# **RESEARCH PROTOCOL**

# Investigating the Relationship Between Cortisol and Paternal Postpartum Depression: A Research Protocol

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#### Abstract

**Introduction:** Postpartum depression (PPD) is a common mental health condition that affects new parents and is often associated with major depressive disorder (MDD). However, research focuses on maternal experiences, overlooking paternal PPD. Cortisol is a stress hormone that can cause dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, impacting the mental state, and serving as a biomarker of depression. This dysregulation could result in fathers experiencing PPD, as decreased levels of cortisol may hinder father-newborn bonding. PPD can develop over a year rather than within the first four weeks post-childbirth. 4% to 25% of new fathers experience PPD, with peak prevalence occurring within 3-6 months after childbirth. The Edinburgh Postnatal Depression Scale (EPDS) is a tool designed to screen for symptoms of PPD. This study examines the correlation between cortisol levels and PPD among fathers.

**Methods:** A total of 100 fathers aged 18-45 will be recruited from urban hospitals in the Greater Toronto Area within 1 month postpartum. Participants will be screened using the EPDS, and blood samples will be collected to measure cortisol levels using an enzyme-linked immunosorbent assay (ELISA). This data will be collected at 1, 3, 6, and 12 months postpartum. Fathers with pre-existing psychiatric conditions, cortisol-altering medications, or significant health conditions will be excluded. Statistical analyses of the data will investigate the association between cortisol levels and paternal PPD.

**Results:** The study expects a statistically significant negative difference in cortisol levels between fathers with PPD and those without, indicating a potential association between cortisol dysregulation and paternal PPD. The study may identify predictors (marital status, previous parenting experience, finances) influencing cortisol levels in fathers, providing insight into cortisol regulation and paternal well-being.

**Discussion:** Findings will indicate cortisol as a biomarker for paternal PPD and assist in early interventions. It can also help with the readiness of healthcare providers to begin mental health services to fathers after delivery.

**Conclusion:** This study investigates the link between low cortisol levels and paternal PPD, hypothesizing a positive correlation with EPDS. Findings may lead to early screening tools and targeted interventions aimed at improving paternal mental health.

Keywords: postpartum depression; cortisol; pregnancy; stress; paternal; mental health

#### Introduction

Postpartum Depression

Postpartum depression (PPD) is a serious mental health condition that primarily occurs within the first few weeks after childbirth. While it is common to experience some mood swings after childbirth, and for people to experience a range of emotions such as irritability and being overly sensitive, PPD is more intense and lasts longer [1]. This is the case since it involves persistent feelings of sadness, anxiety, and hopelessness that can interfere with a parent's ability to function and bond with their child, rather than the temporary mood swings typically experienced after childbirth [1]. Specifically, PPD is diagnosed when there are at least 5 depressive symptoms present for at least 2 weeks, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1]. Symptoms include depressed mood, loss of interest and pleasure in most activities, insomnia, feelings of worthlessness or guilt, suicidal ideation or recurrent thoughts of death, and others [2]. PPD is most prevalent within three to six months postpartum [3].



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Postpartum depression includes many risk factors such as violence and abuse, immigration status, gestational diabetes, cesarean section, a history of depression, vitamin D deficiency, obesity, poor postpartum sleep, lack of social support, traditional dietary patterns, multiple births, preterm or low-birth-weight infants, postpartum anemia, and a negative birth experience [4]. These factors can increase the likelihood of developing PPD by impacting stress, physical health, and emotional well-being. One big factor is hormonal changes, one common hormonal change is seen in the increase in cortisol levels.

#### Cortisol and Postpartum Depression

Cortisol is a crucial hormone in pregnancy that oversees the development and maturation of fetal organ systems [5]. Cortisol linkage is significant in pregnancy because the hypothalamic-pituitary-adrenal (HPA) axis mediates the body's response to threats and stress, which is crucial in basic survival and functioning [6]. It is influenced by social and environmental factors, making cortisol a probable mediator of physiological linkage and co-regulation [7]. Several studies have indicated that couples in close romantic relationships exhibit linked diurnal cortisol activity and cortisol reactivity to stressors [8]. This suggests that postpartum depression in one partner can be linked to the condition in the other. A correlation has been observed where low cortisol levels in one partner with postpartum depression can influence the mental health of the other partner.

Cortisol is a stress hormone that can influence the central nervous system, causing dysregulation of the HPA axis [7]. The HPA axis is known for its role in regulating the body's stress response, maintaining homeostasis, and influencing metabolism, immune function, mood, and other functions [7]. As depicted in Figure 1, when the body perceives stress, whether physical or psychological, the hypothalamus, a region of the brain, releases the corticotropin-releasing hormone (CRH) [7]. CRH then stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH) [7]. ACTH, in turn, stimulates the adrenal glands, specifically the adrenal cortex, to produce and release cortisol, often called the stress hormone [7]. Cortisol helps the body cope with stress by increasing blood sugar levels, suppressing the immune system, and modulating inflammation [7]. Once the stressor is removed, cortisol levels return to normal, allowing the body to return to its baseline state [7]. However, chronic stress or dysregulation of the HPA axis can lead to prolonged elevation of cortisol levels, which can have detrimental effects on health, and can contribute to the development of PPD [7].

