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Effects of maternal anxiety on fetal and maternal circulation

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SUMMARY

OBJECTIVE: The aim of this study was to evaluate the association between maternal anxiety in the third trimester and changes in fetal and maternal circulation assessed by Doppler velocimetry.

METHODS: This is a prospective, cross-sectional study. The inclusion criteria were good health, a singleton pregnancy, maternal age between 18 and 40 years, and gestational age between 34 and 40 weeks. Doppler measurements included mean uterine artery pulsatility index, fetal middle cerebral artery pulsatility index, peak of systolic velocity, umbilical artery, and umbilical vein. The Beck Anxiety Inventory questionnaire, validated for the Brazilian population, with 21 self-reported items, was applied.

RESULTS: The study included 34 pregnant women, and 6 (17.7%) presented a total Beck Anxiety Inventory score showing moderate or severe maternal anxiety. The mean maternal age was 28.1 years (SD 5.7 years); the mean gestational age at interview was 36.5 weeks (SD 1.8 weeks), and the mean Beck Anxiety Inventory total score was 12.3 (SD 9.8). The group with moderate or severe anxiety, compared to the group with minimal or mild anxiety, presented an association with lower maternal age (median 21.5 vs. 29.5 years, p=0.019), lower fetal umbilical vein blood flow (median 189.4 vs. 249.5 mL/min, p=0.047), and lower umbilical vein-corrected blood flow (median 68.5 vs. 84.9 mL/kg/min, p=0.038).

CONCLUSION: Maternal anxiety may affect fetal circulation patterns in late pregnancy and is associated with reduced blood flow in the fetal umbilical vein. The underlying physiopathology needs further investigation.

KEYWORDS: Anxiety. Maternal health. Placental circulation. Umbilical veins.

INTRODUCTION

Several physiological, anatomical, and psychological changes occur in women during gestation that are essential to ensure adequate fetal growth and development. During the pregnancy, expectant mothers usually present anxiety related to the acceptance of body changes, growth of the fetus, and, at the third trimester, maternal anxiety increases related to fear of labor and the need for readjustment of lifestyle with others and the new baby.

Few studies have been done regarding an association between maternal psychological status and maternal-fetal circulation. Fu et al. concluded that poor mental health during pregnancy is found to have an adverse effect on umbilical artery and fetal cerebral circulation evaluated by Doppler ultrasound[1]. Levine et al.[2], in a systematic review, concluded that there is limited evidence that prenatal stress is associated with changes in circulation. In particular, studies of life stress during pregnancy and birth outcomes confirm that the mother's emotional status affects the developing baby. High levels of perceived maternal stress and anxiety are also associated with preterm birth[3], birth weight[4,5], and small-sized infants for gestational age[6].

Doppler velocimetry results of uterine artery (UtA), umbilical artery (UA), fetal middle cerebral artery (MCA), and fetal venous circulation have been linked with adverse perinatal outcomes. However, few studies have assessed their potential relationship with prenatal maternal anxiety. This study was conducted in order to evaluate the association between maternal anxiety in the third trimester and changes in fetal and maternal circulation assessed by Doppler velocimetry.

METHODS

A prospective comparative study was carried out at the prenatal clinic of the University Hospital. The study was approved by the Local Human Research Ethics Committee (CAAE 56059116.9.0000.5505), and all participants signed an informed consent form. The inclusion criteria were pregnant women presenting good health, a singleton pregnancy, maternal age between 18 and 40 years, gestational age between 36 and 40 weeks, and no regular use of medication.

Gestational age was based on the last menstrual period and confirmed by first-trimester ultrasound. Each woman was initially evaluated by ultrasound, and measurements were obtained for fetal biometry and the amniotic fluid index. Fetal Doppler velocimetry measurements were taken of the UtA,

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UA, MCA, and umbilical vein (UV). Doppler measurements were carried out using a real-time ultrasound Voluson 730 Pro (GE Healthcare, Solingen, Germany) with a 2.5-MHz curved-array probe using pulsed and color Doppler options. The high-pass filter was set at minimum, and the sample volume size was adapted to the vessel diameter. All of the recordings used for analysis were obtained in the absence of fetal body and breathing movements at insonation angles as low as possible and always close to 0°. A pulsed Doppler examination of the UA was performed at the free loop of the umbilical cord, and the pulsatility index (PI) was obtained. The MCA could be seen as a major lateral branch in the circle of Willis, and a Doppler sample gate was placed on the proximal portion to obtain waveforms and measure PI. The Doppler assessment of UtA was performed on both the left and right branches, and the mean value of PI was obtained for analysis.

