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ORIGINAL ARTICLE

The association maternal cortisol levels and anxiety during labor with neonatal outcome: a cross-sectional

Cortisol, anxiety and neonatal outcome

Elizabet Catherine **Jusuf** [1,*], Michael Grant **Husain** [2], Marwa **Safa** [1]

[1] Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[2] Teluk Bintuni Regional Public Hospital, West Papua, Indonesia.

***Corresponding Author:** Elizabet Catherine **Jusuf**, M.D., M.Sc, Departement of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University, Perintis Kemerdekaan street KM.10, Makassar, South Sulawesi, Indonesia, 90242.

Email: ecj88@med.unhas.ac.id.

ORCID: 0000-0001-5800-8732.

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Abstract

Objective. This study aims to investigate the association of maternal cortisol levels and anxiety during labor with neonatal outcome in primigravida women.

Materials and methods. A total of 147 pairs of primigravida with their neonates included in the study. The study was conducted from January to May 2023 using cross-sectional design. Labor anxiety were assessed using the Labor Anxiety Questionnaire Kwestionariusz Lęku Porodowego-II (KLP-II). The maternal cortisol was measured using the ELISA at active phase of labor. Data were analyzed using the Chi-Square test and Mann-whitney test.

Results. The mean age and birth weight of 24.52± 4.21 years and 2992± 377.68 gr, respectively. The median serum cortisol concentration was 58.35 ng/ml with an interquartile range of 22.19 – 70.98 ng/ml. There was no association between maternal cortisol levels and anxiety during labor with neonatal outcome (antropometry and APGAR score) (P> 0.05). Labor duration also was not influenced by cortisol levels and anxiety during labor, instead of by birthweight (P< 0.05).

Conclusions. Both maternal cortisol levels and anxiety during primigravida labor was not associated with neonatal outcome. Further research is needed with a larger sample size to confirm whether acute stress anxiety can influence the neonatal outcome.

Keywords

Maternal cortisol; anxiety; labor; neonatal outcome.

Introduction

Childbirth is a stressful event that can trigger anxiety, fear of birth and even tokophobia [1–3]. Some of the suggested reasons contributing to this phenomenon include a lack of trust in the attending obstetrical staff during delivery, incapability of giving birth, fear of suffering injury, fear of the death of themselves or their infant, and intolerance of physical pain [4]. Anxiety and fear of childbirth are more common in primigravida who have never experienced childbirth before and lack of knowledge [5,6]. These issues pose a significant problem for women as they can lead to mothers avoiding pregnancy, causing harm for both the mother and the fetus, and increasing the demand for cesarean sections [7]. Reck et al found that fear of giving birth was the strongest predictor of labor duration [8], and in general it increases the risk of dystocia in pregnant women [2].

Anxiety and fear of birth are associated with an increase in cortisol level [9,10]. Maternal cortisol levels are controlled by the hypothalamic-pituitary-adrenal (HPA) axis. When the body perceives physical or psychological stress, it triggers a stress response that activates the HPA axis. This activation process begins with the release of corticotropin-releasing hormone (CRH) from the hypothalamus, which then stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH). Ultimately, this leads to the adrenal cortex releasing cortisol [11]. Previous studies have shown that cortisol affect neonatal outcomes including gestational age, birth weight, and neonatal outcomes [10,12–18]. Understanding the relationship between maternal anxiety and neonatal outcomes is essential for healthcare providers to provide comprehensive care during pregnancy. By recognizing the impact of maternal anxiety, healthcare professionals can implement interventions to support expectant mothers and mitigate any potential negative consequences on the newborn. Even though relationships between maternal anxiety and cortisol level have been found, most of the study was measured the cortisol level in pregnancy not in the labor. Therefore, this study was conducted to analyze association of maternal anxiety and cortisol levels during primigravida labor with neonatal outcome.

Materials and methods

This cross-sectional was conducted at Khadijah Mother and Child Hospital in Makassar, Indonesia, in January-May 2023. The study was approved by Hasanuddin University Clinical Research Ethics Committee with the protocol number 813/UN4.6.4.5.31/PP36/2022 and informed consent was obtained from all participants

Data related to subject characteristics of respondents and study were collected using a questionnaire through direct interviews. Data was taken from pregnant woman during the first stage of labor at a cervical dilatation of 4–6 cm. The inclusion criteria were single pregnancy,

vaginal birth, gestational age between 37 and 42 weeks, not taking medications that interfere with cortisol levels, and no chronic diseases or hormonal disorders such as Cushing Syndrome, Cushing disease, and Addison's disease. Exclusion criteria were fetal with congenital anomalies, malpresentation, or premature rupture of membranes.