# Paternal Postpartum Depression

In comparison to maternal PPD, paternal PPD is often overlooked because societal expectations frequently focus on mothers, leaving fathers' mental health needs unrecognized [9]. However, 4% to 25% of new fathers experience PPD [10]. The transition to parenthood is challenging for most new fathers due to financial stress, sleep deprivation, and father-child bonding [9]. The emotional and mental health of fathers is often missed throughout the first postpartum year [10]. This can be because men typically avoid medical care in comparison to women [11]. Additionally, 24% to 50% of fathers experience PPD whose partners undergo PPD as well [12]. Making maternal PPD a catalyst for paternal PPD [10]. Paternal PPD can intensify stress and have a negative result on the family. marriage, and child development [9]. Stress can cause fathers to become emotionally unavailable, causing the child's sense of security to plummet [13]. Paternal PPD has been linked to a reduction in positive parent-infant interactions [9]. Furthermore, depressed fathers may not be emotionally available to provide support to their partner, who may also be undergoing PPD. Fathers often face these difficulties without social support [10]. New fathers might express their depression through increased anger and anxiety rather than sadness [10]. Despite these different signs, depression is still a significant issue [10]. Without treatment, paternal PPD can undermine a father's ability to emotionally support his partner and child [10].

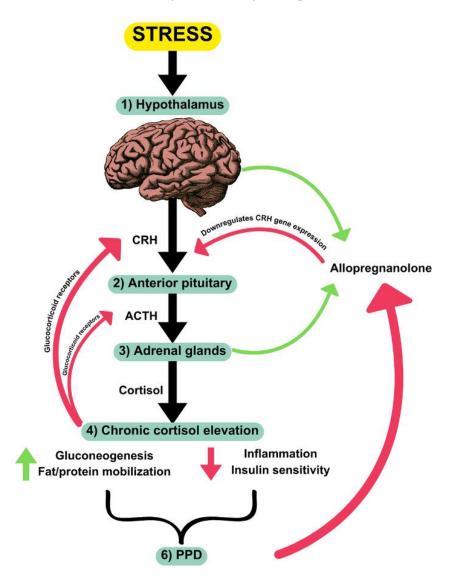
Paternal PPD has crucial implications for early child development and overall physical growth, socio-emotional and psychological well-being [9]. Several factors have been identified as potential triggers for paternal PPD, including strained marital relationships, employment status, and inadequate childbirth education [9]. Thus, raising awareness about this phenomenon and helping fathers overcome PPD is very important.

#### Study Objectives

The objectives of this study are to investigate the link between cortisol levels and PPD in fathers. Specifically, the study seeks to determine whether a relationship exists between cortisol levels and PPD severity (assessed by EPDS). It also aims to explore the potential of using cortisol levels as a predictive tool for early intervention in paternal PPD, which can in turn help to shape improved mental health care for new fathers [1].

#### **Hypotheses**

The study hypothesizes that fathers with lower cortisol levels will exhibit higher EPDS scores, indicating more severe PPD. Additionally, it hypothesizes that there is a significant relationship between cortisol levels and PPD severity, suggesting that cortisol can serve as a biomarker for paternal PPD.



**Figure 1. Impact of Stress on the HPA Axis.** Stressors from becoming first-time parents, finances, and marital relationships can cause the hypothalamus to release CRH [14]. This signals the pituitary gland to produce ACTH [14] This leads to the adrenal glands releasing cortisol [14]. Constant stress can result in dysregulation of cortisol levels [14]. Allopregnanolone regulates this, which reduces the impacts of stress [14].

#### Methods

#### **Participants**

This study is a longitudinal cohort study aimed at assessing PPD within 1-12 months postpartum, as depression gradually increases throughout the first year postpartum [15]. A total of 100 fathers experiencing PPD from hospitals and clinics in urban areas where PPD prevalence is notably high will be recruited from the Greater Toronto Area (GTA). Fathers aged 18-45 years old will be included. This is because males over the age of 45 have lower conception rates [16]. They must be 1 month postpartum and fluent in the language used in the study's questionnaires (e.g., English). Eligible participants will either have been diagnosed with PPD based on a clinical evaluation or score above the threshold on the Edinburgh Postnatal Depression Scale (EPDS) [1].

