



Impact of the peripartum period on the longitudinal course of obsessive–compulsive disorder

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Abstract

Some women are vulnerable to developing new onset obsessive–compulsive disorder (OCD) or having an exacerbation of pre-existing OCD during reproductive cycle events. Reports on the impact of the peripartum period on pre-existing OCD are inconsistent, with both worsening and improving symptom severity described. Studies have primarily been retrospective or have collected few data points, which limits the investigators' ability to capture the range of OCD symptoms during this time period, systematically and prospectively. The objective of this investigation was to add to the existing literature on the impact of the peripartum period on the course of pre-existing OCD. We conducted a secondary analysis of a subset data from the Brown Longitudinal Obsessive Compulsive Study, a prospective, observational study of OCD course. Nineteen women who experienced a pregnancy during the course of the study (9.5% of overall sample of women) were followed on average for 486 ± 133 weeks. Weekly psychiatric status ratings (PSRs) of OCD severity were compared between peripartum and non-peripartum periods. We found that the peripartum period did not significantly impact the course of OCD severity in the majority of women ($N=13$, 69%). Of the minority of women with measurable variability in OCD symptoms, no statistically significant difference in PSR scores was observed between peripartum and non-peripartum periods. In this novel yet small dataset, the severity of OCD does not appear to worsen for most women during the peripartum period.

Keywords Reproductive cycle events · Obsessive–compulsive disorder · Pregnancy · Peripartum · Prospective study

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Introduction

Pregnancy and postpartum have been shown to be a high-risk period for onset or exacerbation of psychiatric illness (O'Hara and Wisner 2014). Much of the literature has focused on mood disorders during this time, but there is less information evaluating the relationship between obsessive–compulsive disorder (OCD) and the perinatal period (Abramowitz et al. 2003). The available data indicates that reproductive cycle events including menarche, pregnancy, and the postpartum period have been shown to be a high-risk period for new onset OCD in women (Forray et al. 2010; Guglielmi et al. 2014; Labad et al. 2005). OCD during pregnancy can have a significant negative impact on physical and psychological health, as well as social relationships, in which disease severity is negatively correlated with quality of life (Gezginc et al. 2008). In one study, mothers with OCD reported decreased self-efficacy and increased marital distress during the postpartum period (Challacombe et al. 2016). They were also less likely to breastfeed and

reported more difficulties with attending to the care of their babies (Challacombe et al. 2016). In addition to the negative impact on mothers, OCD during pregnancy has been associated with unfavorable outcomes in the neonate, including lower birth weight and shorter gestation (Uguz et al. 2015). Given these potential negative outcomes to both mother and infant, it is important to clarify the impact of the peripartum period on severity and symptom course of OCD.

While investigators have focused on reproductive cycle events as a high-risk time for OCD onset, the impact of pregnancy on pre-existing OCD is equivocal with reports showing improvement in 8–28% (Guglielmi et al. 2014), worsening in 17–46% (Uguz et al. 2007; Williams and Koran 1997), and no change in 31–69% (Uguz et al. 2007; Williams and Koran 1997). Report of the postpartum period is similar; most women report no change or exacerbation of OCD symptoms (Guglielmi et al. 2014; Labad et al. 2005; Williams and Koran 1997), albeit a smaller percentage of women (0–10%) report symptom improvement (Guglielmi et al. 2014; Labad et al. 2005). Most data on perinatal OCD symptoms are obtained from retrospective studies which are subject to recall bias and single point, cross-sectional data, which limit ability to track OCD trajectory throughout the peripartum period (Forray et al. 2010; Guglielmi et al. 2014; Labad et al. 2005; Uguz et al. 2007; Williams and Koran 1997).

The only published prospective study following women with obsessive–compulsive symptoms (OCS) during pregnancy and the postpartum period found no change in OCS severity during the perinatal period (House et al. 2016). This study included 52 participants whose symptoms were monitored across pregnancy and 1 year postpartum with the Yale-Brown Obsessive Compulsive Scale (YBOCS). A minimum of three data points were obtained with at least one assessment in pregnancy and one in postpartum. The authors concluded that OCS did not change over the course of pregnancy and postpartum. This study only obtained a few data points and primarily included women with mild or subclinical presentations which again limited the investigators' ability to capture OCD variability and trajectory.

