

The impact of anxiety and depression during pregnancy on fetal growth and the birth outcome

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Background

Maternal depressive and anxiety symptoms during pregnancy have been reported in some, but not all, studies to be associated with an increased risk of preterm birth and intrauterine growth restriction (IUGR).

Objectives

The aim of this study was to estimate the risk of preterm birth and IUGR associated with antenatal anxiety and depression during early pregnancy and to evaluate their impact on fetal growth and the birth outcome.

Patients and methods

The following measures were applied to 54 pregnant mothers: the Edinburgh Postnatal Depressive Scale (EPDS), the Beck Anxiety Inventory (BAI), and fetal biometric data and behavior were recorded during ultrasound examination at 24–36 weeks of gestation and the placental blood perfusion was measured by Doppler assessment of the systolic/diastolic ratio (S/D ratio) of the umbilical artery in the third trimester.

Results

This study revealed that women with depressive and anxiety symptoms in the third trimester of pregnancy exhibit an increased likelihood of having oligohydramnios, IUGR, diminished placental perfusion, and preterm labor.

Conclusion

This study provides evidence that maternal depressive and anxiety symptoms during pregnancy are associated with various fetal developmental problems.

Keywords:

anxiety, birth outcome, depression, pregnancy

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Introduction

Human developmental studies usually consider pregnancy as the starting point of life, suggesting that psychological and behavioral development begins during the gestational period (Field, 2011).

Many stressors commonly affect pregnant women such as low income, difficult employment conditions, heavy family and household responsibilities, problems in intimate relationships, and pregnancy complications (Woods *et al.*, 2010).

Animal experiments have shown that exposure of the pregnant dam to stressful conditions (capture, noise, immobilization, introduction of a strange male, crowding, etc.) often results in a smaller litter size (embryo resorption), structural malformations, growth retardation, lower birth weight, and even a shift in the sex ratio (Beydoun and Saftlas, 2008).

Recent studies have drawn attention to the harmful effects of antenatal anxiety and depression on the developing child. These effects include preterm birth (PTB) (Fransson *et al.*, 2011), low birth weight (Grote *et al.*, 2010), a reduced cognitive ability and increased

fearfulness (Bergman *et al.*, 2007), and an increased incidence of respiratory and skin illnesses in early life (Beijers *et al.*, 2010). Moreover, Kinsella and Monk (2013) concluded that the fetal heart rate, the activity, sleep patterns and movements, all indicators of neurobehavioral development, were significantly affected by maternal stress, depression, and anxiety.

An elevated prenatal maternal cortisol is the strongest predictor of these neonatal outcomes. Newborns of depressed mothers show a biochemical profile that mimics their mothers' prenatal biochemical profile including elevated cortisol and lower levels of dopamine and serotonin (Huynh *et al.*, 2014).

The fetal brain is highly sensitive to minor changes in the intrauterine environment either due to internal and/or external factors. Hypothalamic–pituitary–adrenal axis hormones are suggested to be an important explanation for such effects. However, the nature of stressors and the time of exposure are important determinants of this effect (Davis and Sandman, 2010).

Studies suggest that a significant portion of pregnant women have prenatal anxiety, generally and regarding

their pregnancy (Mahboob *et al.*, 2011). Recent studies estimated a 29% prevalence of antenatal anxiety among pregnant women (Nasreen *et al.*, 2011).

Because of the cultural and socioeconomic environment in various developing regions of the world, sex discrimination and the preference for sons rather than daughters may contribute to anxiety among pregnant women (Waqas *et al.*, 2015). Anxiety during pregnancy is associated with a shorter gestation and lower birth weight, with consequences for infant development (Kinsella and Monk, 2009).

Recently, depression during pregnancy has begun to be recognized as a factor that may affect pregnancy outcomes adversely (Alder *et al.*, 2007). Depression has also been linked to other known risk factors such as smoking, substance, hypertension, preeclampsia, and gestational diabetes (Deave *et al.*, 2008).

Recent estimates of the prevalence of major depression during pregnancy show that from 8.3 to 12.7% of US women experience this condition (Leight *et al.*, 2010). However, many community-based studies found that poor urban women from minority backgrounds are at least twice as likely as middle-class women (Rahman *et al.*, 2007) to meet the diagnostic criteria for major and minor depression during pregnancy (20–25%).

Prenatal and perinatal complications of depression during pregnancy include higher rates of placental abnormalities, pre-eclampsia, and spontaneous miscarriage (Straub *et al.*, 2012).

Depressed women are also more likely to deliver prematurely, and they often have neonates who require intensive care for postnatal complications (Muzik *et al.*, 2009). They are also at a greater risk for being low birth weight (<2500 g) and small for their gestational age (<10th percentile) (Conde *et al.*, 2010).