Labor anxiety were assessed using the Labor Anxiety Questionnaire Kwestionariusz Lęku Porodowego-II (KLP-II), consisting of 9 Likert scale questions with point values ranging from 0 to 3. Scores could vary from 0 to 27 points, with different ranges indicating varying levels of anxiety. Cortisol levels were measured via the ELISA method at the Clinical Pathology Laboratory of Hasanuddin University Hospital, with samples collected in EDTA tubes.

Statistical analysis was performed using SPSS 24.0 for Windows software, with KLP-II scores and cortisol levels presented as mean ± standard deviation. Baseline characteristics were reported as frequencies and percentages. Differences in KLP-II scores and cortisol levels among groups were analyzed using the Mann-Whitney U test for non-normally distributed data, while differences in baseline characteristics were assessed using the chi-square test. Statistical significance was set at a p-value of <0.05.

Results

A total of 147 primigravida women and their neonates were included in the study, with a mean age and a mean birth weight of 24.52± 4.21 years and 2992± 377.68 g, respectively. Cortisol was not associated with KLP-II score (r = 0.03, p-value = 0.715) (Fig. 1) The median serum cortisol concentration was 58.35 nmol/L with an interquartile range of 22.19 – 70.98 ng/ml (Fig. 2). The cortisol concentration did not differ between low birth weight (< 2500g) (57.62 ± 5.02 nmol/L) and normal birth weight (≥ 2500gr) (56.80±9.18 nmol/L) (P = 0.925).

Based on the median serum concentration, patients were categorized into low (<58.35 ng/ml) or high (≥58.35 ng/ml) cortisol groups. Maternal and perinatal characteristics not associated with maternal cortisol level (Table 1). Neonatal outcomes and duration of labor are also not associated with cortisol levels. In addition, anxiety (KLP score) is not associated with neonatal outcomes or the duration of labor (Table 2).

Duration of labor (Stage 1 and Stage 2) only influenced by birth wieght (P = 0.01 and P = 0.045, respectively). Birth weight was influenced by birth length (P < 0.001), and APGAR at 1 minute was influenced by the frequency of antenatal care (P = 0.041).

Discussion

This study provided the first insights about association of maternal cortisol levels and anxiety during labor with neonatal outcome. Anxiety during labor can have significant implications for both the mother and the newborn. Maternal anxiety can impact the health and well-being of the fetus and subsequently the newborn. Maternal anxiety is a complex issue that can lead to adverse effects on pregnancy and childbirth. It is crucial to address maternal anxiety not only for the mother's mental health but also for the optimal development and health of the newborn [19].

Based on median of cortisol, there is no significant demographic differences in low and high cortisol, so the potential impact of confounding factors was reduced [20,21]. Gestational age

and gravidity was controlled on inclusion sampling. In the study, there was no association between anxiety and neonatal anthropometry both birth weight and birth length as found in the study of Gregor et al [22]. The meta-analysis study showed that chronic stress is associated with a statistically significant risk of low birth weight (OR = 1.50, 95% CI = [1.13; 1.99], $p \leq 0.02$) which was supported by five of nine studies. However, this meta-analysis did not exclusively assess anxiety in pregnant women, but used several questionnaires that also assessed levels of depression and stress [23]. Previous study also found that higher scores on the Perceived Stress Survey (PSS) throughout pregnancy were not associated with alterations in neonatal anthropometry including birth weight, length, head and abdominal circumferences, even after accounting for important confounders [24]. Large data cohort studies showed no association was found for maternal prenatal anxiety with birth weight after multiple covariates and family environment were controlled. However, there was an association between prenatal maternal anxiety at 30th week only with gestational age, suggesting a timing effect for maternal anxiety in the third trimester [25].

