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Psychosocial predictors of fetoplacental blood flow during pregnancy

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Abstract

Background: Although a number of studies have found significant associations between maternal psychological distress, anxiety and changes in fetoplacental blood flow, findings remain inconsistent. A recent pilot study by our group highlighted some of these inconsistencies. In the current study, we expanded this pilot analysis to include psychological distress, anxiety and a range of antenatal variables, with the aim of identifying predictors of fetoplacental blood flow.
Methods: Healthy pregnant women (n = 148) underwent Doppler flow studies on uterine, umbilical and fetal arteries; as well as assessments of distress, anxiety and other antenatal variables (e.g. perceived social support, resilience, nicotine and alcohol use) in each trimester.
Results: Stepwise regression analyses found that state anxiety was associated with lower mid-cerebral artery pulsatility index at trimester 3.
Limitations: Subjects were recruited from selected midwife obstetric units in the same health district, so the generalizability of our results may be limited. While most subjects received Doppler assessment at trimesters 2 and 3, only approximately half of our sample was assessed at trimester 1.
Conclusion: The finding that anxiety is associated with increased blood flow to the fetal brain during trimester 3 of pregnancy, coincide with previous work. The findings emphasize a growing appreciation of the potential importance of psychological well-being during pregnancy for infant development. However, as associations were small and variable, further research using multivariate models to determine the precise mechanisms underlying these associations would be warranted.
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1. Introduction

A number of antenatal variables may be associated with adverse changes in fetoplacental blood flow. For example, Doppler flow velocity studies have found that maternal psychological distress or anxiety during pregnancy may be associated with an increased uterine artery resistance index (RI) and an increased umbilical artery pulsatility index (PI) (both of which indicate impaired blood flow within the maternal and fetal components of the placenta); as well as decreased mid-cerebral artery (MCA) PI (a marker of compensatory increased fetal cerebral flow due to vasodilatation triggered by fetal hypoxaemia) [1,2]. Variability in these fetoplacental parameters is seen both in normal and abnormal pregnancies. In normal cases, uterine and umbilical artery PI decrease physiologically over time [3,4]. Temporal changes in normal MCA PI follow an inverted U-shape, increasing until about 30 weeks' gestation and decreasing thereafter [3]. Certain pathological conditions, such as pregnancy induced hypertension, may be associated with increased uterine artery resistance [5]. Increased umbilical artery PI and decreased MCA PI are both associated with intrauterine growth restriction [6]. A recent meta-analysis has shown that maternal anxiety is significantly correlated with increased risk of preterm birth (delivery before 37 weeks of gestation) and low birth weight (birth weight less than 2.5 kg), and of adverse child outcomes [7]. Yet, the biological mechanisms by which anxiety may affect outcomes remain unclear. Vascular factors are under-investigated in determining birth outcomes [8]. Therefore, it is of scientific and clinical importance to clarify these underlying mechanisms and to delineate the associations between antecedent maternal psychological distress and downstream changes in fetoplacental blood flow.

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To date, studies of the associations of psychological distress and anxiety with fetoplacental blood flow have yielded inconsistent results. Of those studies that have shown interactions, these were mainly found later in pregnancy [1,2]. For example, women with features of state and trait anxiety have been found to have significantly increased uterine artery RI during the third trimester [2]. State and trait anxiety respectively refer to transitory perceived apprehension associated with certain stimuli, and a relatively stable personality characteristic of anxiety proneness [9]. Trait anxiety has also been found to be associated with increased umbilical artery PI, and decreased fetal MCA PI towards the end of pregnancy [1]. Despite these positive findings, a number of studies have also failed to demonstrate associations in any trimester [10–13]. In addition, associations between distress, anxiety and increased ductus venosus PI for veins—another potentially important indicator of fetal compromise [14]—have not been investigated.

Reviews have sought to provide reasons for this inconsistency in findings. Since most significant findings were moderate at best, it is suggested that psychological distress and anxiety only contribute partially to the variation in blood flow parameters; and that multidimensional models should be used, as several factors likely determine antenatal psychological distress levels and blood flow [8]. Such factors include individual-level variables such as medical factors, distress levels, emotion, and coping ability and behaviour; interpersonal factors such as social support and socio-economic status; and the possible interrelations among these factors. While social support and resilience have been found to predict distress and anxiety levels at each trimester of pregnancy [15], there is also evidence that these variables may only have small positive effects on fetoplacental blood flow [16]. In turn, nicotine and/or alcohol use may negatively influence fetoplacental blood flow [17,18], for example, nicotine use may cause increased uterine blood flow resistance [19].

Furthermore, differing methodologies may explain the inconsistencies. In their recent systematic review of 115 studies on the validity of 43 measures used to assess psychological distress and anxiety during pregnancy (in relation to various biological and other variables) and outcomes, Nast and colleagues [20] found that the studies defined the construct of psychological distress differently and used many different scales. Meta-analysis showed that, although the scales used did not always measure *pregnancy-specific* distress and anxiety; the Spielberger State Trait Inventory (STAI), Kessler's K-10 and Cohen's Perceived Stress Scale (PSS) were most valid to assess psychological distress and anxiety during pregnancy. (These findings concerning anxiety are consistent with those published by Newham et al. [21]). The authors suggest that, as the aforenamed scales validly measure different stress constructs, e.g. the STAI measures anxiety, while the PSS measures daily hassles; they should all be included in multivariate models in prenatal stress research in order to cover different aspects relating to stress.

A pilot study from our group sought to delineate these complex associations [22]. While findings in this relatively small sample were somewhat inconclusive, a significant association between significant distress (K-10 score above 20 [23]) and increased uterine artery PI was found at trimester 3, when controlling for nicotine and alcohol use. In the current study, we aimed to expand our pilot analyses and to add to the limited existing body of work in the field. In order to identify predictors of fetoplacental blood flow in a larger sample; and to determine their relative contribution, we used multivariate regression models, validated measures of distress and anxiety (STAI, K-10 and PSS), and a number of other relevant antenatal variables (e.g. perceived social support, resilience, nicotine and alcohol use).

2. Methods

2.1. Subjects

Pregnant women were recruited randomly at midwife obstetric units in the Eastern Metropole region of Cape Town (Western Cape, South Africa) during their first antenatal visit. These units are situated in low socio-economic status areas. Women were included after initial screening and signing of written consent if they were fluent in Afrikaans and/or English; in good health; had no history of significant adverse pregnancy-related conditions or terminations; and had a normal ultrasound scan with singleton pregnancy at the screening session. The cut-off gestational age for recruitment was 20 weeks, as determined by ultrasound. Clinical records indicated that women generally did not book their first appointment early. Women were excluded if they had a multiple pregnancy; were >85 kg in weight; had experienced one or more previous pregnancy losses during the second or third trimesters, or more than two trimester 1 losses; had a history of preterm labour, abruption, or early onset/severe pregnancy-induced hypertension; or had a serious current medical condition including diabetes mellitus, heart disease and epilepsy. The study was approved by the Research Ethics Committee of Stellenbosch University and was conducted in accordance with the international Declaration of Helsinki 2008.

2.2. Procedures

In addition to their routine antenatal visits, women attended two or three assessment sessions at the ultrasound unit of Tygerberg Hospital. The number of study sessions was dependent on the gestational age of subjects at recruitment. Women were assessed longitudinally at gestation 13–14 weeks (trimester 1), 22–23 weeks (trimester 2), and 32–33 weeks (trimester 3). At each study visit, subjects received a detailed ultrasound scan including a Doppler assessment, and completed self-report questionnaires (with guidance and assistance from the study team) on demographics, medical health, obstetric history including parity

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