However, information about psychiatric disorders during pregnancy regarding mothers and their offspring in developing countries are still lacking; more accurate information about the mental health status of women during pregnancy and its effects on the birth outcome are needed.

There are many conflicting data regarding the effect of pregnant mothers' psychological state on fetal growth and activity.

Patients and methods

This study was conducted at the obstetric outpatient clinic (OPC), Mansoura University Hospitals (MUH).

All patients gave their formal consent. The protocol was approved the Ethical committee of the Faculty of Medicine, Ain Shams university.

The study took place during the period from February to September 2014. A total of 72 pregnant women were asked to join this study: 11 of them refused (not interested, personal causes), and seven did not continue. Finally, 54 pregnant women participated in this study. Mothers with medical and/or obstetric complications were excluded. After informed consent, which included permission for recording the fetal growth, the mother's sociodemographic data were collected. At the late second trimester of pregnancy, the Edinburgh Postnatal Depressive Scale (EPDS) and the Beck Anxiety Inventory (BAI) were administered. Fetal growth and activity were assessed during the ultrasound examination. Fetal growth measures included the biparietal diameter, the head circumference, the abdominal circumference, and the femur length. In addition, a Doppler waveforms study of the umbilical vessels after 30 weeks' gestation was performed for the assessment of the systolic/diastolic (S/D) ratio of the umbilical artery. S/D ratios higher than 3 were considered as an early sign of placental blood flow insufficiency. These measures were obtained by the obstetrician of the research team using standard clinical measurement protocols.

PTB was defined as delivery of the baby before completing 37 weeks' gestation. Intrauterine growth restriction (IUGR) was defined as a fetal weight lower than the 10th percentile for the gestational age as determined through ultrasound growth curves, and low birth weight was defined as neonates delivered with less than 2500 g weight (Suri *et al.*, 2007).

Measures

The BAI was used to measure the severity of anxiety. The BAI consists of a 21-item self-report inventory in which each item describes a common symptom of anxiety. The respondent was asked to rate each symptom over the preceding week on a four-point scale (0–3). Scores of 0–7 reflect minimal anxiety, 8–15 mild anxiety, 16–25 moderate anxiety, and a score of 26–63 indicates severe anxiety (Beck *et al.*, 1988).

The EPDS is a 10-item self-report scale assessing symptoms of depression such as dysphoric mood, anxiety, feeling of guilt, suicidal ideas, and 'not coping'. Each item is scored on a four-point scale (0–3) and rates the intensity of depressive symptoms during the previous 7 days. The scale is specifically designed to screen for postpartum depression, but can also be used as a valid measure of depression through the various stages of pregnancy and

the puerperium. A cutoff level of at least 10 reduces detection failure in the postnatal period. When selecting this threshold, the sensitivity for the detection of major depression increased to almost 100% and the specificity to 82% (Cox *et al.*, 1987). In this study, we used a cutoff level of at least 10 to define symptoms of depression.

Results

Results as shown in Table 1 demonstrated that 54 pregnant women participated in this study, and their mean age was 24.94 ± 3.65 years. About 66.7%

Table 1 Sociodemographic data of the pregnant mothers

GA	Mean \pm SD	Range
Age	24.94 ± 3.65	21–34
Number of deliveries	1.11 ± 1.25	0–4
Gestational age	31.67 ± 3.12	24–36
Residence [<i>n</i> (%)]		
Rural		36 (66.7)
Urban		18 (33.3)
Occupation [<i>n</i> (%)]		
Housewife (nonemployer)		33 (61.1)
Physician		9 (16.7)
Engineering		3 (5.6)
Pharmacist		3 (5.6)
Teachers		6 (11.1)
Education level [<i>n</i> (%)]		
Basic		7 (12.9)
Secondary		18 (33.3)
High		29 (53.7)

GA, gestational age.

were from rural areas; most of them (61.1%) were housewives, and 53.7% received a high educational level. Their mean number of deliveries was 1.11 ± 1.25 , and their mean gestational age 31.67 ± 3.12 weeks.

Table 2 highlights that 61.11% of the pregnant women had symptoms of depression. No significant relation was detected with regard to the age of the pregnant women, the number of deliveries, the education level, and the gestational age during administration of the scale.

The gestational age at delivery was significantly reduced in the depressed group (37.45 ± 1.75) ($P = 0.020$), although the mean age was just at maturity.

About 63.6% of the cases of depression were among housewives ($P \leq 0.001$), and 54.5% were from rural areas ($P = 0.018$).