Various theories exist regarding the impact of maternal anxiety on fetal growth. One proposed mechanism involves alterations in maternal hypothalamic-pituitary-adrenal (HPA) axis activity. Specifically, it is postulated that maternal anxiety during pregnancy may elevate the production of stress hormones like cortisol and catecholamines. Research using animal models has demonstrated that these stress hormones can affect uterine blood flow and immune system functioning, potentially leading to a higher likelihood of shortened gestational periods and reduced fetal growth [26,27]. Another possible explanation for this association could be the increased susceptibility to infections resulting from stress. Studies have indicated that heightened stress levels may compromise immune function, thereby raising the risk of infections during pregnancy that could contribute to shortened gestation [25].

Cortisol, which is considered a stress hormone, also did not affect neonatal anthropometry. Previous research has conflicting views on the impact of cortisol on fetal weight. Some studies suggest that high levels of cortisol in pregnant women may increase the risk of low birth weight in newborns [15,28–35], while other studies have reported contradictory findings [36–38]. During pregnancy, a woman's baseline cortisol secretion increases significantly, up to four times higher than non-pregnancy levels, with the peak levels typically observed in the third trimester in anticipation of childbirth[39]. This natural elevation in cortisol is essential to support fetal growth and development, yet external stressors, both physiological and psychological, can lead to abrupt short-term fluctuations in cortisol levels [40]. While in the uterus, the placental enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) keeps the fetus blocked from maternal cortisol by by converting it into an inactive form. Despite this protective mechanism, a small fraction of maternal cortisol is able to cross the placental barrier and reach the fetus, which has been associated with adverse effects on fetal development such as reduced birth weight and shortened gestation period due to compromised blood flow essential for oxygen and nutrient delivery [38]. The lack of association between anxiety, cortisol levels, and neonatal anthropometry observed in this study could be attributed to the acute nature of anxiety experienced during delivery. It is suggested that chronic anxiety and prolonged exposure to cortisol are necessary to impact neonatal outcomes.

Duration of labor (stage 1 and stage 2) was not influenced by anxiety and maternal cortisol in this study. Studies in pregnant women < 20 weeks showed no relationship between anxiety and the prolongation of the stage 1 [41]. While another studies involving women at less than 20

weeks and 34 weeks of gestation did not find a significant correlation between anxiety and labor duration [42]. A study by Adams et al. involving 2206 pregnant women at 32 weeks of gestation reported that women experiencing fear of childbirth had a longer duration of labor compared to those without such fears [43]. Studies in women with Covid-19 infection who are known to be at risk for anxiety also showed no difference in the duration of delivery[44–46].

Various techniques have been developed to alleviate stress during childbirth, such as the Lamaze relaxation method, hydrotherapy, emotional support, and the inclusion of family members or partners in the delivery process [47]. WHO recommends that pregnant women should be accompanied by someone they trust and feel safe with, such as friends, spouses, midwives, or family[48]. A study involving 114 pregnant women indicated that having family members (such as mothers, sisters, friends, or husbands) present and providing support during labor can help in managing pain, instill a sense of security, and enhance satisfaction among pregnant women. This support system may also mitigate the challenges of childbirth, improve both mental and physical well-being, and boost maternal contentment with the birthing experience.[49]

This study shows the importance of appropriate timing of cortisol sampling to predict maternal and neonatal outcomes. Anxiety is associated with elevated cortisol but it seems that cortisol is not an acute marker because of the blunted cortisol response in pregnant women. In addition, suppression of HPA-axis reactivity during pregnancy makes non-severe stressors not evoke cortisol so in educating a doctor can explain how the long-term impact of cortisol is[50].

Limitation

The variation observed may due to disparities in gestational age, the types of questionnaires utilized, and the methodologies employed for sampling. This investigation focused on evaluating anxiety levels during the active phase of labor, where labor pain can increase patient anxiety. Furthermore, the subjective nature of anxiety poses challenges in its precise measurement and may be subject to cultural influences, thereby limiting generalizability across diverse regions. Consequently, it is imperative to approach this issue from an alternative standpoint. Moreover, relying solely on clinical studies to examine the relationship between anxiety, and duration of labor may prove inadequate, as such studies predominantly rely on interviews with expectant mothers, which are susceptible to various biases including recall bias, selection bias, nonconformist bias, and active co-operator bias. Additionally, the circadian rhythm can impact blood cortisol levels, serving as a potential confounding variable.

