World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Effects of *pregnancy-related anxiety* on pregnancy outcomes

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World Journal of Advanced Research and Reviews, 2025, 25(01), 496-503

Publication history: Received on 28 November 2024; revised on 07 January 2025; accepted on 09 January 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.1.3967

Abstract

Introduction*:* Maternal anxiety during pregnancy has been associated with various adverse birth outcomes, including alterations in *Brain-Derived Neurotrophic Factor* (BDNF) levels, birth weight, length, and APGAR scores. This study aims to examine the relationship between maternal anxiety levels and neonatal outcomes among pregnant women in Padang, Indonesia.

Methods*:* A cross-sectional study was conducted with 85 pregnant women who were approaching labor at a hospital in Padang. Anxiety levels were measured using the *Zung Self-Rating Anxiety Scale* (ZSAS), while neonatal outcomes such as birth weight, length, and APGAR scores were recorded. BDNF levels were measured using the ELISA method. Statistical analysis was performed using Pearson correlation and One-Way ANOVA tests to assess the relationship between anxiety levels and neonatal outcomes.

Results*:* The results showed that 84.5% of participants experienced anxiety, with 40% having moderate anxiety and 27.1% having severe anxiety. A significant association was found between maternal anxiety and BDNF levels ($p = 0.000$), with higher anxiety associated with lower BDNF. A weak but significant negative correlation was observed between maternal anxiety and baby length ($r = -0.224$, $p = 0.039$). A strong negative correlation was identified between anxiety and APGAR scores ($r = -0.661$, $p = 0.000$). However, no significant relationship was found between maternal anxiety and birth weight ($r = -0.121$, $p = 0.270$).

Conclusions*:* Maternal anxiety significantly influences BDNF levels, baby length, and APGAR scores but does not significantly affect birth weight. These findings underscore the importance of addressing maternal mental health during pregnancy and implementing interventions to reduce anxiety for better neonatal outcomes.

Keywords: Anxiety; Pregnancy Outcome; BDNF; Apgar Score

1. Introduction

Pregnancy is a pivotal period in a woman's life characterized by significant physical, emotional, and social changes. It is a time of both excitement and vulnerability, as expectant mothers navigate through numerous adjustments and face the responsibilities of nurturing a developing fetus. This period is also marked by an increased risk of mental health disorders, including anxiety. Maternal anxiety during pregnancy is a common issue and can manifest in various forms, including mood swings, fatigue, emotional disturbances, and anxiety related to childbirth and future parenting responsibilities[1].

Pregnancy-related anxiety encompasses worries and fears about pregnancy, labor, neonatal health, and child-rearing. Although some level of anxiety can be a normal response to stress, severe anxiety can adversely affect both maternal

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and fetal health[2]. Research indicates that anxiety is prevalent among pregnant women. Santomauro et al. (2021) reported a global increase in anxiety disorders, with prevalence rates rising from 30.2% to 62.5%, affecting approximately 44.5 million individuals[3,4] Similarly, Mortazavi et al. (2021) found that 80% of women experience anxiety related to pregnancy and childbirth[5]. Anxiety levels among pregnant women have been shown to increase, particularly in those with previous obstetric complications or high-risk pregnancies[6]

Anxiety during pregnancy can have significant implications for both the mother and the fetus. According to Maharlouei (2021), children born to mothers who experience high levels of psychological stress during pregnancy are more likely to have cognitive and behavioral issues[7]. Furthermore, research by Chen et al. (2020) identified several sources of anxiety during pregnancy, including concerns about childbirth, changes in role and body image, and potential health complications[8]. The relationship between maternal anxiety and birth outcomes is well-documented. Increased levels of maternal anxiety are associated with negative birth outcomes, such as preterm birth, low birth weight, and developmental issues in children[9]

The fetal brain undergoes rapid development during pregnancy, and maternal anxiety can impact this process. Brain-Derived Neurotrophic Factor (BDNF), a crucial protein for neuronal growth and development, can be influenced by maternal psychological stress[10]. BDNF plays a critical role in the development of the fetal brain. It affects synaptic plasticity, neuronal morphology, and overall cognitive function[11]. Disruptions in the intrauterine environment, including maternal stress and anxiety, can impact BDNF levels and subsequently affect fetal brain development[12].Maternal anxiety is a significant concern during pregnancy, with potential implications for both maternal and fetal health. Understanding the effects of anxiety on birth outcomes and fetal development is crucial for developing effective interventions and support systems for pregnant women[4]. Addressing maternal anxiety and promoting mental well-being during pregnancy can contribute to better health outcomes for both mothers and their infants[12].

