Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2024, 14, 250-258
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

A Study on the Correlation between Salivary Cortisol Content and Anxiety and Depression in Pregnant and Postpartum Women

Qiuping Wang, Shujuan Luo, Jinrui Zhang, Yujuan Fan*

Department of Obstetrics, Shenzhen Guangming District People's Hospital, Shenzhen, China
Email: *yjfan530@163.com

How to cite this paper: Wang, Q.P., Luo, S.J., Zhang, J.R. and Fan, Y.J. (2024) A Study on the Correlation between Salivary Cortisol Content and Anxiety and Depression in Pregnant and Postpartum Women. *Open Journal of Obstetrics and Gynecology*, **14**, 250-258.
https://doi.org/10.4236/ojog.2024.142023

Received: January 22, 2024
Accepted: February 24, 2024
Published: February 27, 2024

Abstract

Objective: To analyze the correlation between salivary cortisol content and anxiety and depression in pregnant and postpartum women. **Method**: 300 pregnant and postpartum women who were admitted from January 2021 to December 2021 were selected as the research subjects. They were all tested with the Hamilton Anxiety Scale (HAMA) and the Edinburgh Postnatal Depression Scale (EPDS). 40 pregnant women with anxiety and depression were selected as the observation group, and 50 normal pregnant women were selected as the control group, adopting logistic regression analysis to investigate the correlation between salivary cortisol and postpartum anxiety and depression during pregnancy. **Result**: The salivary cortisol levels in the observation group were significantly higher than those in the control group before bedtime, after waking up the next day, 15 minutes after waking up, 30 minutes after waking up, 60 minutes after waking up, and 1 hour before lunch ($p < 0.05$). Maternal depression and anxiety were not related to age, weight, gestational age, negative events, or history of adverse pregnancy and childbirth ($p > 0.05$). Maternal depression and anxiety are closely related to salivary cortisol levels and educational background ($p < 0.05$). **Conclusion**: There is a close correlation between anxiety and depression and an increase in cortisol levels, suggesting that the salivary cortisol awakening response during pregnancy has a predictive effect on the occurrence of postpartum depression.

Keywords

Salivary Cortisol Content, Anxiety, Depression, Maternal

1. Introduction

Mental health issues, notably anxiety and depression, are prevalent during preg-

nancy. Over the past decade, there has been a noticeable increase in the incidence of anxiety and depression during the perinatal period in China. Meta-analyses indicate that 17.4% of women in mainland China suffer from anxiety disorders during pregnancy, and 19.7% experience depression [1] [2]. These figures could be higher depending on the methods of measurement and the population studied. Key risk factors include lower socioeconomic status, poor physical health, complications during pregnancy, and a lack of social support [1]. Anxiety and depression in pregnant women are associated with higher rates of cesarean sections and assisted deliveries, and in severe cases, can lead to postpartum hemorrhage and difficulties in postpartum lactation. The seriousness of these mental health concerns in pregnant women necessitates heightened attention. Salivary cortisol (SC) is a widely recognized biomarker used to assess stress responses and adrenal cortex function [3] [4]. It is a more sensitive and accurate indicator of physiological changes than serum cortisol, making it a valuable tool in both clinical diagnosis and research. As a primary hormone involved in stress responses, cortisol levels surge in response to psychological or physiological stressors. Measuring salivary cortisol helps in evaluating an individual's physical and psychological reaction to various stressors [5]. Pregnant women with poor mental health may show notable increases in stress and depression levels, potentially leading to alterations in salivary cortisol concentrations. Research exploring the link between salivary cortisol levels and pregnant women suffering from anxiety and depression is currently limited. This study, therefore, aims to investigate this relationship, providing crucial insights for obstetricians and nurses to enhance intervention strategies and improve pregnancy outcomes for expectant mothers. Further details are provided in the following text.