The objective of this investigation was to determine the impact of the peripartum period on the course of pre-existing OCD. Utilizing weekly data from a prospective longitudinal study of OCD course, we sought to explore individual trajectories of OCD severity during the peripartum period and compare symptom course between peripartum and non-peripartum states. Based on the study conducted by House and colleagues (House et al. 2016), we hypothesized a waxing and waning course of symptoms would be observed, but overall OCD course would not be significantly affected by the peripartum period.

Materials and methods

Participants

We conducted a secondary analysis of a subset of data from women who experienced a pregnancy while participating in the Brown Longitudinal Obsessive Compulsive Study (BLOCS), a prospective, observational study of OCD course with 200 females (177 adults, 23 adolescents). A detailed description of the sample characteristics and study methodology has been reported elsewhere (Pinto et al. 2006). Briefly, treatment-seeking participants with a primary psychiatric diagnosis (primary psychiatric disorder across their lifetime) of OCD as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (*DSM-IV*) were recruited from inpatient, partial hospital, and outpatient settings from 2001 to 2006. The only exclusion criterion was the presence of a mental disorder due to a medical condition. All participants consented to having their data collected, analyzed, and used in publication. The study was approved by the institutional review board at Butler Hospital and Brown University.

Measures

The Structured Clinical Interview for *DSM-IV* Axis I Disorders-Patient Edition¹ was used to establish Axis I diagnoses at intake (First et al. 2002). Demographic and clinical history were assessed using the Butler Hospital OCD Database (Rasmussen 1993). The YBOCS was used to assess OCD symptoms and severity at the initial assessment (Goodman et al. 1989a, b). The YBOCS is widely considered the gold standard instrument for OCD symptom assessment and has well-established reliability and validity (Goodman et al. 1989a, b). Psychiatric diagnoses and YBOCS total scores in this study have been found to have good to excellent inter-rater reliability as reported elsewhere (Eisen et al. 2010). Medication inventory was taken at baseline.

Participants underwent annual follow-up interviews either in person or by telephone. This assessment included the Longitudinal Interval Follow-Up Evaluation (LIFE), a semi-structured instrument designed to assess the longitudinal course of psychiatric disorders (Keller et al. 1987). Using information obtained through the LIFE, weekly psychiatric status ratings (PSRs) were made to determine whether participants met diagnostic criteria for specific psychiatric disorders. The 6-point OCD PSR indicated

¹ One participant entered this study at the age of 14 and became pregnant as an adult during the follow-up period. Intake diagnoses for this participant were made using the Kiddie Schedule for Affective Disorders and Schizophrenia (Kaufman et al. 1997) and the child version of the YBOCS (Scahill et al. 1997).

whether participants met criteria for OCD on a range of severity, distress, and impairment. This range included no symptoms (PSR 1), minimal symptoms (PSR 2), mild symptoms (PSR 3), moderate symptoms (PSR 4), severe symptoms (PSR 5), or extreme symptoms (PSR 6). A PSR of ≥ 4 indicates full criteria are met for the disorder. Psychiatric status ratings are frequently used in longitudinal studies and provide reliable and valid ratings of ongoing disorder severity (Warshaw et al. 1994). Inter-rater and test–retest reliability for OCD PSR ratings in this sample are excellent and have been reported elsewhere (Eisen et al. 2010), as have our methods for establishing and maintaining long-term reliability (Pinto et al. 2006).