The UV was identified in its intra-abdominal portion, and waveforms were plotted for the straight part. The venous Doppler parameters included time-averaged maximum velocities (TAMxV) measured with insonation along the vessel axis. The evaluation of TAMxV was not recorded simultaneously to adjacent arterial vessels; the measurements were performed during the mean time to include five or more heart cycles. The UV diameter was measured in insonation perpendicular to the vessel wall with the color Doppler mode switched off and the vessel image zoomed in. The blood flow (Q) was calculated as follows: $Q=\pi(D/2)^2\times h\times TAMxV$, where D is the vein diameter and h is the coefficient for the blood velocity profile (0.5)[7].

The intra- and interobserver variability of UV measurements was previously assessed. Intraclass correlation coefficient for the UV TAMxV mean measures was 0.938 (95% confidence interval [CI] 0.888–0.969) and interclass correlation coefficient for the UV TAMxV mean measures was 0.798 (95%CI 0.635–0.889)[8].

Following the Doppler ultrasound measurements, the Beck Anxiety Inventory (BAI) questionnaire was handed out; it is easy to apply and is answered by pregnant women. The BAI is a questionnaire with 21 self-reported items for assessing the severity of a woman's anxiety. Each item describes a common symptom of anxiety and is rated on a 4-point Likert scale, ranging from 0 (for not at all) to 3 (for severely). The respondent is asked to rate each symptom and then the total score is calculated (0–63). A high overall score indicates a high level of anxiety. Score from 0 to 10 reflects minimal anxiety; from 11 to 19, mild anxiety; from 20 to 30, moderate anxiety; and from 31 to 63, severe anxiety. The Brazilian version of the BAI used in this study was validated using the Brazilian population[9].

Data were analyzed using the MedCalc program, version 11.5.1.0 (MedCalc Software, Belgium). Descriptive statistics are presented as mean and standard deviation (SD), median and range, or frequency and percentage. The sample size was estimated based on the study of Fu et al.[1] to detect a difference of 0.20 in the UA-PI, and it was verified that a minimum sample size of 30 cases was required. Data were compared using the Mann-Whitney U test for independent samples, the chi-square test, or the Fisher's exact test. A statistical significance level was set at $p<0.05$.

RESULTS

The study included 34 pregnant women, and 6 (17.7%) presented a total BAI score showing moderate or severe maternal anxiety. Table 1 displays the maternal characteristics and the main Doppler results. The mean BAI total score was 12.3 (SD 9.8). No preterm delivery occurred and all babies had adequate parameters for their gestational age at birth.

Table 1. Maternal, perinatal characteristics, and Doppler parameters at third trimester (n=34).

Characteristic	Value
Maternal age (years)	28.1 (5.7)
Nulliparity	21 (61.8%)
Gestational age at exam (weeks)	36.5 (1.7)
Estimated fetal weight (g)	2,852 (488)
Amniotic fluid index (cm)	12.9 (2.5)
UtA PI	0.72 (0.67–0.77)
UA PI	0.81 (0.16)
MCA PI	1.62 (0.25)
MCA PSV	51.2 (10.1)
UV TAMxV (cm/s)	20.42 (3.79)
UV flow (mL/min)	226.3 (197.0–269.9)
UV flow, normalized (mL/min/kg)	79.7 (69.2–96.1)
Total BAI score	10.5 (7.0–13.0)
Maternal anxiety	
Minimal	17 (50.0%)
Mild	11 (32.4%)
Moderate	4 (11.8%)
Severe	2 (5.9%)

Data expressed as n (%), mean (SD), or median (95%CI for the mean). UtA: uterine artery; PI: pulsatility index; UA: umbilical artery; MCA: middle cerebral artery; PSV: peak systolic velocity; UV: umbilical vein; TAMxV: time averaged maximum velocity; BAI: Beck Anxiety Inventory.

