Women and Birth 28 (2015) 179–193

Contents lists available at ScienceDirect

Women and Birth

journal homepage: www.elsevier.com/locate/wombi

Review article

The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review

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ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 9 February 2015
Accepted 12 February 2015

Keywords:
Pregnancy
Depression
Anxiety
Stress
Preterm birth

ABSTRACT

Background: Experiencing psychological distress such as depression, anxiety, and/or perceived stress during pregnancy may increase the risk for adverse birth outcomes, including preterm birth. Clarifying the association between exposure and outcome may improve the understanding of risk factors for prematurity and guide future clinical and research practices.
Aim: The aims of the present review were to outline the evidence on the risk of preterm associated with antenatal depression, anxiety, and stress.
Methods: Four electronic database searches were conducted to identify quantitative population-based, multi-centre, cohort studies and randomised-controlled trial studies focusing on the association between antenatal depression, anxiety, and stress, and preterm birth published in English between 1980 and 2013.
Findings: Of 1469 electronically retrieved articles, 39 peer-reviewed studies met the final selection criteria and were included in this review following the PRISMA and MOOSE review guidelines. Information was extracted on study characteristics; depression, anxiety and perceived stress were examined as separate and combined exposures. There is strong evidence that antenatal distress during the pregnancy increases the likelihood of preterm birth.
Conclusion: Complex paths of significant interactions between depression, anxiety and stress, risk factors and preterm birth were indicated in both direct and indirect ways. The effects of pregnancy distress were associated with spontaneous but not with medically indicated preterm birth. Health practitioners engaged in providing perinatal care to women, such as obstetricians, midwives, nurses, and mental health specialists need to provide appropriate support to women experiencing psychological distress in order to improve outcomes for both mothers and infants.
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1. Introduction

Research has identified that amongst women who experience psychological adversities during pregnancy there is a trend towards sub-optimal birth outcomes, including mortality and morbidity, shorter gestation, and lower birth weight.[1] According to the World Health Organization, 2009, preterm birth (PTB) is the leading cause of infant mortality and, morbidity. Infants born preterm (<37 weeks of completed gestation) are at a greater risk of various health and developmental problems, and present a considerable emotional and economic cost to families, as well as significant implications for public-sector services. Despite decades of investigation, the incidence of preterm birth has not declined and its aetiology remains unexplored.

PTB has been linked to a complex cluster of overlapping biomedical, social and psychological factors. While some studies report no link between maternal mental health during pregnancy and birth outcomes,[2] there is emerging evidence of the relationship between maternal mental health during pregnancy and

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http://dx.doi.org/10.1016/j.wombi.2015.02.003
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pregnancy outcomes, including PTB (for reviews see 1). However, evidence of the specific effects of antenatal depression, anxiety and stress on birth outcomes remains unclear and at times conflicting. Therefore, the main objective of this review is to identify and examine the impact of overall maternal psychological distress during pregnancy, specifically the three most prevalent diagnostic (clinical) and symptomatological (sub-clinical) presentations of psychological distress, i.e., depression, anxiety and perceived stress (referred to subsequently as DAS) during pregnancy.

Depression is one of the most common complications during pregnancy and the childbearing years. The prevalence of major depressive disorder defined by diagnostic criteria during pregnancy is 12.7%, while as many as 37% of women report experiencing depressive symptoms at some point during their pregnancy.[3] Anxiety is known to be more prevalent than depression at all stages of pregnancy although there is a high level of comorbidity of about 60% between the two.[3,4] Additionally, the way a woman perceives and interprets various stressful events in her environment during pregnancy has gained increasing research attention, especially in respect to the contribution to adverse birth outcomes.

Experiencing depression, anxiety, or stress (DAS) during pregnancy may expose both mother and infant to (1) many psychological risks, including an impaired bonding with the foetus and with the new-born, increased risk of poor psychological postnatal adjustment, postnatal depression, and (2) physiological consequences, including low birth weight, intra-uterine growth restriction, and preterm birth. This review will focus on studies reporting PTB, defined as birth prior to the completion of 37 weeks gestation.