Life events were assessed with Life Event Assessment (LEA) which captured the month and year for each pregnancy occurring in each follow-up interval (Dohrenwend et al. 1978). We used an algorithm to estimate the peripartum period. The algorithm defined the start of the peripartum period as 4 weeks prior to the first day of the month in which the pregnancy was documented. We defined the end of the peripartum window as 12 weeks after the first day of the month in which a birth or miscarriage occurred. This time window was chosen to demarcate the peripartum period in line with the theory of four trimesters of pregnancy (Tully et al. 2017). Additionally, this period is reflected in the *DSM-5* which defines “with peripartum onset” as an episode occurring during pregnancy as well as 4 weeks postpartum. We extended our postpartum period to 12 weeks as this is consistent with epidemiological data that found elevated rates of psychiatric contacts through the first 3 months after childbirth (Kendell et al. 1987; Munk-Olsen et al. 2006), and proposals that the *DSM-5* peripartum specifier does not adequately describe at-risk periods across moderate and severe perinatal psychiatric episodes (Munk-Olsen et al. 2016).

When a birth occurred without a pregnancy indicated in the database, we defined the start of the peripartum period as 44 weeks prior to the first day of the month in which the birth occurred. Similarly, if a miscarriage occurred without knowledge of a pregnancy, the start of peripartum period was set as 12 weeks prior to the first of the month. Thus, the algorithm provided peripartum epochs that varied within and between individuals, depending upon documentation within the database.

Detailed descriptions of rater training are reported in Pinto et al. (2006). Briefly, all interviewers had at least a bachelor’s degree and were supervised by MD- and PhD-level experts in OCD research and treatment. Interviewers completed a series of observational, didactic, and participatory training activities including conducting assessment with feedback from experienced interviewers and audiotaping for inter-rater reliability calculations. New interviewers were required to achieve excellent inter-rater reliability with trainers (interclass correlation coefficient > 0.85) for the SCID, YBOCS total score, and the LIFE. Through the study,

fidelity to training was monitored via weekly meetings to review ratings as well as periodic, random calculation of inter-rater reliability statistics.

Statistical analysis

Our analyses focused on the primary outcome of OCD PSR (range: 1–6). We created individual participant profile plots to illustrate longitudinal symptom course over the observed period. The original analysis plan called for a mixed-effects or a generalized estimating equation model to determine whether OCD PSR scores changed during the peripartum period. We planned to account for within-participant correlation through either random effects or appropriate covariance assumptions. However, since all participants entered the study with a $PSR \geq 3$, we observed little variability in outcome over time. This resulted in challenges with model convergence, which was true whether we modeled outcome as continuous, ordinal, or dichotomous based on $PSR \geq 4$. Therefore, we simplified analyses and collapsed data for each participant on peripartum and non-peripartum states. We calculated an average OCD PSR score for each participant during these periods and used a Wilcoxon signed-rank test to evaluate differences in mean OCD PSR scores between peripartum and non-peripartum states. For participants with measurable variability, we constructed individual logistic regression models for $OCD\ PSR \geq 4$. The models contained a peripartum-by-week interaction and corresponding main effects. Individual estimates for the change in log-odds of $OCD\ PSR \geq 4$ for 1-week increase in time (i.e., the interaction between peripartum indicator and week) were captured and summarized using a random effects meta-analysis with the restricted maximum-likelihood estimator (REML) for between- “study” (i.e., between participant) variance, τ^2 . We performed analyses using R (3.5.3, 2019, The R Foundation) and assumed a two-sided, 5% level of significance. Meta-analysis was conducted using the *metaphor* package (Viechtbauer 2010). Since this was a secondary data analysis, no formal power and sample size calculation was performed.

Results

We identified 19 women (9.5% of women in the BLOCS cohort) who had a pregnancy, birth, or miscarriage documented in the database. Just more than half of the women ($N = 10$, 52.6%) reported more than one pregnancy through the course of follow-up. The average length of follow-up was 486 ± 133 weeks, ranging from 208 to 676 weeks. Participant demographics, medication use, and psychiatric history were obtained at study intake. The mean age was 25.9 years ($SD = 6.2$; range of 14–38 years) with the majority being white (94.7%), employed (63.2%), with some college or

graduate school education (89.5%), and no reported disability. The majority of women (73.7%) reported a history of comorbid major depressive disorder. Additional comorbidities included history of an anxiety disorder (36.8%), eating disorder (21.1%), tic disorder (15.8%), or substance abuse (5.3%). Most participants ($N=16$, 84.2%) were prescribed a serotonin reuptake inhibitor. Additionally, 2 participants were treated with a neuroleptic and 3 participants were treated with a benzodiazepine.