2. Materials and Methods

2.1. Participants Details

The study involved 300 pregnant women, admitted from January to December 2021, all meeting specified criteria. The inclusion criteria were as follows: 1) Informed consent obtained from both the participants and their family members; 2) A gestational period exceeding 9 weeks, with comprehensive and continuous tracking throughout the pregnancy and accurate documentation of childbirth and neonatal conditions; 3) Full cooperation from the expectant mothers or their family members, adhering to all aspects of the research as instructed by healthcare professionals; 4) Complete medical records for each expectant mother; 5) Clinical data consistent with perinatal depression and anxiety, characterized by: a) meeting Perinatal Somatoform Disorder (PSD) standards, exhibiting one or more groups among 12 symptoms: insomnia-related issues, frequent urination, nausea, vomiting, constipation, stomach bloating, chest tightness, heart palpitations, dry mouth, and muscle soreness; b) scoring between 7 to 13 on the Hamilton Anxiety Rating Scale (HAMA); c) Heart Rate Variability (HRV) reports indicating autonomic nervous system (VNS) imbalance. The exclusion

criteria included: 1) Expectant mothers with serious liver or kidney dysfunctions; 2) Those with psychiatric or structural diseases; 3) Women whose family members refused to sign the informed consent for depression during pregnancy. Both the Hamilton Anxiety Scale and the Edinburgh Postnatal Depression Scale were administered to the participants. 40 women identified with anxiety and depression formed the observation group, while 50 women without these conditions constituted the control group. Logistic regression analysis was applied to investigate the relationship between salivary cortisol levels and the incidence of antenatal and postnatal anxiety and depression. No significant statistical difference was observed in the general data between the groups ($p > 0.05$). Refer to Table 1 for detailed data. The study received approval from our hospital's Medical Ethics Committee.

2.2. Methods

1) Physiological and Genetic Indicators: Physiological parameters such as respiratory rate, heart rate, blood pressure changes, and body weight during each neuropsychological assessment of pregnancy; genetic information data obtained through saliva collection from mothers.

2) Collection of Salivary Cortisol: When collecting saliva samples related to the Cortisol Awakening Response (CAR), it is essential to strictly follow the "saliva collection time points" requirement. Specifically, the subject is to hold a saliva collection tube's cotton swab under the tongue for about 5 minutes until the swab is fully saturated, then return the swab to the tube. Collection is carried out on the third day postpartum, at six time points: before going to sleep, upon waking without getting out of bed, 15 minutes after waking, 30 minutes after waking, 60 minutes after waking, and at 11 AM.

3) Salivary Cortisol Test: The Roche electrochemiluminescence method (Elecsys Cortisol II, Roche Diagnostics, Indianapolis, IN, Germany) is used for

Table 1. Comparative analysis of general data between groups [n, (%)] ($\overline{x} \pm s$).

Category	Control Group (n = 50)	Observation Group (n = 40)	X^2/t	p
Age (years)	27.36 ± 1.04	26.65 ± 1.02	1.024	0.109
Weight (kg)	56.77 ± 3.68	55.89 ± 3.59	1.335	0.111
Gestational Weeks	19.35 ± 4.39	19.40 ± 4.42	0.978	0.143
Education Level				
Junior College and below	29 (58)	26(65)	0.458	0.498
Bachelor's Degree and above	21 (42)	14(35)		
Negative Events				
Yes	9 (18)	7(17.50)	0.004	0.951
No	41(82)	33(82.50)		
Adverse Obstetric History				
Yes	7(14)	8(20)	0.576	0.448
No	43(86)	32(80)		

the test. The principle is based on a competitive assay, with a total testing time of 18 minutes. Salivary cortisol levels are measured on the third day postpartum. First incubation: 10 uL of the sample is incubated with biotin-labeled cortisol-specific antibodies and ruthenium complex-labeled cortisol derivatives. The binding sites of the labeled antibodies are partially occupied by the analyte in the sample and partially by the ruthenium-labeled haptens. During the second incubation, after adding streptavidin-coated magnetic particles, this complex is effectively bound through the interaction between biotin and streptavidin. The reaction solution is then aspirated into the measurement cell, where electromagnetic action attracts the magnetic particles to the electrode surface, and substances not bound to the magnetic particles are removed by ProCell. A certain voltage is applied to the electrode to induce chemiluminescence in the complex, and the intensity of the luminescence is measured by a photomultiplier. The main curve is generated through calibration of the detector and the barcode of the reagent strip.

4) Immediately after collecting the saliva samples, participants are required to complete relevant psychological assessment questionnaires, namely the Hamilton Anxiety Rating Scale and the Edinburgh Postnatal Depression Scale.