Table 2 presents the results of Doppler parameters in the group of moderate or severe anxiety, compared to the group of minimal or mild anxiety, and presents an association with lower maternal age (p=0.019), lower fetal UV blood flow (p=0.047), and lower UV-corrected blood flow (p=0.038). No significant association was found between moderate or severe maternal anxiety and fetal growth (p=0.651), mean UtA PI (p=0.175), UA PI (p=0.752), MCA PI (p=0.401), and MCA PSV (p=0.191). No significant differences were detected regarding the type of delivery when comparing the groups: the cesarean section rate was 33.3% (n=2) in the group with moderate or severe anxiety and 32.1% (n=9) in the group with mild or minimal anxiety (p=1.0, Fisher's exact test).

Figure 1 shows the median fetal UV blood flow and UV-corrected blood flow in both groups of moderate or severe anxiety, compared to group of minimal or mild anxiety. A reduction in the UV blood flow occurs in the mothers presenting anxiety.

Table 2. Maternal characteristics and Doppler values of uterine artery, umbilical artery, middle cerebral artery, and umbilical vein according to maternal anxiety.

Characteristics	Minimal or mild anxiety (n=28)	Moderate or severe anxiety (n=6)	p-value*
Maternal age (years)	29.5 (25.3–34.8)	21.5 (18.6–29.2)	0.019
Nulliparity	18 (64.3)	3 (50.0)	0.855
Gestational age at exam (weeks)	36.5 (35.3–37.7)	35.5 (34.3–38.1)	0.442
Amniotic fluid index (cm)	13.0 (11.6–14.3)	12.5 (10.0–15.6)	0.910
Estimated fetal weight (g)	2940 (2499–3139)	2583 (2234–3517)	0.651
UtA PI	0.72 (0.68–0.81)	0.64 (0.55–0.75)	0.175
UA PI	0.85 (0.75–0.91)	0.78 (0.65–0.96)	0.712
MCA PI	1.59 (1.49–1.70)	1.69 (1.37–1.77)	0.401
MCA PSV	49.5 (43.9–54.6)	54.6 (45.4–71.3)	0.191
UV TAMxV (cm/s)	20.9 (19.5–22.1)	18.2 (15.8–23.2)	0.343
UV flow (mL/min)	249.5 (201.3–294.1)	189.4 (133.8–249.7)	0.047
UV flow, normalized (mL/min/kg)	84.9 (73.0–103.3)	68.5 (59.9–76.2)	0.038
Total BAI score	8.0 (6.0–11.0)	25.0 (22.0–45.1)	<0.001

*Mann-Whitney U test. Data expressed as n (%) or median (95%CI for the mean). UtA: uterine artery; UA: umbilical artery; PI: pulsatility index; MCA: middle cerebral artery; PSV: peak systolic velocity; UV: umbilical vein; TAMxV: time averaged maximum velocity; BAI: Beck Anxiety Inventory.