At intake, participants reported a moderate degree of OCD severity with a mean YBOCS score of 18.9 ($SD=8.2$). Symmetry or exactness was the most common obsession (26.3%) followed by a fear of harming others (15.8%) (Fig. 1). At study entry, all women scored between 3 and 5 points on the PSR, representing a range of symptom severity from mild to severe, with the majority (52.6%) scoring a PSR of 4, representing moderate

symptom presentation (Table 1). No evidence of a statistically significant difference in participant average PSR scores was observed between peripartum and non-peripartum states (paired [pseudo] median difference: -0.0082 ; 95% CI: $[-0.25, 0.18]$; Wilcoxon rank-sum p -value= 0.90).

The symptom PSR scores varied little within participants overall, where subject 7 had the same score for over 300 weeks (Fig. 1). Scores remained constant during the peripartum period for seven participants (1, 7, 9, 13, 15, 16, and 19). Six participants (2, 3, 5, 8, 14, and 18) exhibited enough variability in PSR to model PSR scores over time. We conducted the aforementioned meta-analysis using these participants' data (Fig. 2). Despite the fact that 3 of the 6 participants (2, 3, 5) had a significant 2-way interaction between peripartum state and time, overall there was insufficient evidence to suggest that the association between time and OCD PSR ≥ 4 differed between peripartum