Conclusions

The correlation between maternal anxiety and neonatal outcomes underscores the need for a holistic approach to maternal healthcare during pregnancy. But in study, maternal anxiety and cortisol levels during primigravida labor was not associated with neonatal outcome and labor duration. Maternal cortisol level and anxiety was not a reliable indicator that was predictive of adverse neonatal outcomes.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

E.C.J.: Conceptualization, data curation, investigation, formal analysis, validation, visualization. M.G.H.: Formal analysis, validation, visualization. M.S.: Formal analysis, validation, visualization

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Study registration

N/A.

Disclosure of Interest

None of the authors have any conflict of interests related to this work.

Ethical approval

This study was approved by the Ethics Committee of Hasanuddin University of Medical Sciences (No. 813/UN4.6.4.5.31/PP36/2022).

Informed Consent

Informed consent was obtained from all participants.

Data Sharing

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Abdollahi S, Faramarzi M, Delavar MA, Bakouei F, Chehrazi M, Gholinia H. Effect of Psychotherapy on Reduction of Fear of Childbirth and Pregnancy Stress: A Randomized Controlled Trial. Front Psychol. 2020 May 26;11:787. doi: 10.3389/fpsyg.2020.00787

2. Hishikawa K, Kusaka T, Fukuda T, Kohata Y, Inoue H. Anxiety or nervousness disturbs the progress of birth based on human behavioral evolutionary biology. J Perinat Educ. 2019; doi: 10.1891/1058-1243.28.4.218

3. Hofberg K, Ward M. Tokophobia Tokophobia: A Profound Dread and Avoidance of Childbirth (When Pathological Fear Effects the Consultation). In: Cockburn J, Pawson ME, editors. Psychological Challenges in Obstetrics and Gynecology [Internet]. London: Springer London; 2007 [cited 2024 Feb 19]. p. 165–72. doi: 10.1007/978-1-84628-808-1_16

4. Sjögren B. Reasons for anxiety about childbirth in 100 pregnant women. J Psychosom Obstet Gynecol. 1997 Jan;18(4):266–72. doi: 10.3109/01674829709080698

5. Hassanzadeh R, Abbas-Alizadeh F, Meedya S, Mohammad-Alizadeh-Charandabi S, Mirghafourvand M. Fear of childbirth, anxiety and depression in three groups of primiparous

pregnant women not attending, irregularly attending and regularly attending childbirth preparation classes. BMC Womens Health. 2020; doi: 10.1186/S12905-020-01048-9

6. Hendrix YM, Baas M, Vanhommerig J, Jongh A de, Pampus MV van. Fear of childbirth in nulliparous women. Front Psychol. 2022; doi: 10.3389/FPSYG.2022.923819

7. Aksoy M, Aksoy AN, Dostbil A, Celik MG, Ince I. The Relationship between Fear of Childbirth and Women's Knowledge about Painless Childbirth. Obstet Gynecol Int. 2014;2014:1–7. doi: 10.1155/2014/274303

8. Reck C, Zimmer K, Dubber S, Zipser B, Schlehe B, Gawlik S. The influence of general anxiety and childbirth-specific anxiety on birth outcome. Arch Womens Ment Health. 2013 Oct;16(5):363–9. doi: 10.1007/s00737-013-0344-0

9. Kane HS, Dunkel Schetter C, Glynn LM, Hobel CJ, Sandman CA. Pregnancy anxiety and prenatal cortisol trajectories. Biol Psychol. 2014 Jul;100:13–9. doi: 10.1016/j.biopsycho.2014.04.003

10. Fan F, Zou Y, Zhang Y, Ma X, Zhang J, Liu C, et al. The relationship between maternal anxiety and cortisol during pregnancy and birth weight of chinese neonates. BMC Pregnancy Childbirth. 2018 Dec;18(1):265. doi: 10.1186/s12884-018-1798-x

11. Field T, Diego M. Cortisol: The culprit prenatal stress variable. Int J Neurosci. 2008; doi: 10.1080/00207450701820944

12. Shriyan P, Sudhir PM, Schayck OV van, Babu G. Association of high cortisol levels in pregnancy and altered fetal growth. Results from the MAASTHI, a prospective cohort study, Bengaluru. Lancet Reg Health - Southeast Asia. 2023; doi: 10.1016/J.LANSEA.2023.100196