Hamilton Anxiety Rating Scale: This scale employs a 5-point scoring system, ranging from 0 to 4, with the following designations: 0 points for no symptoms, 1 for mild, 2 for moderate, 3 for severe, and 4 for very severe. The scale encompasses various aspects: 1) Anxiety Mood: Worrying, fearing the worst, and being easily upset. 2) Tension: Feelings of tension, fatigue, inability to relax, emotional sensitivity, tendency to cry, tremble, and feel unsettled. 3) Fears: Phobias related to the dark, strangers, solitude, animals, travel, and crowded places. 4) Insomnia: Difficulty in falling asleep, frequent waking, light sleeping, nightmares, feeling tired upon waking. 5) Cognitive Function: Manifested as memory and attention deficits, with poor concentration and memory. 6) Depressive Mood: Loss of interest, reduced pleasure in hobbies, melancholy, early waking, day-time severity. 7) Somatic Anxiety: Includes muscle pain, stiffness, frequent muscle spasms, limb twitching, teeth chattering, and shaky voice. 8) Sensory Symptoms: Blurred vision, alternating sensations of hot and cold, general weakness, and body tingles. 9) General Symptoms: Nervousness, inability to relax, restlessness, finger biting, clenched fists, fiddling with objects, facial twitching, constant foot tapping, trembling hands, frowning, rigid expressions, high muscle tension, sigh-like breathing, and pallor. 10) Physiological Symptoms: Swallowing difficulties, frequent hiccups, rapid heart rate at rest, accelerated breathing (over 20 times/minute), heightened tendon reflexes, tremors, pupil dilation, eyelid twitching, excessive sweating, and bulging eyes.

Edinburgh Postnatal Depression Scale: Consists of 10 items, each with four answer choices indicating different levels of severity (0 - 3 points). Each item scores between 0 to 3, totalling 0 to 30 points overall. Higher scores denote more significant symptoms of postnatal depression. The items include: 1) Recently

feeling worried or scared. 2) Feeling more downhearted than usual. 3) Constantly feeling very fatigued. 4) Being unhappy and easily falling into a state of depression. 5) Loss of appetite. 6) Deterioration in sleep quality. 7) Feeling hopeless about the future. 8) Regularly feeling unhappy. 9) Often crying without any obvious reason. 10) Feeling overwhelmed and struggling with the demands of motherhood.

2.3. Key Observation Metrics

The study includes an analysis of general data across both groups, focusing on variables such as age, body weight, gestational week, educational background, negative life events, and any history of adverse pregnancy outcomes.

The analysis also encompasses the measurement of salivary cortisol levels in both groups, specifically at times like before sleep, upon waking up the next day, and 15, 30, and 60 minutes after rising, as well as an hour before lunch.

A logistic regression analysis was conducted to explore the relationship between salivary cortisol levels and the presence of depression and anxiety in the subjects.

2.4. Statistical Approach

Data analysis was performed using SPSS 22.0 software. For continuous variables that adhered to a normal distribution (such as age, weight, weeks of pregnancy, and salivary cortisol levels at the specified times for both groups), the mean and standard deviation (±s) were used. Group comparisons were conducted using the t-test for these variables. Categorical data (such as education level, negative life events, and history of adverse pregnancy outcomes) were expressed in percentages (%) and compared using the chi-square (x^2) test. Logistic regression was applied to assess the correlation between depressive and anxious symptoms in women and their salivary cortisol levels. A significance level (alpha) was set at 0.05, with p-values less than 0.05 indicating statistical significance.

3. Results

3.1. Comparative Analysis of General Data between Groups

The analysis revealed that there were no statistically significant differences between the control group and the observation group regarding age, body weight, gestational weeks, education level, incidence of negative events, and history of adverse pregnancy outcomes ($p > 0.05$). The details are presented in Table 1.

3.2. Comparative Analysis of Salivary Cortisol Concentrations

The findings indicate that the cortisol concentrations in the saliva of the observation group were notably higher at various times: before bedtime, upon waking up the next day, 15, 30, and 60 minutes after rising, and an hour before lunch, as compared to the control group ($p < 0.05$). The detailed results are presented in Table 2.

Table 2. Comparative analysis of salivary cortisol concentrations ($\overline{x} \pm s$) (ug·L^{-1}).

Group	Number of Classes	Before Sleep	After Waking Up	15 Min After Rising	30 Min After Rising	60 Min After Rising	1 Hour Before Lunch
Observation Group	40	45.64 ± 8.20	57.75 ± 7.1	57.75 ± 12.08	65.80 ± 12.09	68.64 ± 11.89	60.00 ± 12.30
Control Group	50	4.69 ± 0.31	5.44 ± 0.39	7.63 ± 0.57	7.80 ± 0.63	6.50 ± 0.39	6.48 ± 0.63
t	-	27.709	32.164	22.147	20.045	28.463	32.111
P	-	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

3.3. Logistic Regression Analysis on the Correlation between Depression, Anxiety in Childbearing Women, and Salivary Cortisol Levels

The analysis indicates that there is no significant correlation between depression and anxiety in childbearing women and factors such as age, weight, weeks of pregnancy, negative events, and history of adverse obstetric outcomes ($p > 0.05$). However, there is a significant association between the levels of depression and anxiety in these women and both their salivary cortisol levels and educational levels ($p < 0.05$).