Additionally, participants must provide informed consent. Fathers with a pre-existing diagnosis of major depressive disorder (MDD) or other severe psychiatric conditions prior to the postpartum period will be excluded [1]. Participants using medications known to significantly impact cortisol levels, such as corticosteroids [17], or those with significant medical conditions affecting cortisol production, like Cushing's syndrome or Addison's disease [17], will also be excluded. Furthermore, individuals with significant alcohol use, smoking habits, poor nutrition, or irregular sleep patterns, as these can affect cortisol and mental health, may be excluded or have their habits recorded

as part of the study's questionnaire [11]. Non-biological fathers or those who were not the primary caregivers in the postpartum period, as well as those unable or unwilling to provide informed consent, will be excluded. Additionally, data on whether participants are first-time fathers will be collected, as this may influence the experiences and stressors they encounter during the postpartum period.

#### Procedure

1. *Recruitment*: Fathers will be recruited from hospitals and clinics, at 1-month postpartum. Flyers and digital advertisements will be used to inform potential participants about the study. The study will be conducted in urban hospitals and clinics in the GTA, where the prevalence of PPD is typically higher. As stated in existing literature, higher rates of PPD are observed in urban settings due to various socioeconomic and environmental stressors [1].

2. *Consent*: Participants will receive a detailed consent letter explaining the study's purpose, procedures, potential risks, and benefits. Informed consent will be obtained from all participants before any data collection [1].

3. *Blood Sample Collection*: Blood samples for cortisol level analysis will be collected at designated hospital or clinic laboratories by trained phlebotomists [1]. Cortisol levels will be measured using blood samples using enzyme-linked immunosorbent assay (ELISA). These levels will indicate the degree of physiological stress and potential HPA axis dysregulation in participants [17]. Blood samples will be collected at various times depending on the individual. Cortisol levels are often higher in the mornings and lower during the first phase of sleeping [18]. Doctors or nurses will create a schedule for collecting blood samples after inquiring the individual about their sleeping schedule. Blood samples will be collected at

1-, 3-, 6-, and 12-months post-childbirth. ELISA is a reliable method for cortisol detection due to its sensitivity [19]. To verify that the method is measuring cortisol accurately, the assay will be internally calibrated, meaning it will be tested against known cortisol concentrations to determine if it provides the same result as the known standards. Any potential biases introduced by timing or reporting discrepancies will be addressed through careful scheduling and rigorous protocol adherence.

4. *Questionnaire Administration*: The EPDS will be used to assess the severity of depressive symptoms in fathers. This 10-item questionnaire is designed to identify possible PPD [1]. 8 of which correspond to depressive symptoms and 2 which address anxiety symptoms [15]. Participants will complete the Edinburgh Postnatal Depression Scale (EPDS) to assess the severity of PPD. The EPDS is a validated and widely used screening tool to diagnose PPD [1]. 5. *Data Collection*: Blood samples will be analyzed to measure cortisol levels. EPDS scores and demographic data will be collected for each participant [1].

# Anticipated Results

The results of this study are expected to reveal significant correlations between cortisol levels and PPD severity among fathers.

#### **Descriptive Statistics**

We anticipate that using descriptive statistics will provide a clear profile of the study participants, including demographic factors such as age, employment status, and whether they are first-time fathers. We expect the baseline cortisol levels to vary across the participant pool, providing a broad spectrum for analysis [1].

#### Correlation Analysis

The correlation analysis will show a statistically significant positive correlation between cortisol levels and EPDS scores. Lower cortisol levels are expected to correlate with higher EPDS scores, suggesting that fathers with low cortisol levels may experience more severe symptoms of PPD.

#### **Regression Analysis**

The use of a multiple regression analysis can demonstrate that cortisol levels are a significant predictor of PPD severity, even when controlling for other descriptive variables such as age, employment status, and a patients' health history. We anticipate the regression analysis will explain the variance in EPDS scores, indicating that cortisol could serve as a reliable biomarker for assessing the risk and severity of paternal PPD [1].

# **Comparative Analysis**

We expect the comparative analysis to reveal significant differences in EPDS scores between fathers with high cortisol levels and those with low cortisol levels. Fathers with lower cortisol levels are anticipated to report higher levels of depressive symptoms, further supporting the hypothesis that cortisol dysregulation is linked to the severity of PPD [17].

#### Statistical Analysis

1. *Descriptive Statistics*: Demographic data and baseline cortisol levels will be summarized using descriptive statistics [1].

2. *Correlation Analysis*: Pearson correlation coefficients will be calculated to assess the relationship between cortisol levels and EPDS scores [17].

3. *Regression Analysis*: Multiple regression analysis will be performed to evaluate the influence of cortisol levels, demographic factors, and other relevant variables on PPD severity [1].

4. *Comparative Analysis*: Group comparisons (e.g., high vs. low cortisol levels) will be conducted using t-tests or ANOVA to identify significant differences in EPDS scores [1].