13. Zijlmans MAC, Riksen-Walraven JM, Weerth C de. Associations between maternal prenatal cortisol concentrations and child outcomes: A systematic review. Neurosci Biobehav Rev. 2015; doi: 10.1016/J.NEUBIOREV.2015.02.015

14. Heuvel MI van den, Assen MALM van, Glover V, Claes S, Bergh BV den. Associations between maternal psychological distress and salivary cortisol during pregnancy: A mixed-models approach. Psychoneuroendocrinology. 2018; doi: 10.1016/J.PSYNEUEN.2018.06.005

15. Bolten M, Wurmser H, Buske-Kirschbaum A, Papoušek M, Pirke K-M, Hellhammer DH. Cortisol levels in pregnancy as a psychobiological predictor for birth weight. 2011; doi: 10.1007/S00737-010-0183-1

16. Nath A, Murthy GVS, Babu GR, Renzo GCD. Effect of prenatal exposure to maternal cortisol and psychological distress on infant development in Bengaluru, southern India: a prospective cohort study. BMC Psychiatry. 2017; doi: 10.1186/S12888-017-1424-X

17. Field T, Hernandez-Reif M, Diego M, Figueiredo B, Schanberg SM, Kuhn CM. Prenatal cortisol, prematurity and low birthweight. Infant Behav Dev. 2006; doi: 10.1016/J.INFBEH.2005.12.010

18. Cherak SJ, Giesbrecht GF, Metcalfe A, Ronksley PE, Malebranche M. The effect of gestational period on the association between maternal prenatal salivary cortisol and birth

weight: A systematic review and meta-analysis. Psychoneuroendocrinology. 2018; doi: 10.1016/J.PSYNEUEN.2018.04.023

19. Azizi S. Correlation of maternal anxiety and some of neonatal outcomes. Int J Pregnancy Child Birth [Internet]. 2018 Jul 12 [cited 2024 Mar 31];4(4). doi: 10.15406/ipcb.2018.04.00107

20. Manyeh AK, Kukula V, Odonkor G, Ekey RA, Adjei A, Narh-Bana S, et al. Socioeconomic and demographic determinants of birth weight in southern rural Ghana: evidence from Dodowa Health and Demographic Surveillance System. BMC Pregnancy Childbirth. 2016 Dec;16(1):160. doi: 10.1186/s12884-016-0956-2

21. Jeena PM, Asharam K, Mitku AA, Naidoo P, Naidoo RN. Maternal demographic and antenatal factors, low birth weight and preterm birth: findings from the mother and child in the environment (MACE) birth cohort, Durban, South Africa. BMC Pregnancy Childbirth. 2020 Dec;20(1):628. doi: 10.1186/s12884-020-03328-6

22. Gregor K, Banaś E, Malec M, Ilska M, Jagielska A, Rak K, et al. Labor anxiety – risk factors and impact on the course of labor, puerperium and neonatal condition.

23. Matsas A, Panopoulou P, Antoniou N, Bargiota A, Gryparis A, Vrachnis N, et al. Chronic Stress in Pregnancy Is Associated with Low Birth Weight: A Meta-Analysis. J Clin Med. 2023 Dec 14;12(24):7686. doi: 10.3390/jcm12247686

24. Wing DA, Ortega-Villa AM, Grobman WA, Hediger ML, Grewal J, Pugh SJ, et al. Maternal stress and neonatal anthropometry: the NICHD Fetal Growth Studies. Am J Obstet Gynecol. 2017 Jul;217(1):82.e1-82.e7. doi: 10.1016/j.ajog.2017.02.039 PMID: 28263750

25. Bekkhus M, Lee Y, Brandlistuen RE, Samuelsen SO, Magnus P. Maternal Anxiety and Infants Birthweight and Length of Gestation. A sibling design. BMC Psychiatry. 2021 Dec;21(1):609. doi: 10.1186/s12888-021-03620-5

26. Coussons-Read ME, Lobel M, Carey JC, Kreither MO, D'Anna K, Argys L, et al. The occurrence of preterm delivery is linked to pregnancy-specific distress and elevated inflammatory markers across gestation. Brain Behav Immun. 2012 May;26(4):650–9. doi: 10.1016/j.bbi.2012.02.009