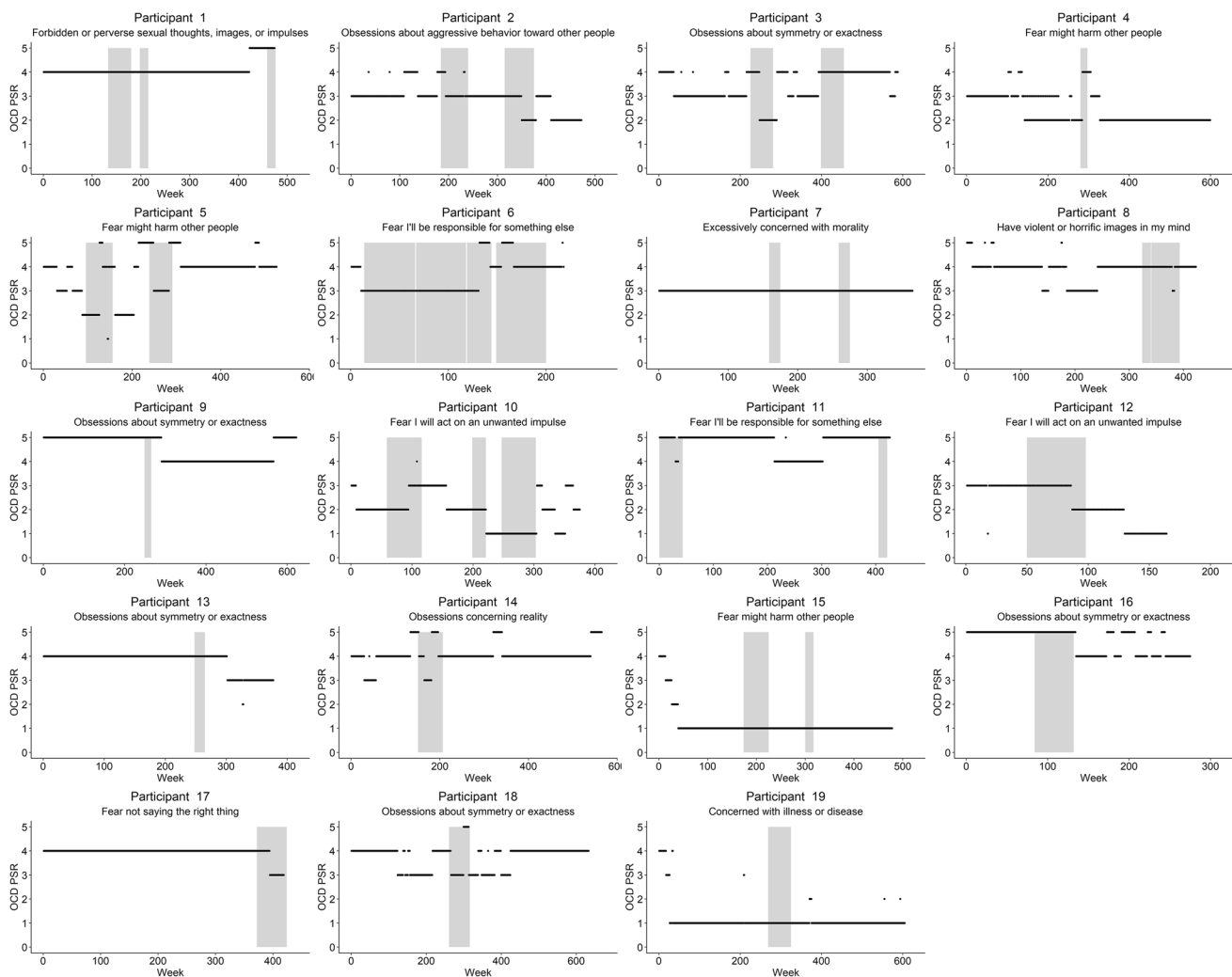


Fig. 1 Distribution of obsessive-compulsive disorder psychiatric status rating (OCD PSR) scores over time and stratified by peripartum state. A 6-point OCD PSR was used to indicate a range of OCD severity where PSR 1 indicated no symptoms and PSR 6 indicated extreme symptoms. These graphs depict all nineteen participant's

OCD trajectories via weekly PSR scores, represented as black horizontal dots. These PSR scores are graphed spanning peripartum and non-peripartum periods, where peripartum time windows are depicted with a vertical gray box. The participant's predominant obsession is also documented with each graph

Table 1 Summary of baseline obsessive–compulsive disorder psychiatric status rating (OCD PSR) scores in the sample

OCD PSR	Overall (<i>n</i> = 19)
1	0 (0%)
2	0 (0%)
3	5 (26.3%)
4	10 (52.6%)
5	4 (21.1%)
6	0 (0%)

OCD PSR scores indicate level of severity of OCD with higher scores representing more severe symptom presentation

and non-peripartum states for these women (*n* = 6; overall odds ratio for OCD PSR \geq 4: 0.99; 95% confidence interval: (0.96, 1.02); *p*-value = 0.57).

Discussion

The peripartum period does not appear to be associated with a worsening of OCD symptom severity for most women in our study. Throughout the peripartum period, symptoms were unchanged for the majority (69%) of participants. A subset of patients (31.6%) reported variability with improvement or worsening of symptoms; however, the change in overall symptom severity during the individual woman's peripartum state compared to her non-peripartum state was not clinically significant. Consistent with prior investigations (Forray et al. 2010; Guglielmi et al. 2014; House et al. 2016; Labad et al. 2005; Williams and Koran 1997), we found that

the peripartum period did not exacerbate pre-existing OCD for most women. However, in one retrospective study (Uguz et al. 2007), a slightly higher proportion of women experienced worsening or improvement of symptoms (46.1% and 23.1%, respectively) compared to women with no change (30.8%). This difference in findings may be explained by cross-sectional data collection in the third trimester, which limits the investigators' ability to assess the impact of the full course of the peripartum period on OCD trajectory. Broader longitudinal follow-up studies of this sample underscore the chronicity of OCD (Eisen et al. 2013) and our findings, and the majority of previous studies, suggest that this may also be true for OCD during the peripartum period.

The strengths of this prospective study include a well-characterized sample with a long period of observation. Weekly PSR data through peripartum and non-peripartum periods allowed us to examine the impact of the peripartum period on overall trajectory of OCD. Our participants had a moderate level of symptom severity, which expands upon past research that included women with mild or subclinical presentations (House et al. 2016).

