Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an International Consortium

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Summary

Background The perinatal period is a time of high risk for onset of depressive disorders and is associated with substantial morbidity and mortality, including maternal suicide. Perinatal depression comprises a heterogeneous group of clinical subtypes, and further refinement is needed to improve treatment outcomes. We sought to empirically identify and describe clinically relevant phenotypic subtypes of perinatal depression, and further characterise subtypes by time of symptom onset within pregnancy and three post-partum periods.

Methods Data were assembled from a subset of seven of 19 international sites in the Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium. In this analysis, the cohort was restricted to women aged 19–40 years with information about onset of depressive symptoms in the perinatal period and complete prospective data for the 10-item Edinburgh postnatal depression scale (EPDS). Principal components and common factor analysis were used to identify symptom dimensions in the EPDS. The National Institute of Mental Health research domain criteria (RDoC) functional constructs of negative valence and arousal were applied to the EPDS dimensions that reflect states of depressed mood, anhedonia, and anxiety. We used k-means clustering to identify subtypes of women sharing symptom patterns. Univariate and bivariate statistics were used to describe the subtypes.

Findings Data for 663 women were included in these analyses. We found evidence for three underlying dimensions measured by the EPDS: depressed mood, anxiety, and anhedonia. On the basis of these dimensions, we identified five distinct subtypes of perinatal depression: severe anxious depression, moderate anxious depression, anxious anhedonia, pure anhedonia, and resolved depression. These subtypes have clear differences in symptom quality and time of onset. Anxiety and anhedonia emerged as prominent symptom dimensions with post-partum onset and were notably severe.

Interpretation Our findings show that there might be different types and severity of perinatal depression with varying time of onset throughout pregnancy and post partum. These findings support the need for tailored treatments that improve outcomes for women with perinatal depression.

Funding Janssen Research & Development.

Introduction

In recent decades, a robust literature has documented the perinatal period as a time of high risk for onset of depressive disorders with substantial morbidity for mother, infant, and family that includes increased risk for low birthweight and prematurity, impaired mother–infant attachment, and infant malnutrition during the first year of life.[1,2] Maternal suicide is a leading cause of maternal mortality.[3] Perinatal depression, broadly defined by WHO as onset of a major depressive episode during pregnancy or the first 12 months post partum, has a lifetime prevalence of 10–15% in developed countries[2] and higher risk in low-income countries.[4] The greatest point prevalence for onset of symptoms is the acute post-partum period,[5] but there is growing evidence that many women have onset of symptoms during pregnancy.[6] The public

health importance of identifying women who have perinatal depression was highlighted by new recommendations of the US Preventive Services Task Force for screening for depression during pregnancy and post partum.[7] These recommendations are consistent with guidelines from the National Institute for Health and Care Excellence (NICE) in the UK,[8] the Australian Perinatal Depression Initiative,[9] and WHO recommendations.[10]

An analysis of data from the international Postpartum Depression: Action Towards Treatment (PACT) Consortium, which represents 19 institutions in seven countries, showed substantial heterogeneity in symptoms of perinatal depression.[11] This study used latent class analysis and described three specific latent classes (subtypes) of women with post-partum depression who differed by symptom severity, timing of onset (pregnancy *vs* post

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Research in context

Evidence before this study

We did two comprehensive searches to identify all relevant articles. First, we searched PubMed with the keywords "perinatal depression", "postpartum depression", "time of onset", "pregnancy", and "phenotypes" from inception until Feb 6, 2017. We did not restrict by year of publication and included all published articles. Next, we searched PsycInfo with the same keywords. The search yielded 38 articles from PubMed and four additional articles from PsycInfo that were applicable to our study objective. Previous work in this area is scant and few studies have examined the differences between women who develop depression during pregnancy compared with women who develop symptoms in the post-partum period. Furthermore, previous studies are limited by either very small sample sizes or inadequate phenotyping by time of symptom onset. Overall, research that investigates symptom constructs that may differentiate meaningful differences between depression during pregnancy versus post partum is rare, and no previous studies have examined the time of symptom onset in each trimester of pregnancy and three post-partum periods (0 to <4 weeks, ≥4 to <8 weeks, and ≥8 weeks) in relation to specific symptom dimensions that are based on a framework to understand the underlying pathophysiology.

Added value of this study

The Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium includes anonymised data from 19 international sites. We used data from seven of these sites to examine the time of onset of symptoms in the perinatal period.

We examined National Institute of Mental Health research domain criteria (RDoC) functional constructs (ie, negative valence and arousal/regulatory systems) on the basis of patient report of symptoms assessed with the Edinburgh postnatal depression scale (EPDS) in the PACT Consortium. We found evidence for three underlying dimensions of depressed mood, anxiety, and anhedonia in perinatal depression. On the basis of these dimensions, we identified five distinct subtypes of perinatal depression that had clear differences in symptom quality and time of onset. Anxiety and anhedonia emerged as prominent symptom dimensions with post-partum onset and were notably severe. Our findings have important public health implications to address the morbidity and mortality associated with perinatal depression. First, clinicians should be aware that different types and severity of perinatal depression exist, with varying time of onset throughout pregnancy and post partum. Second, we identified five distinct subtypes of perinatal depression and found clear differences related to time of depression onset in the perinatal period.

Implications of all the available evidence

There is growing evidence that a one-size-fits-all approach can no longer be applied to adequately meet the mental health needs of women with perinatal psychiatric illness. Different types and severities of perinatal depression exist. Further research into tailoring treatment on the basis of subtype to improve outcomes for women with different phenotypes and severity of perinatal depression is needed.

partum), history of previous mood or anxiety disorder, pregnancy or obstetric complications, and presence of suicidal ideation. These findings supported the need for further investigation to increase our understanding of the different phenotypes and type and quality of presentation associated with perinatal depression in women with onset during pregnancy versus post partum. These findings extended previous work documenting that comorbid anxiety is an important symptom in women with the most severe illness (eg, worry, ruminating thoughts).[12] Additionally, these findings were consistent with results of a clinical trial that showed differential treatment response by time of symptom onset in women with post-partum depression.[13]

Anxiety and mood symptoms in perinatal depression have not been adequately described. We postulated that women who become depressed during pregnancy will differ in type and quality of presentation compared with those with post-partum onset. We wanted to examine this important issue in the PACT Consortium dataset, which had not been previously addressed in the first PACT study.[11] We hypothesised that the underlying causes for onset and quality of symptoms across the perinatal period could be different on the basis of underlying

pathophysiological mechanisms such as the hormonal fluctuations that characterise the perinatal period.[14] Therefore, rather than focus on traditional diagnostic criteria for perinatal depression that do not account for co-occurring anxiety symptoms, we sought to examine the symptom constructs described in the National Institute of Mental Health (NIMH) research domain criteria (RDoC).[15] The NIMH RDoC was developed to create a framework for research on pathophysiology that helps to inform future neuroscience-based diagnostic classification systems and ultimately leads to novel treatment and detection of subtypes for treatment selection.[16] Application of the RDoC framework to examine the performance of mapping screening or diagnostic measures of depression to RDoC constructs has been an informative approach in other studies.[17] We examined the RDoC functional constructs (ie, negative valence and arousal/regulatory systems)[16] on the basis of patient report of symptoms assessed with the Edinburgh postnatal depression scale (EPDS) in the PACT Consortium.[18] Examination of the EPDS factor structure has been described in the literature with consistent reports of subscales measuring mood and anxiety.[19] A few studies have also described a potential third EPDS subscale for anhedonia[20] or suicidal thoughts.[21]