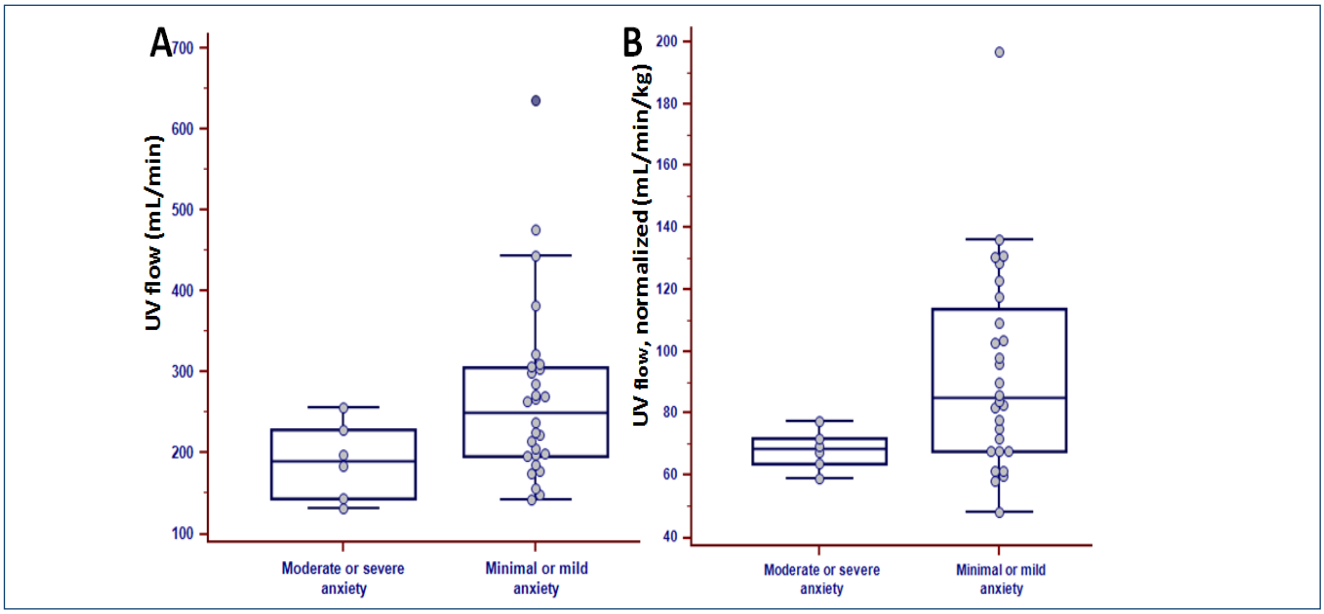

Figure 1. Box-and-whisker plot for median and 95%CI of umbilical vein flow (A) and normalized umbilical vein flow by estimated fetal weight (B) according to maternal anxiety.

DISCUSSION

In our study, fetal UV circulation patterns are associated with maternal anxiety. Maternal anxiety appears to be related to reduced UV blood flow. These changes suggest that the fetal supply of oxygenated blood flow may be reduced in conditions of moderate or severe maternal anxiety. Color Doppler ultrasound is a sensitive and safe technique for examining changes in fetal blood flow and provides a comprehensive and objective assessment of the fetus[10].

No difference is found with the UtA, UA, and MCA changes in both groups, according to maternal anxiety. It agrees with Kent et al.[11] Interestingly, as opposed to the study of Fu et al.[1], we found no difference in Doppler velocimetry indices in the UA. Possible reasons might be the small sample size or an unknown possible physiological mechanism of how maternal stress affects the fetus.

Anxiety is increasing in our society due to several factors and represents an important health problem. Maternal anxiety in the first trimester is a risk factor for later development of fetal complications. A study was performed to identify the biopsychosocial risk associated with the development of adverse obstetric outcomes. Ramiro-Cortijo et al.[12] found women with fetal complications showed a significantly higher score in anxiety compared to women without fetal complications. Our data show that maternal psychological features like anxiety exert an influence on fetal UV blood flow.

Elevated maternal psychological distress during pregnancy is linked to adverse outcomes. Prenatal brain development in the setting of elevated maternal distress has adverse infant social and cognitive outcomes. Wu et al.[13] studied mother-infant dyads and found an association between prenatal maternal stress and infant cognitive outcome mediated by fetal left hippocampal volume. McGuinn et al.[14] found that higher levels of pregnancy-specific anxiety in the mother were associated with higher anxiety symptoms in the child. Changes in fetal circulation due to maternal anxiety may be related to long-term effects on the offspring.

The different positions adopted by pregnant women may affect the maternal uteroplacental blood flow and interfere in fetal circulation[15]. As uterine blood flow may change in the maternal supine position, the exams in the present study were performed to avoid this aspect.

The strength of this study is the prospective examination of fetal venous blood flow in a population of pregnant women attending for routine care and assessment of maternal anxiety. The main limitation of the study is the limited number of cases and the data confined to the third trimester of pregnancy. The sample size of the groups does not allow the analysis of changes in Doppler flow regarding anxiety that may affect the fetus and play a role in medical decision-making. Studies with a larger number of cases are needed to better understand the effects of maternal anxiety on the fetus that may influence obstetric management.

CONCLUSION

Maternal anxiety may affect fetal circulation patterns in late pregnancy and is associated with reduced blood flow in the fetal UV. Effective use of these Doppler indices allows fetal assessment of changes in maternal characteristics and medical history that affect these measurements in normal pregnancies. However, the underlying physiopathology of these changes needs further investigation.

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AUTHORS' CONTRIBUTIONS

RMYN: Conceptualization, Data curation, Formal Analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. **TFJ:** Conceptualization, Data curation, Formal Analysis, Writing – original draft, Writing – review & editing.

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