There was a significant increase in the S/D ratio of the umbilical artery in depressed mothers (2.95 ± 0.73) ($P = 0.023$). About 45.5% ($P = 0.018$) of the women with depressive symptoms showed IUGR, and all women who had oligohydramnios ($n = 9$) and had depression ($P = 0.009$) (Table 3).

About 38.88% of the women had mild anxiety, 27.77% had moderate anxiety, and about 16.66% of them had minimal and severe grades of anxiety. Severe anxiety was more at the gestational age of 32.33 ± 2.78 weeks, whereas minimal anxiety was seen at 29.67 ± 4.27 weeks ($P = 0.007$).

Table 2 Results of the Edinburgh Depression Scale in relation to sociodemographic and fetal developmental data

GA	Edinburgh Depression Scale		t-Test	P
	Absent (<i>n</i> = 21) (38.88%)	Present (<i>n</i> = 33) (61.11%)		
Age	24.86 ± 3.61	25.00 ± 3.72	0.139	0.890
GA at examination	30.86 ± 3.12	32.18 ± 3.06	1.540	0.130
Number of deliveries	1 (0–3)	1 (0–4)	328.50 ^a	0.736
GA at delivery	38.57 ± 1.54	37.45 ± 1.75	2.393	0.020*
			χ^2 -Test	P
Residence [<i>n</i> (%)]				
Rural	18 (85.7)	18 (54.5)	5.610	0.018*
Urban	3 (14.3)	15 (45.5)		
Occupation [<i>n</i> (%)]				
Housewife	12 (57.1)	21 (63.6)	21.868	<0.001*
Doctor	9 (42.9)	0 (0)		
Engineering	0 (0)	3 (9.1)		
Pharmacist	0 (0)	3 (9.1)		
Teacher	0 (0)	6 (18.2)		
Education level [<i>n</i> (%)]				
Basic	3 (14.3)	6 (18.2)	1.689	0.430
Secondary	3 (14.3)	9 (27.3)		
High	15 (71.4)	18 (54.5)		
S/D ratio of umbilical artery	2.51 ± 0.53	2.95 ± 0.73	2.346	0.023*
IUGR	3 (14.3)	15 (45.5)	5.610	0.018*
Oligohydramnios	0 (0)	9 (27.3)	6.873	0.009*

IUGR, intrauterine growth restriction; ^aThe Mann–Whitney *U*-test was used; *Significant at $P < 0.05$; GA, gestational age.

Almost 100% of the women who had severe anxiety were from rural areas, whereas 80% of them with moderate anxiety were from urban areas ($P \leq 0.001$).

Housewives represented 66.7 and 80% of the cases with severe and moderate anxiety, respectively ($P \leq 0.001$).

The gestational age at delivery was higher in women with minimal anxiety (39.33) and lower in those with severe anxiety (36.33) that was beyond maturity. The S/D ratio of the umbilical artery was higher with moderate and severe anxiety (3.22 ± 0.62 and 2.77 ± 0.93 , respectively) ($P = 0.010$). Oligohydramnios was also detected with moderate and severe anxiety (40 and 33.3%, respectively) ($P = 0.003$).

Discussion

This study revealed that women with depressive and anxiety symptoms in the third trimester of pregnancy exhibit an increased likelihood of having oligohydramnios, IUGR, diminished placental perfusion, and preterm labor.

Our findings on the impact of maternal depression and anxiety on fetal development and the birth outcome were consistent with recent researches that suggested that prenatal depression may itself have a direct, negative impact on neonatal health such as intrauterine growth retardation (Alder *et al.*, 2007) (a fetal weight lower than the 10th percentile for the gestational age), preterm labor (Parker Dominguez *et al.*, 2008) (delivery of the baby before completing 37 weeks' gestation), and babies with low birth weight (Goedhart *et al.*, 2010; Chan *et al.*, 2013) (neonates delivered with less than 2500 g weight).

In addition, a Doppler waveforms study of the umbilical vessels after 30 weeks' gestation was conducted for the assessment of the systolic/diastolic (S/D) ratio of the umbilical artery. An S/D ratio higher than 3 was considered as an early sign of placental blood flow insufficiency. Another important finding in this study was that depression and anxiety during pregnancy were associated with a significant increase in the S/D ratio similar to the results of Chen *et al.* (2014).

Newport *et al.* (2002) reported that depression during pregnancy may in fact be 'a child's first adverse life event'.

Another prospective study of maternal prenatal depression found a negative relation between depression and child cognitive and language development, independent of antidepressant medication exposure (Davis and Sandman, 2010).

In addition to depression, a direct link between anxiety disorders and adverse infant health may also exist. Recent literature indicates that prenatal maternal stress is negatively related to birth outcomes and child health (Glover *et al.*, 2009).