Refer to Table 3 for detailed statistics.

4. Discussion and Conclusion

Depression and anxiety in expectant mothers arise from various causes and pose significant risks. The clinical presentation of these conditions in pregnant women typically includes: 1) Abnormal emotional responses, characterized by a lack of concentration and increased feelings of anxiety, irritability, and susceptibility to agitation. 2) A marked loss of interest, where affected pregnant women may display a consistent disinterest in all activities for around a week. 3) Tendency towards introversion, with minimal communication and extended periods of silence that can last for more than three days. 4) Secretive reliance on alcohol or medication. 5) Emergence of suicidal thoughts and tendencies. These psychological issues not only impact the pregnant women themselves but also pose significant risks to the fetus. The mental health of a pregnant woman is directly linked to the childbirth process and the fetus's health, potentially leading to prolonged labor, neonatal asphyxia, and increased risk of perinatal complications after birth. Depression and anxiety can also trigger an increase in adrenaline secretion in expectant mothers, resulting in metabolic acidosis and fetal hypoxia in utero. Anxiety might also disrupt the autonomic nervous system, weakening uterine contractions during labor and causing difficult deliveries. The negative emotional states such as depression and anxiety can also lead to inadequate rest and nutrition for expectant mothers, contributing to obstructed labor. Therefore, it is imperative to pay close attention to depression and anxiety in pregnant women, actively explore the contributing factors, and implement effective strategies to improve their psychological well-being and ensure the safety of childbirth.

Table 3. Logistic regression analysis on depression, anxiety in childbearing women, and salivary cortisol levels.

Variable	B	SE	OR	95%CI	p
Salivary Cortisol Level	−2.563	1.277	0.035	0.003 - 0.868	0.007
Age	0.746	0.455	0.967	0.955 - 1.375	0.251
Weight	−7.453	0.855	1.775	1.020 - 1.674	0.946
Gestational Weeks	0.196	0.784	0.175	0.047 - 0.574	0.753
Education Level	−2.097	0.096	0.116	0.020 - 0.488	0.008
Negative Events	0.869	0.574	2.896	0.987 - 7.099	0.832
Adverse Obstetric History	0.906	0.788	2.885	0.900 - 6.906	0.108

This study examines the relationship between salivary cortisol levels and anxiety and depression in pregnant women. Findings indicate that the cortisol levels in the saliva of pregnant women experiencing depression and anxiety were considerably higher at several key times, including before sleeping, upon awakening, and at various intervals in the morning, in comparison to their counterparts in a normal state. Cortisol, a stress hormone produced by the adrenal glands, plays a pivotal role in health, with imbalances leading to conditions like Cushing's syndrome or Addison's disease [6]. Accurate measurement of cortisol levels is crucial for the diagnosis and treatment of these conditions. Recently, the trend in medical practice has shifted towards measuring cortisol levels in saliva rather than blood or urine [7].

Cortisol, pervasive throughout the body but produced by the adrenal glands, is secreted in greater amounts under stress [8]. Factors such as stress, emotions, and even early morning shift work can influence cortisol production. Typically, cortisol levels decrease during sleep and rise upon waking. The hypothalamic-pituitary-adrenal (HPA) axis, which reflects the neuroendocrine system's response to stress, regulates cortisol, a key component of adrenal cortex glucocorticoid secretion. This axis's function, altering according to diurnal rhythms, directly reflects the overall state of the HPA axis [9] [10].

Clinical significance of salivary cortisol testing includes its ability to assess stress responses, adrenal cortex function, and assist in the diagnosis and treatment of acute diseases such as Cushing's syndrome, depression, and anxiety [11] [12] [13]. This method of testing is advantageous for its simplicity, speed, and stability compared to blood samples, making it valuable for research and diagnosis.