It is likely that, beyond the established bio-medical factors, depression, anxiety and perceived stress may contribute in different ways to PTB, activating different pathways in the process. Furthermore, the co-morbidity of depression, anxiety and perceived stress may pose an even higher risk for PTB. Therefore, the secondary objective of this review is to examine the effects of depression, anxiety and perceived stress as individual and as combined exposures.

Additionally, it is recognised that the relationship between DAS and PTB and the interpretation of findings is expected to be influenced by the operationalisation of DAS and PTB, the antenatal measures used and potential modifying and confounding variables. Consequently, the third objective of this review is to critically consider these methodological influences in determining the relationship between DAS and PTB.

2. Methods

The protocol for the review was developed and agreed by the authors prior to commencement. It followed all aspects recommended in the reporting of systematic reviews, namely the PRISMA Checklist and MOOSE Guidelines.[5,6] Epidemiological studies (both observational and experimental) that explored the association between DAS during pregnancy and PTB were considered for this review. Depression and anxiety were conceptualised as defined by DSM-IV-TR criteria on mood disorders (2000). Stress was conceptualised as an individual's response to a stressful situation through a validated self-report measure of stress and not only the occurrence of specific stressors (such as daily, occupational, chronic, etc., stressors only). Principal summary measures for associations were odds ratios (OR), relative risks (RR), hazard ratios (HR), regression coefficients, and a discriminate predictive function. The protocol was not submitted for registration.

2.1. Eligibility criteria and search strategy

MEDLINE, CINAHL, PsycInfo, and Cochrane databases searches were conducted by the first author (AS), with the help of an experienced health sciences librarian (JD). Search terms, inclusion and exclusion criteria applied in the review can be found in Table 1.

All articles were entered into EndNote X6 (Thomson Reuters, Carlsbad, CA, USA). Subsequent manual searches were performed through reference lists of the papers and of other published reviews. A study selection table detailing inclusion and exclusion criteria (Table 1) was used by two reviewers (AS and FB), who independently judged a random sample of studies to enhance reliability of selection. Subsequently, studies that were under question for inclusion ($n = 20$) were re-examined by the second reviewer (FB). Of 1469 reviewed studies, 39 met the inclusion criteria and were selected for final quality assessment.

2.2. Assessment of quality and risk of bias

The methodological quality and risk of bias of each study were assessed using an adapted checklist developed by a knowledge synthesis group for the specific purpose of review of the evidence relating to determinants of preterm and low birth weight births.[7] The checklist is applicable across study types and details criteria and standards for selection, exposure assessment, outcome assessment, confounding factors, analytical, and attrition bias assessment with classifications ranging from *None* to *High*, and *Cannot Tell* (see Table 2). Adjustments were made regarding exposure and outcome descriptions, definitions criteria, and criteria for confounding factors, where the lowest (none) levels of bias were ascertained to studies that controlled for all common and adjusted confounders and high bias was assigned to studies that did not consider or report on any confounders. Overall bias

Table 1
Search terms, inclusion and exclusion criteria.

Search terms (keywords, index words, MeSH headings, and their combinations using Boolean AND/OR operators)	1. "in pregnancy" OR "in pregnant women" OR "during pregnancy" OR "whil* pregnant" OR prenatal OR antenatal OR prepartum OR antepartum; 2. anxiety OR depress* OR anxious OR stress* OR mental OR distress*; {Anxiety} OR {Anxiety Disorders} OR {Anxiety Management} OR {Depression (Emotion)} OR {Major Depression} OR {Stress} 3. preterm OR premature OR "early delivery" OR "early onset of labour" OR "early onset of labor" OR prematurity OR gestational age; {Premature birth}
Included	English-language articles published between 1980 and 2013 Quantitative primary research articles (population-based, multi-centre, cohort studies and randomised-controlled trials) Measured depression, anxiety and stress symptoms in all pregnant women by means of self-reported questionnaires or structured psychiatric interview Reported the use of validated diagnostic or screening tools to determine either one of depression, anxiety, or stress
Excluded	Reviews or theoretical papers Retrospective design was used to measure antenatal depression, anxiety or stress Duplicate articles using the same data Primarily focus was on the use of antidepressant medication, rather than the measurement and diagnosis of depression

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