27. Dunkel Schetter C, Tanner L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. Curr Opin Psychiatry. 2012 Mar;25(2):141–8. doi: 10.1097/YCO.0b013e3283503680

28. Spicer J, Werner E, Zhao Y, Choi CW, Lopez-Pintado S, Feng T, et al. Ambulatory assessments of psychological and peripheral stress-markers predict birth outcomes in teen pregnancy. J Psychosom Res. 2013 Oct;75(4):305–13. doi: 10.1016/j.jpsychores.2013.07.001

29. Kivlighan KT, DiPietro JA, Costigan KA, Laudenslager ML. Diurnal rhythm of cortisol during late pregnancy: Associations with maternal psychological well-being and fetal growth. Psychoneuroendocrinology. 2008 Oct;33(9):1225–35. doi: 10.1016/j.psyneuen.2008.06.008

30. Hompes T, Vrieze E, Fieuws S, Simons A, Jaspers L, Van Bussel J, et al. The influence of maternal cortisol and emotional state during pregnancy on fetal intrauterine growth. Pediatr Res. 2012 Sep;72(3):305–15. doi: 10.1038/pr.2012.70

31. Guardino CM, Schetter CD, Saxbe DE, Adam EK, Ramey SL, Shalowitz MU, et al. Diurnal salivary cortisol patterns prior to pregnancy predict infant birth weight. Health Psychol. 2016;35(6):625–33. doi: 10.1037/hea0000313

32. Gilles M, Otto H, Wolf IAC, Scharnholz B, Peus V, Schredl M, et al. Maternal hypothalamus-pituitary-adrenal (HPA) system activity and stress during pregnancy: Effects on gestational age and infant's anthropometric measures at birth. Psychoneuroendocrinology. 2018 Aug;94:152–61. doi: 10.1016/j.psyneuen.2018.04.022

33. Giesbrecht GF, Campbell T, Letourneau N. Sexually dimorphic adaptations in basal maternal stress physiology during pregnancy and implications for fetal development. Psychoneuroendocrinology. 2015 Jun;56:168–78. doi: 10.1016/j.psyneuen.2015.03.013

34. D'Anna-Hernandez KL, Hoffman MC, Zerbe GO, Coussons-Read M, Ross RG, Laudenslager ML. Acculturation, Maternal Cortisol, and Birth Outcomes in Women of Mexican Descent. Psychosom Med. 2012 Apr;74(3):296–304. doi: 10.1097/PSY.0b013e318244fbde

35. Braithwaite EC, Hill J, Pickles A, Glover V, O'Donnell K, Sharp H. Associations between maternal prenatal cortisol and fetal growth are specific to infant sex: findings from the Wirral Child Health and Development Study. J Dev Orig Health Dis. 2018 Aug;9(4):425–31. doi: 10.1017/S2040174418000181

36. Bublitz MH, Vergara-Lopez C, O'Reilly Treter M, Stroud LR. Association of Lower Socioeconomic Position in Pregnancy with Lower Diurnal Cortisol Production and Lower Birthweight in Male Infants. Clin Ther. 2016 Feb;38(2):265–74. doi: 10.1016/j.clinthera.2015.12.007

37. Bublitz MH, Bourjeily G, D'Angelo C, Stroud LR. Maternal Sleep Quality and Diurnal Cortisol Regulation Over Pregnancy. Behav Sleep Med. 2018 May 4;16(3):282–93. doi: 10.1080/15402002.2016.1210147

38. Peterson A, Toledo-Corral CM, Chavez T, Naya C, Johnson M, Eckel S, et al. Prenatal Maternal Cortisol Levels and Infant Birth Weight in a Predominately Low-Income Hispanic Cohort. Int J Environ Res Public Health. 2020 Sep 21;17(18):6896. doi: 10.3390/ijerph17186896

39. Jung C, Ho JT, Torpy DJ, Rogers A, Doogue M, Lewis JG, et al. A Longitudinal Study of Plasma and Urinary Cortisol in Pregnancy and Postpartum. J Clin Endocrinol Metab. 2011 May;96(5):1533–40. doi: 10.1210/jc.2010-2395

40. Johnson ML, Virostko A, Veldhuis JD, Evans WS. Deconvolution Analysis as a Hormone Pulse-Detection Algorithm. In: Methods in Enzymology [Internet]. Elsevier; 2004 [cited 2024 Apr 2]. p. 40–54. doi: 10.1016/S0076-6879(04)84004-7