Undoubtedly, anxiety and depression during pregnancy are associated with some risky health behaviors, such as poor nutrition and hygiene, a lack of motivation to obtain prenatal care or to follow medical recommendations, and smoking and/or alcohol and substance abuse, all of which affect pregnancy outcomes adversely (Neggers, *et al.*, 2006).

Different mechanisms were described to answer the question of how maternal stress influences neonatal health.

Anxiety or depression during pregnancy might promote adverse birth outcomes through the dysregulation of the hypothalamic–pituitary–adrenocortical axis, stimulating the release of stress hormones, such as cortisol and catecholamines, reaching the fetus through transplacental transport of maternal hormones. These biological changes may result in placental hypofusion (reduction in blood flow) and consequent restriction of oxygen and nutrients to the fetus, leading to fetal growth restriction and/or precipitation of PTB (O'Donnell *et al.*, 2009).

Other mechanisms include the possibility that antenatal depression might compromise the immune system functioning, which in turn may lead to reproductive tract infection, triggering PTB (Dunkel Schetter, 2010).

Limitations

Limitations of the study include the inability to control for several variables such as anemia, weight gain during pregnancy, and smoking (although smoking was uncommon among the women of our study population). Also, the sample size was relatively small, and further investigations with larger samples are needed.

Conclusion

This study found a strong link between maternal depressive and anxiety symptoms in the third trimester of pregnancy and various fetal developmental problems such as oligohydramnios, IUGR, diminished placental perfusion, and preterm labor.

Therefore, the early detection and management of depressive and anxiety symptoms during pregnancy should be provided routinely for all pregnant women

Table 3 Results of the Beck Anxiety Inventory in relation to sociodemographic and birth developmental data

GA	The Beck Anxiety Inventory				F-test	P
	Minimal (n = 9) (16.66%)	Mild (n = 21) (38.88%)	Moderate (n = 15) (27.77%)	Severe (n = 9) (16.66%)		
Age	24.00 ± 1.50	24.29 ± 3.66	26.60 ± 4.79	24.67 ± 2.18	1.521	0.220
GA at examination	29.67 ± 4.27	33.14 ± 2.71	30.40 ± 1.92	32.33 ± 2.78	4.507	0.007*
Number of deliveries	0 (0–2)	1 (0–2)	3 (0–4)	1 (0–2)	6.025 ^a	0.110
GA at delivery	39.33 ± 1.00	38.71 ± 1.31	36.80 ± 1.78	36.33 ± 0.50	13.653	<0.001*
					χ ² -Test	P
Residence [n (%)]						
Rural	9 (100)	15 (71.4)	3 (20)	9 (100)	23.914	<0.001*
Urban	0 (0)	6 (28.6)	12 (80)	0 (0)		
Occupation [n (%)]						
Housewife	3 (33.3)	12 (57.1)	12 (80)	6 (66.7)	51.912	<0.001*
Doctor	6 (66.7)	3 (14.3)	0 (0)	0 (0)		
Engineering	0 (0)	0 (0)	0 (0)	3 (33.3)		
Pharmacist	0 (0)	0 (0)	3 (20)	0 (0)		
Teacher	0 (0)	6 (28.6)	0 (0)	0 (0)		
Education level [n (%)]						
Basic	0 (0)	3 (14.3)	6 (40)	0 (0)	19.987	0.003*
Secondary	0 (0)	3 (14.3)	6 (40)	3 (33.3)		
High	9 (100)	15 (71.4)	3 (20)	6 (66.7)		
S/D ratio of umbilical a	2.33 ± 0.22	2.66 ± 0.60	3.22 ± 0.62	2.77 ± 0.93	4.199	0.010*
IUGR	0 (0)	6 (28.6)	6 (40)	6 (66.7)	9.514	0.023*
Oligohydramnios	0 (0)	0 (0)	6 (40)	3 (33.3)	13.680	0.003*

No significant relation was found between anxiety and the age or the number of deliveries; IUGR, intrauterine growth restriction; ^aThe Kruskal–Wallis test was used; *Significant at $P < 0.05$; GA, gestational age.

in Egypt, which will not only reduce the burden on mothers but is also an important preventive measure for serious developmental problems in our children.

Recommendations

It may be useful in future studies to follow-up the infants of mothers who had depression and anxiety during pregnancy to evaluate the developmental milestones, cognitive functions, and behavior outcomes of the infants. Also, biological markers of the hypothalamic–pituitary–adrenal axis functioning, such as cortisol levels, could be used to help further understand how the fetus is affected by the mother's psychological status.

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Conflicts of interest

There are no conflicts of interest.

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