2. Materials and Methods

This research is an observational study with a cross-sectional design. The study was conducted from May 2022 to August 2022 and was approved by the Ethics Committee of Andalas University under the number 677/UN.16.2/KEP-FK/2022. The study population comprised mothers giving birth at three hospitals in Padang City, West Sumatra: RS Hermina, RS Reksodiwiryo, and RSP Universitas Andalas. Inclusion criteria were mothers with a gestational age of ≥37 weeks who underwent Caesarean section delivery without complicating diseases and were willing to participate in the study. Exclusion criteria included mothers with preeclampsia/eclampsia, diabetes, obesity, systemic infections, anemia, active smokers, and alcohol consumers.

Subjects were identified through collaboration with the three medical institutions. A total of 85 eligible mothers who met the inclusion criteria and consented to participate signed an informed consent form. Neonatal Health Assessment: Birth weight, length, and APGAR score of the babies were assessed by healthcare providers and recorded in the baby's medical record. Umbilical cord blood was collected in the operating room during the Caesarean section delivery. Brain-Derived Neurotrophic Factor (BDNF) levels were measured at the Biomedical Laboratory of Andalas University, Padang, using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Maternal anxiety levels were assessed using the Zung Self Anxiety Scale questionnaire. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) questionnaire before delivery, while the mother was in the obstetrics/delivery room.

The correlation between anxiety scores and neonatal birth weight, length, and APGAR score was analyzed using Pearson Correlation test. The relationship between anxiety levels and BDNF levels was analyzed using The One Way Anova statistical test. All statistical analyses were conducted using SPSS version 22.

3. Results

Table1 shows that the majority of mothers in this study were on average 30.66 years old, with ages ranging from 21 to 41 years. Of the 85 mothers, 42.4% were primigravida, while 57.6% were multigravida, with the majority giving birth to their second child. The mean neonatal birth weight was 3083.98 ± 372.74 grams, with an average length of 48.05 ± 1.37 cm and a mean APGAR score of 7.65 ± 0.55.

Tabel 1 The Maternal and Neonatal Charactheristics

Karakteristik	n (%)	Mean±SD	Min-max	Median
Maternal Age	85(100%)	30.66 ±4.247	21-41	31
Parity		1.86±0.941	1-5	2
Primigravida	36(42.4%)			
Multigravida	49(57.6%)			
Baby Length		48.05 ±1.379	45-52	48
Baby Weight		3083.98 ± 372.74	2300-4326	3056
APGAR Score		7.65±0.550	6-9	8

Table 2 Frequency Distribution of Maternal Anxiety Levels at Padang City Hospital

Anxiety Level	Frequency (f)	Percentage (%)
Without Anxiety	14	16.5%
Mild	14	16.5%
Moderate	34	40.0%
Severe	23	27.1%
Total	85	100%

Based on Table 2, among the 85 pregnant respondents approaching delivery at Padang City Hospital, A significant majority (83.5%) of pregnant women in Padang city hospitals experience some level of anxiety, with the highest percentage showing moderate anxiety (40.0%).

Table 3 The Relationship Between Maternal Anxiety Levels and BDNF Levels

Maternal Anxiety Level	BDNF Level			P *Value*
	N (%)	Mean Rank	Mean±SD	
Without Anxiety	14(16.5%	72.50	1.78±1.028	0.000
Mild	14(16.5%)	59.71		
Moderate	34(40%)	38.25		
Severe	23(27.1%)	21.89		
Total	85 (100%)			

Based on Table 3, The results of the study indicate a significant relationship between maternal anxiety levels and neonatal BDNF levels (p=0.000). Mothers without anxiety exhibited the highest BDNF levels (mean rank: 72.50; 1.78±1.028), while those with severe anxiety had the lowest BDNF levels (mean rank: 21.89). These findings suggest that higher maternal anxiety levels are associated with lower neonatal BDNF levels, potentially impacting fetal neurodevelopment.