41. Slade P, Sheen K, Weeks A, Wray S, De Pascalis L, Lunt K, et al. Do stress and anxiety in early pregnancy affect the progress of labor: Evidence from the Wirral Child Health and Development Study. Acta Obstet Gynecol Scand. 2021 Jul;100(7):1288–96. doi: 10.1111/aogs.14063

42. Sanni K-R, Eeva E, Noora SM, Laura KS, Linnea K, Hasse K. The influence of maternal psychological distress on the mode of birth and duration of labor: findings from the FinnBrain Birth Cohort Study. Arch Womens Ment Health. 2022 Apr;25(2):463–72. doi: 10.1007/s00737-022-01212-0

43. Adams S, Eberhard-Gran M, Eskild A. Fear of childbirth and duration of labour: a study of 2206 women with intended vaginal delivery. BJOG Int J Obstet Gynaecol. 2012 Sep;119(10):1238–46. doi: 10.1111/j.1471-0528.2012.03433.x

44. Libretti A, Troìa L, Cappello AM, Casarotti C, D'Amato AT, Dallarda G, et al. Pregnancy and neonatal outcomes of SARS-CoV-2 infection discovered at the time of delivery: a tertiary center experience in North Italy. J Perinat Med. 2024 Feb 26;52(2):215–21. doi: 10.1515/jpm-2023-0280

45. Yazdi Moghaddam H, Karimi FZ, Jesmani E, Abdollahi M. Relationship between fear of COVID-19 and mental health in pregnant women. Ital J Gynaecol Obstet. 2024 Jun;36(02):151. doi: 10.36129/jog.2023.119

46. Fernández-Alonso AM, Mayoral-César V, Díaz-Goicoechea M, Díaz-Goicoechea M, Vicente-García G, Rodríguez-Castillo C, et al. Expectations of childbirth and anxiety in at term pregnant women during the SARS-CoV-2 pandemic in Spain: A pilot study. Ital J Gynaecol Obstet. 2023 Dec;35(04):503. doi: 10.36129/jog.2023.94

47. Hodnett ED, Gates S, Hofmeyr GJ, Sakala C. Continuous support for women during childbirth. Cochrane Database Syst Rev. 2013;2013(7). doi: 10.1002/14651858.CD003766.pub5 PMID: 23076901

48. Chaote P, Mwakatundu N, Dominico S, Mputa A, Mbanza A, Metta M, et al. Birth companionship in a government health system: a pilot study in Kigoma, Tanzania. BMC Pregnancy Childbirth. 2021;21(1):1–17. doi: 10.1186/s12884-021-03746-0 PMID: 33863306

49. Chunuan S, Pinjaroen S. Effect of the Presence of Family Members During the First of Labor Childbirth Outcomes in a Provincial Hospital in Songkhla Province Background a nd Significance. 2010;(June 2018).

50. Evans LM, Myers MM, Monk C. Pregnant women's cortisol is elevated with anxiety and depression — but only when comorbid. Arch Womens Ment Health. 2008 Jul;11(3):239. doi: 10.1007/s00737-008-0019-4

Table 1. Maternal and neonatal characteristics and their association with maternal cortisol levels

Perinatal characteristics	categories	Serum cortisol concentration < 58.35 ng/ml (n= 73)	Serum cortisol concentration ≥ 58.35 ng/ml (n=74)	P value
Maternal Age	Continous (Mean ± SD)	25 ± 5	24.5 ± 5	0,793
Maternal Age	<20 years	10 (6.8)	11 (7.5)	1
	20-35 years	63 (42.9)	63 (42.9)	
Employment status	not employed	72 (49)	74 (50.3)	0,497
	Employed	1 (0.7)	0 (0)	
Education	Junior High School	3 (2)	7 (4.8)	0,368
	Senior High School	64 (43.5)	63 (42.9)	
	Diploma	6 (4.1)	4 (2.7)	
Income	< Minimum wage	71 (48.3)	74 (50.3)	0,245
	≥ Minimum wage	2 (1.4)	0 (0)	
ANC Frequencies	<4	16 (10.9)	20 (13.6)	0,761
	4-7	49 (33.3)	47 (32)	
	>8	8 (5.4)	7 (4.8)	
Anxiety	Normal	11 (7.5)	9 (6.1)	0,827
	Elevated	28 (19)	28 (19)	
	High	21 (14.3)	26 (17.7)	
	very high	13 (8.8)	11 (7.5)	
KLP Score	Continous (Median ± IQR)	15 ± 3	15.5 ± 3	0,796
Gender	Male	33 (22.4)	39 (26.5)	0,457
	Female	40 (27.2)	35 (23.8)	
First phase duration	Continous (Median, Min-max), hours	8 (2-15)	8 (3-14)	0,846
Second phase duration	Continous (Median, Min-max), minute	15 (10-120)	15 (10-35)	0,99

