lifetime psychiatrics comorbidity at wave 1: any substance use disorders (including abuse or dependence to alcohol, cannabis, sedatives, tranquilizers, opiates, stimulants, hallucinogens, crack/cocaine, inhalants/solvents, heroin, and other drugs), any anxiety disorders (including panic disorder, specific phobia, social phobia, and generalized anxiety disorder), and any personality disorders (paranoid, schizoid, histrionic, antisocial, avoidant, dependent and obsessive-compulsive).

### 2.5. Three-year course of bipolar disorder

Three-year incidence of at least one MDE, mania and hypomania was assessed at wave 2, using the AUDADIS-IV. Questions on hospitalization, suicide attempts and suicidal ideation were assessed for the period between the two interviews using the same wordings than during the first interview.

### 2.6. Statistical analyses

Weighted percentages, means and standard-errors (SEs) were computed using SUDAAN, version 11.01 (Research Triangle Park, NC). Because of the weighting and clustering used in the NESARC design, SUDAAN implements a Taylor linearization method.

We divided women sample of the NESARC into 4 independent groups as follows: (1) women without child, (2) women with one child, (3) women with two children and (4) women with three or more children.

We compared these groups according to (1) severity criteria including: type of BD, age of onset, number of episode(s), hospitalization, suicide attempts and psychiatric comorbidities; (2) evolution criteria including: incidence of mood episode, hospitalization, suicide attempts. Women without child were considered as the reference group.

Multivariate logistic regressions were conducted with simultaneous entry of sociodemographic characteristics (Pignon et al., 2017). Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were derived to presented to reflect association strength and significance.

As a sensitivity analysis, we compared women reporting a pregnancy within the 3 years of follow-up with those reporting no pregnancy within this timeframe. Similarly, we re-analyzed our results in the subsample of participants in childbearing age (aged 50 year old or less).

## 3. Results

### 3.1. Sample

Of the 34,653 participants, 14,564 were women in which 1190 met criteria for. Among them, 322 had no child (27%), 199 had one child (17%), 299 had two children (25%) and 370 had three children or more (31%). *Age-adjusted prevalence for bipolar disorder by parity was 5.65% (SE: 0.36%) in women with no child, 5.44% (SE: 0.51%) in women with one child, 5.81% (SE: 0.42%) in women with two children and 6.23% (SE: 0.54%) in women with 3 children or more.*

### 3.2. Sociodemographic characteristics

The sociodemographic characteristics are summarized in Table 1. The majority of women was white, married, less than 44 years old with, educated and mainly lives in rural areas. All women with BD and with children (1, 2 or more) were less likely to be never married, more likely to be older than 29 years old, and more likely to benefit from a public