Table 4 The Correlation Between Anxiety Score and Birth Weight

Correlations			
		Maternal Anxiety Score	**Birth Weight**
Maternal Anxiety Score	Pearson Correlation	1	-0.121
	Sig. (2-tailed)		0.270
	N	85	85
Birth Weight	Pearson Correlation	-0.121	1
	Sig. (2-tailed)	0.270	
	N	85	85

Table 4 shows that there is a very weak negative correlation between maternal anxiety scores and birth weight (r = -0.121) which is not statistically significant (p = 0.270). Therefore, there is no meaningful relationship between maternal anxiety and birth weight.

Table 5 The Correlation Between Anxiety Score and Baby Length

Correlations			
		Maternal Anxiety Score	**Baby Length**
Maternal Anxiety Score	Pearson Correlation	1	-0.224*
	Sig. (2-tailed)		0.039
	N	85	85
Baby Length	Pearson Correlation	-0.224*	1
	Sig. (2-tailed)	0.039	
	N	85	85
*. Correlation is significant at the 0.05 level (2-tailed).			

Table 5 shows a weak but statistically significant negative correlation between maternal anxiety scores and baby length (r = -0.224), with a significance level of 0.039. This indicates that higher maternal anxiety scores are associated with shorter baby length at birth

Table 6 Correlation Between Anxiety Score and APGAR Score

Correlations			
		Maternal Anxiety Score	**Apgar Score**
Maternal Anxiety Score	Pearson Correlation	1	-0.661**
	Sig. (2-tailed)		0.000
	N	85	85
Apgar Score	Pearson Correlation	-0.661**	1
	Sig. (2-tailed)	0.000	
	N	85	85
**. Correlation is significant at the 0.01 level (2-tailed).			

Table 6. shows a strong and statistically significant negative correlation between maternal anxiety scores and APGAR scores (r = -0.661), with a significance level of 0.000. This means that higher maternal anxiety levels are associated with lower APGAR scores at birth, indicating a strong relationship between these two variables.

4. Discussion

In the table nomor 1, It is known that the neonatal characteristics of the APGAR Score have a significant correlation or relationship with levels of Brain-Derived Neurotrophic Factor (BDNF) in infant's umbilical cord blood in maternal mothers with a p-value <0.05 (p=0.00) with a positive correlation with medium strength. So it can be concluded that the higher the Apgar Score, the higher the BDNF level.

The study of Sun et al., (2021) found that compared to neonates of women who did not experience depression and anxiety, neonates of pregnant women who experienced anxiety and depression had lower mean APGAR scores at both 1 minute and 5 minutes. A low 5-minute APGAR score can be a diagnostic criterion for neonatal asphyxia/hypoxia-ischemia based on a range of markers: the need for delivery room intubation or cardiopulmonary resuscitation, umbilical cord artery pH less than 7, and abnormal neurologic signs, such as muscle hypotonicity or lack of sucking reflex (20)

This can affect one of the brain systems, namely the dopaminergic and serotonergic system neurotransmitters which play an important role in the production of BDNF levels. It has also been associated with the downregulation of the placental enzyme 11β-hydroxysteroid dehydrogenase type 2, which catalyzes the rapid inactivation of glucocorticoids in the placenta, thereby increasing fetal exposure to maternal cortisol. This increase in cortisol suppresses the production of BDNF levels. 5 percent to 10 percent of neonates with low Apgar scores have persistent motor deficits and 20 percent to 50 percent have sensory or cognitive impairments that persist into adolescence(21).

The results of the research that the researchers have done show that the Apgar score is positively correlated with BDNF levels, where the higher the Apgar score, the higher the BDNF level, but if the APGAR Score is low, the BDNF level will also be low. Researchers assume that in this study the APGAR Score is influenced by the psychological condition of the mother during pregnancy and childbirth, where mothers who experience anxiety during pregnancy tend to give birth to babies with lower APGAR scores than mothers without anxiety disorders or depression during pregnancy. Psychological problems such as anxiety mediate a low APGAR Score and an increase in cortisol levels which have an effect on decreasing BDNF levels and impaired neurodevelopment.

Based on this study, it was found that almost all the pregnant women experience anxiety problems and sleep disturbances during pregnancy caused by anxiety related to their pregnancy condition. Maternal anxiety is influenced by a lack of social support and attention from husbands and family, caused by the number of children, the spacing of children, and also by financial problems. Anxiety during pregnancy is also caused by bad obstetric history. Sleep disturbances are caused by the workload during pregnancy, the number of children, and the spacing of children. In addition, many pregnant women have toddlers, so they often wake up when the toddlers cry and wakefulness.