Neonates Birth Weight	Continous (Median, Min-max), gr	2950 (1750-3950)	3000 (2300-4200)	0,473
Neonates Birth length	Continous (Median, Min-max), cm	48 (42-51)	48 (44-52)	0,115
1st minute APGAR	Continous (Median, Min-max)	8 (4-8)	8 (6-8)	0,543
5th minute APGAR	Continous (Median, Min-max)	10 (6-10)	10 (7-10)	0,948

Table 2. neonatal characteristics and their association with maternal anxiety

Perinatal characteristics	categories	Normal-increased anxiety (n=76)	High and Very high Anxiety (n=71)	P value
Gender	Male	37 (25.2)	35(23.8)	1
	Female	39 (26.5)	36 (24.5)	
First phase duration	Continous (Median ± IQR), hours	8 (2-15)	8 (2-14)	0,413
Second phase duration	Continous (Median ± IQR), minute	15 (10-90)	15 (10-120)	0,558
Neonates Birth Weight	Continous (Median ± IQR), gr	2950 (1750-4100)	3000 (2250 - 4200)	0,726
Neonates Birth length	Continous (Median ± IQR), cm	48 (42-52)	48 (43-52)	0,645
1st minute APGAR	Continous (Median ± IQR), `	8 (4-8)	8 (4-8)	0,486
5th minute APGAR	Continous (Median ± IQR),	10 (6-10)	10 (6-10)	0,484

Figure 1

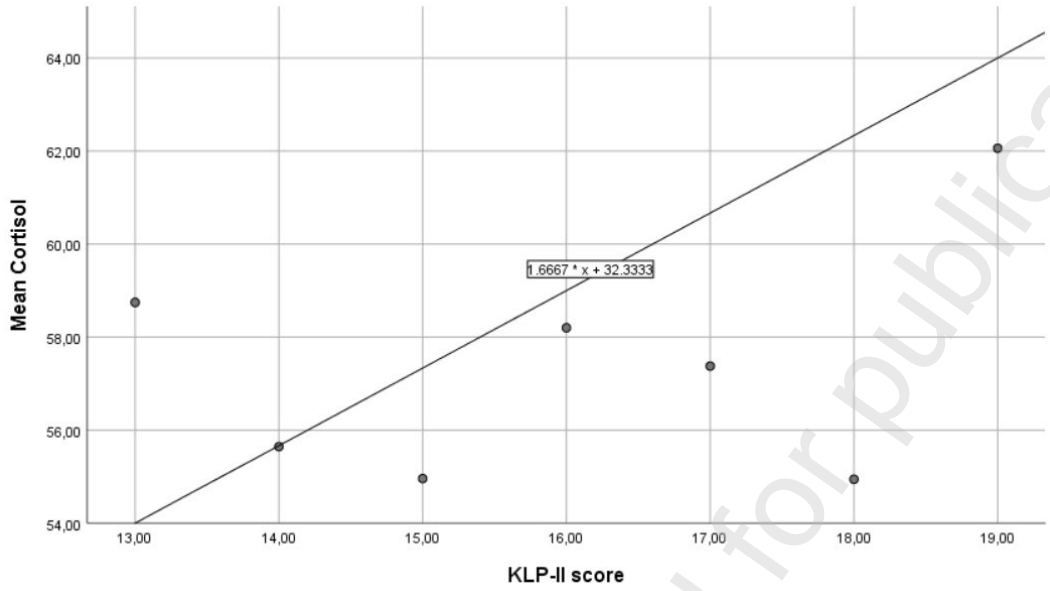

Figure 2