Although there were a large number of observations per participant, the primary limitation of this study is the small sample size and limited variability in OCD PSR. These restricted the statistical methods that could be performed. In addition, inclusion of multiple events (pregnancy, birth, and miscarriage) as one category assumes that they have the same impact on OCD symptoms. Psychiatric treatment (medication, psychotherapy) was uncontrolled so we are not able to draw conclusions about its effects on our analyses. Finally, the sample was predominantly white and all participants were treatment seeking, which limits the generalizability of these results.

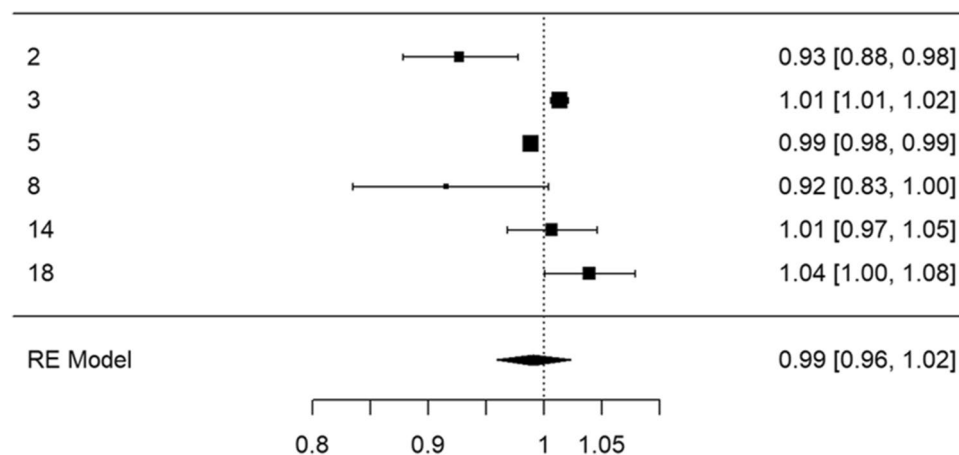


Fig. 2 Meta-analysis of subjects with higher variability in obsessive–compulsive disorder psychiatric status rating (OCD PSR) scores in the peripartum. Of the nineteen participants in this study, six participants demonstrated higher variability in OCD PSR scores during the peripartum. OCD PSR scores represent a marker of OCD severity, with higher numbers indicating a greater severity. The OCD PSR

scores were dichotomized to PSR < 4 and PSR \geq 4, where PSR \geq 4 indicates full criteria is met for the disorder. An odds ratio and 95% confidence interval were calculated to determine if there was a change between these two dichotomized PSR scores across peripartum and non-peripartum states

Despite these limitations, our observations comprise real-world experiences in a population of women with OCD in long-term follow-up. We provide new data that the severity of OCD does not appear to be impacted by the peripartum period. Additionally, we show that while the peripartum period does not typically impact the overall trajectory of OCD, there is potential for symptom variability in some women. This demonstrates a heterogeneity of response with either improvement or worsening of symptoms consistent with past literature (Forray et al. 2010; Guglielmi et al. 2014; House et al. 2016; Labad et al. 2005; Uguz et al. 2007; Williams and Koran 1997). Future studies should distinguish obsessions/compulsions in pregnancy from postpartum as research suggests certain obsessions like symmetry may be associated with higher disease severity and comorbidity (Sibrava et al. 2016) and the postpartum period may be a higher risk time for OCD exacerbation (Guglielmi et al. 2014; Labad et al. 2005).

Conclusion

In conclusion, OCD severity does not appear to change across the peripartum period for the majority of women in our study. This study adds to our knowledge of the longitudinal impact of perinatal events on OCD symptomatology and provides clinicians with considerations as to how to counsel and monitor patients with OCD during the peripartum.

Author contribution CB, KW, CC, JC, and JS contributed to the concept and design of the paper. CB, SR, MM, JE, KZ, JC, CC, and KW and contributed to the acquisition, analysis, and interpretation of data. KW and JC contributed to statistical analysis. AC and JS drafted the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content and approved the final manuscript.

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Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study received IRB approval and informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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