#### Discussion

The anticipated results will aid in indicating a relationship between male cortisol levels and paternal PPD as well as aid in enhancing the awareness of paternal PPD. This research identifies demographic factors associated with low cortisol levels, early screening and proactive support for at-risk fathers so that resources may become more feasible. Moreover, this research can enhance awareness of paternal PPD among healthcare professionals, equipping them with important insights and tools to provide effective support to fathers during the postpartum period. For instance, nurses working in pediatric, or labor and delivery units can play a pivotal role in raising public awareness about paternal postpartum depression [10]. They can educate families about available counselling resources and facilitate referrals to appropriate agencies [10]. Given that nurses frequently interact with expectant and new parents in both professional and social settings, as well as within their own communities, they are uniquely positioned to influence and support families during this critical period [10].

# **Limitations**

Although this study aims to provide valuable insights into the relationship between cortisol levels and paternal PPD, several limitations must be considered to fully understand the implications of the findings. Due to the sample size of 100 fathers, this may not be large enough for generalizability. Another contributing factor is the focus on urban hospitals and clinics, which might not capture the experiences of fathers in rural or less socio-economically stressed environments. Urban settings might have unique stressors that do not apply elsewhere, such as noise pollution. Additionally, there may be bias skewing the results. For example, self-reporting bias could occur because participants are aware they are being studied, potentially influencing their responses on the EPDS and other measures. Selection bias may also be a concern, particularly since we are recruiting individuals already seeking help or part of hospital databases, which could lead to discrepancies between those seeking help and those who are not. Additionally, this study focuses on fathers 3-6 months postpartum, this period may result in altered outcomes. Another limitation would include the differences in cortisol levels per individual based on the time the sample is collected. Cortisol levels can differ per individual as the levels are highest around 7 am and lowest during the evening [18]. Additionally, steroids and other medications can also impact cortisol levels [18]. Next Steps

The anticipated results of this study are expected to contribute valuable insights into the physiological basis of paternal PPD. If our hypotheses are supported, the study will

underscore the potential of cortisol screening as an early intervention tool, helping to identify fathers at risk for PPD and enabling timely support and treatment [1]. However, acknowledging the aforementioned limitations is crucial for interpreting the results accurately and guiding future research. Future research can improve this study in several ways. Firstly, replicating this study in diverse settings beyond the urban areas (e.g., rural areas) can determine whether the findings are applicable across different populations and environments beyond the GTA. Secondly, we can use statistical methods such as power analysis and effect size estimation to improve the generalizability of the results. To further minimize biases, incorporating random sampling techniques to reduce selection bias can be implemented. Potentially, future research can also explore the role of other biomarkers such as testosterone to provide a more comprehensive understanding of the physiological factors involved in paternal PPD [1]. These improvements can help create the basis for an intervention study which can focus on the effectiveness of cortisol screening in hand with initial treatment. The evaluation of these approaches can help to determine which helps to reduce the severity of PPD symptoms. Such would help to provide evidence of the benefits associated with identifying paternal PPD early and associated treatment. Future research can help initiate programs catered to men's mental health in hospitals, so that paternal PPD can be diminished early on.

### Conclusion

Overall, this study aims to enhance our understanding of PPD by examining the relationship between cortisol levels and depressive symptoms among new fathers. With the hypothesis that low cortisol levels are positively correlated with higher EPDS scores, our findings are anticipated to reveal significant correlations between decreased cortisol levels and increased severity of PPD symptoms, as measured by the EPDS. Through descriptive, correlation, regression, and comparative analyses, it is expected that cortisol dysregulation is a substantial factor in paternal PPD. If the hypothesis is supported, cortisol levels could serve as a valuable biomarker for early identification and intervention in fathers experiencing PPD. By underlining the physiological reasons for paternal PPD, this study could contribute to more effective screening and support strategies, potentially improving outcomes for both fathers and their families.

#### List of Abbreviations

ACTH: adrenocorticotropic hormone CRH: corticotropin-releasing hormone DSM-5: diagnostic and statistical manual of mental disorders EPDS: edinburgh postnatal depression scale HPA: hypothalamic-pituitary-adrenal MDD: major depressive disorder PPD: postpartum depression

# **Conflicts of Interest**

The authors declare that they have no conflicts of interest.

#### **Ethics Approval and/or Participant Consent**

Due to the involvement of human participants, Research Ethics Board (REB) approval will be required and obtained.

#### **Authors' Contributions**

GO: Contributed equally to the creation of the 437 manuscript, including the study design. Contributed to the abstract, introduction, limitations, conclusion, and gave final approval of the version to be published. HP: Contributed equally to the creation of the 437 manuscript, including the study design. Contributed to abstract, introduction, discussion, next steps, and gave final approval of the version to be published. AR: Contributed equally to the creation of the 437

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