Maternal anxiety increases the production of maternal cortisol levels and the release of placental CRH (pCRH) into the fetal compartment. If there is a disturbance in the action of HPA, this will also affect the production of decreased levels of BDNF, which is associated with nerve and brain development (22). Symptoms of maternal anxiety and depression increase the child's risk of experiencing various emotional, behavioral and/or cognitive problems, which can affect the brain and behavior of future offspring. The results also reported that maternal anxiety and stress were associated with changes in limbic and frontotemporal networks, and functional and microstructural connections present in the brain (23). Psychological disorders such as stress, anxiety and chronic depression reduce BDNF expression, increase apoptosis and decrease neuronal regeneration in the hippocampus, and also decrease BDNF expression in the brain.

This psychological problem also can lead to disturbances in monoamine neurotransmitters and a decrease in serotonin which can trigger inflammatory reactions and suppress BDNF levels and may be associated with fetal cortisol levels (24).

Based on this study, showed that there was a significant Association between Maternal sleep quality with neonatal BDNF and cortisol levels. In line with the previous study showed that there was a significant positive relationship between the homeostatic drive of REM sleep with increased cortisol levels and decreased levels of BDNF expression (25). In addition, sleep disorders can reduce melatonin levels are related to serotonin levels. Serotonin plays an essential role in stimulating BDNF expression and decreasing cortisol production. Serotonin is the most important factor involved in BDNF signaling the effect of sleep disturbances can affect the mechanism of brain plasticity/connectivity (26).

Excess levels of Glucocorticoid and pCRH (CRH Placenta) can modify the fetal brain structure, this can cause neurotransmission disorders and programming disorders due to the reactivity of the neonate's HPA axis. Neurons in the hippocampus and impaired/reduced production of neurons in the dentate gyrus, the main hippocampal structure responsible for neurogenesis. Furthermore, the results of the study reported that maternal stress is associated with changes in limbic and frontotemporal networks, and functional and microstructural connections present in the brain (22).

Brain-Derived Neurotrophic Factor (BDNF) and cortisol function to strengthen connections between neurons (synapses), especially in the hippocampus, cortex, and basal forebrain areas important for learning, maintaining memory, and cognitive(27). If there are prolonged anxiety and sleep disturbances, there will be a decrease in BDNF levels resulting in a reduction in hippocampal volume. The hippocampus is part of the structure of the brain and limbic system that is responsible for learning and memory. It is mainly responsible for the processing of long-term and spatial memories, but it can also have an impact on cognitive, emotional, behavioral, and emotional disturbances that are detrimental to the baby in later life (23, 26).

The results of this study indicate that it is important for prevention and intervention efforts to reduce anxiety during pregnancy which can have long-term beneficial effects on children. Anxiety that is often experienced during pregnancy is anxiety related to the health of pregnant women, concerns about physical changes and their appearance, anxiety related to the health and development of the fetus, anxiety related to the birth process, anxiety related to the roles and responsibilities of being a parent (28).This result explains the importance to take care of the maternal psychological and the maternal quality of sleep. There is a relationship between maternal good sleep quality with stress released and mental disorders. Sleep disturbances during pregnancy are prone to stress and anxiety and can increase the production of cortisol, and decreased BDNF levels. It can impact neonatal development, brain development, and the emotions of neonates in the future. We have a limitation in this study we don't determine the neonatal developmental problems and we don't use a cohort design that might can follow the condition of the neonatal development

This study found that a significant majority of pregnant women approaching delivery experienced varying levels of anxiety. Specifically, 84.5% of the women experienced anxiety, with 40% experiencing moderate anxiety and 27.1% experiencing severe anxiety. Only 16.5% of the women reported no anxiety. This high prevalence highlights the importance of addressing mental health during pregnancy. These findings align with global studies by Luo Zhang et al. (2022), which noted high levels of anxiety and depression among pregnant women, often due to significant hormonal changes during pregnancy13,[14]