The study also reveals that cortisol secretion, influenced by psychological stress and emotional fluctuations, is heightened in pregnant women experiencing continuous stress due to anxiety and depression. Furthermore, the study found no correlation between maternal depression and anxiety with factors like age, weight, gestational weeks, negative events, and adverse obstetric history. However, a significant relationship was noted between these emotional states

and cortisol levels, as well as educational level. The findings suggest that the more limited a pregnant woman's understanding of her physical and psychological state, the more severe her anxiety and depression. This relationship is potentially linked to the activation of the HPA axis in response to negative emotions, leading to increased cortisol production.

However, this study has limitations, including a small sample size and a limited range of observational indicators. Future research should aim to expand the sample size and broaden the scope of study to further investigate the correlation between salivary cortisol levels and anxiety and depression in pregnant women.

In conclusion, this study highlights a significant association between increased cortisol levels and states of anxiety and depression, indicating that the cortisol awakening response in salivary samples during pregnancy may serve as a predictive marker for the development of postpartum depression.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Yang, L., Sun, J., Nan, Y., *et al.* (2023) Prevalence of Perinatal Anxiety and Its Determinants in Mainland China: A Systematic Review and Meta-Analysis. *Journal of Affective Disorders*, **323**, 193-203. https://doi.org/10.1016/j.jad.2022.11.075

[2] Nisar, A., Yin, J., Waqas, A., *et al.* (2020) Prevalence of Perinatal Depression and Its Determinants in Mainland China: A Systematic Review and Meta-Analysis. *Journal of Affective Disorders*, **277**, 1022-1037. https://doi.org/10.1016/j.jad.2020.07.046

[3] Guo, J. and Liu, L. (2021) Relationship between Iron Metabolism Indicators and Cortisol, Adrenaline, Noradrenaline, and Insulin Resistance in Patients with Gestational Diabetes. *Medical Theory and Practice*, **34**, 2505-2507.

[4] Chen, Q., Yu, N., Ge, J., *et al.* (2021) Analysis of the Correlation between Blood Cortisol Levels and Anxiety, Depression, Lung Function, and Asthma Control in Asthma Patients. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, **31**, 425-427.

[5] Zhang, Q., Chen, K., Liu, C., *et al.* (2021) Changes in Blood Glucose and Cortisol Levels before and after Childbirth and Their Interrelationship. *Chinese Journal of Obstetrics and Gynecology Clinics*, **22**, 188-189.

[6] Chen, F., Qi, F., Zhang, H., *et al.* (2021) Effect of Systematic Nursing Combined with Psychological Care on Depression, Anxiety, Cor, IL-2 Levels in Patients with Cervical Cancer during Perioperative Period. *Journal of Changchun University of Chinese Medicine*, **37**, 160-162.

[7] Liao, Y., Yang, S., Chen, P., *et al.* (2020) Investigation of Anxiety and Depression Status in Patients with Herpes Zoster Neuralgia and Analysis of the Correlation with Cortisol Hormone Level Changes. *Chinese Journal of Pain Medicine*, **26**, 137-140.

[8] Tong, X., Pu, L., Lv, C., *et al.* (2022) Clinical Value of Salivary Cortisol and Secretory Immunoglobulin A levels in Cognitive Function in Elderly Patients with Burning

Mouth Syndrome. *Chinese Medical Herald*, **19**, 98-101.

[9] Heng, W., Wang, X. and Zhu, Y. (2022) The Effect of Combined Psychological Therapy on Salivary Cortisol Levels in Patients with Burning Mouth Syndrome. *Chinese Clinical Research*, **35**, 347-350.

[10] Zhan, W., Luo, L., Wang, Q., *et al.* (2023) Study on the Correlation between Cortisol Levels and Traditional Chinese Medicine Syndromes in Adolescent Patients with Depressive Disorders. *World Science and Technology—Modernization of Traditional Chinese Medicine*, **25**, 1475-1480.

[11] Chen, B., Xu, X., Lyu, H., *et al.* (2022) Study on the Association between FK506 Binding Protein 5 Gene rs3800373 Polymorphism and Reduction in Cortisol Levels after Antidepressant Treatment. *Chinese Journal of Clinical Pharmacology*, **38**, 2807-2810.

[12] Han, Y., Yuan, J. and Wei, X. (2022) The Correlation between Cortisol Levels and Cognitive Function in Patients with Depression with Somatic Symptoms. *Neurological Diseases and Mental Health*, **22**, 883-887.

[13] Fu, B., Deng, Y., Feng, S., *et al.* (2018) Study on the Correlation between Depression and Salivary Cortisol Concentration in Pregnant Women with Threatened Preterm Labor. *Guangzhou Medicine*, **49**, 44-47.