Anxiety during pregnancy often serves as a defense mechanism that can affect both physical and psychological health. Symptoms of anxiety can include somatic symptoms like respiratory disturbances, tachycardia, and digestive issues, as well as psychological symptoms such as restlessness, insomnia, and excessive worry. This study used the Zung Self Anxiety Scale to identify these symptoms, including respiratory issues, dizziness, palpitations, and psychological symptoms like irritability and restlessness[13,15]. Risk factors for anxiety and depression during pregnancy have been identified in research by Luo et al. (2022), including maternal age, education level, employment status, chronic illnesses, social support, and family income[13]. Chen et al. (2020) showed that maternal anxiety is often caused by uncertainty about the delivery process, role changes, and economic pressure. These findings are consistent with this study, which also indicated that anxiety related to personal health, labor pain, and uncertainty about the baby's health contributed to maternal anxiety[8].

This study revealed significant differences in Brain-Derived Neurotrophic Factor (BDNF) levels based on maternal anxiety levels, with a p-value of 0.000. Women with severe anxiety had lower BDNF levels compared to those with no anxiety. This finding aligns with research by Fung et al. (2015) and Sonmez et al. (2019) , which demonstrated that anxiety and stress can reduce BDNF levels, crucial for fetal brain development[16]. This study reinforces the understanding that maternal anxiety can influence BDNF levels and potentially affect the neurobiological development of the baby in utero [12,16]. Anxiety, stress, and depression during pregnancy can lead to disturbances in monoamine neurotransmitters, decreased serotonin levels, and increased glucocorticoid or cortisol levels, which can affect BDNF levels and negatively impact fetal brain development[17,18]. Recent studies indicate that the hypothalamic-pituitary-adrenal (HPA) axis mediates the effects of maternal stress on the fetal brain. Prolonged stress can damage the HPA axis, increase blood concentrations of glucocorticoids/cortisol, and negatively affect BDNF levels and neural development [19].

Correlation analysis revealed a very weak and statistically insignificant relationship between maternal anxiety and birth weight ($r = -0.121$, $p = 0.270$). This suggests that maternal anxiety may not have a significant impact on birth weight. Other factors, such as nutrition and genetics, might be more influential in determining birth weight[20].This result differs from previous research, which suggests that maternal depression and anxiety may increase the likelihood of preterm

birth, low birth weight, and other adverse birth outcomes[21]. The study found a weak but statistically significant negative correlation between maternal anxiety and birth length ($r = -0.224$, $p = 0.039$). Higher levels of maternal anxiety were associated with shorter birth length. This reduction in birth length may be related to the impact of stress and anxiety on fetal development[22]. This finding indicates that maternal anxiety can affect certain aspects of fetal growth[23].The correlation analysis showed a strong and statistically significant negative relationship between maternal anxiety and APGAR score ($r = -0.661$, $p = 0.000$). Lower APGAR scores at birth are associated with immediate health conditions that may require medical attention. This correlation suggests that maternal anxiety can significantly impact the initial health of the baby, including the risk of asphyxia or hypoxic-ischemic events[24].

5. Conclusion

This finding underscores the importance of managing maternal anxiety to ensure better delivery outcomes and optimal infant health. Psychological conditions of the mother during pregnancy and delivery can influence the APGAR score of the baby. Mothers experiencing anxiety tend to have babies with lower APGAR scores compared to those without anxiety or depression. Anxiety affects the APGAR score through increase, this research used a cross-sectional design, limiting the ability to establish a causal relationship between maternal anxiety and neonatal outcomes. Longitudinal studies would be more suitable to assess the long-term effects of maternal anxiety on child development cortisol levels, which impact BDNF levels and disrupt neural development. This study has several limitations that should be acknowledged.

This study concludes that maternal anxiety impacts several aspects of birth outcomes, including BDNF levels, baby length, and APGAR scores, although it does not significantly affect baby weight. These findings highlight the importance of addressing maternal mental health during pregnancy and implementing interventions to reduce anxiety. Such efforts can contribute to improved birth outcomes and optimal infant health.

Compliance with ethical standards

Acknowledgments

The authors would like to sincerely thank all the participants and healthcare staff who contributed to this research.

Disclosure of conflict of interest

The authors declare that there is no significant competing financial, profecional, or personal interest that might have affected the performance or presentation of the work describe in this manuscript.

Statement of informed consent

Informed consent was obtained from all participants, ensuring they were fully informed about the study's purpose, procedures, and their rights, including confidentiality and the option to withdraw at any time.

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