



RESEARCH ARTICLE

Early postpartum cortisol and malondialdehyde trajectories in non-depressed mothers: A pilot study in Surabaya, Indonesia

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Abstract

The days immediately following childbirth are characterized by rapid biological and psychological changes. Stress and oxidative biomarkers cortisol and malondialdehyde (MDA) in particular have been implicated in postpartum mood disturbance. However, their early postpartum trajectories in healthy, non-depressed mothers, particularly in the Indonesia context, remain poorly documented. This pilot study therefore investigated changes in cortisol and MDA levels during the first three days postpartum women in Surabaya, Indonesia. A quantitative time-series study was conducted at the Surabaya, Indonesia. Thirty postpartum mothers were assessed on day 1 and day 3 after delivery. Serum cortisol and MDA levels were measured using ELISA and TBARS methods. Depressive symptoms were evaluated using the Edinburgh Postnatal Depression Scale (EPDS) and analyzed as a continuous variable. Data were tested for normality and homogeneity, followed by paired comparisons and correlation analyses. No significant differences were observed in cortisol (p-value = 0.900) and MDA levels on day 1 and day 3 (p-value = 0.211). EPDS scores decreased from 9.80 ± 3.21 to 8.00 ± 4.46 , but not statistically significant (p-value = 0.244). A significant moderate positive correlation was found between cortisol levels and EPDS scores on day 1 ($r = 0.519$; p-value = 0.003), but not on day 3. Meanwhile, no significant relationship was found between MDA and EPDS scores. Maintained cortisol and MDA levels after 3 days postpartum may reflect normal recovery patterns in mothers without depression. These findings provide a basic for further research and support the development of integrated psychosocial and biological screening strategies, in line with SDG 3 (Healthy Lives and Well-being).

1. INTRODUCTION

Postpartum psychological distress remains a significant global health concern. Research indicates that postpartum depression affects between one-tenth and one-fifth of women worldwide. However, this prevalence is observed to be higher in low- to middle-income economies like Indonesia. Moreover, even mothers that do not experience full clinical depression often experience emotional instability and some level of mild stress in the immediate postpartum

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period, particularly in the first week after giving birth. Maternal psychological changes during this early period may not be recognized, but can affect maternal recovery and bonding with the baby (1). The early postpartum period involves massive physiological and hormonal changes that can affect multiple biomarkers in the mother such as cortisol and malondialdehyde (MDA). This is a transition time during which the hypothalamic-pituitary-adrenal (HPA) axis adapts and is a major factor in controlling cortisol production. Cortisol is essential to the physiological stress response process as well as other metabolic and homeostatic functions. Chronic perinatal stress can affect the regulation of the HPA-axis and/or result in a chronic increase in cortisol, which can impact maternal and infant health (2,3). At the same time, oxidative stress may be evaluated by measuring the end product of lipid peroxidation, MDA, which is a measure of oxidative damage to the cell membranes. Higher concentrations of MDA can thus be a marker of higher oxidative stress and inflammation related to the physiological changes of the postpartum period (4). In addition to these biological changes, the postpartum adjustment also takes place in a sociocultural environment. Family involvement, family expectations on motherhood, breastfeeding and cultural view on maternal resilience can influence maternal stress in Indonesia. All of these factors could be working together in the early postpartum period to affect psychological adjustment and physiological stress response (5).

The knowledge of changes in cortisol and MDA in the early postpartum period could be of great value to shed light on the physiological and psychological adjustment of the mother after childbirth. Alterations in these biomarkers have been associated with maternal psychological well-being and postpartum adjustment, suggesting a potential link between biological stress responses and maternal health outcomes (6). This relationship is particularly relevant in Indonesia, where sociocultural expectations and maternal responsibilities may contribute to the stress experienced by women during the postpartum period (7). Furthermore, biological responses to childbirth may vary across populations, highlighting the importance of examining these biomarkers within specific population and sociocultural contexts (8). A better understanding of early postpartum biological adaptation may provide preliminary evidence to support the development of maternal health strategies that address both physiological and psychological well-being. This clinically relevant because postpartum stress has been associated with difficulties in maternal infant bonding, breastfeeding, and sleep, as well as an increased vulnerability to postpartum mood disturbances.

There are remaining controversies despite numerous findings on postpartum health. Many studies have focused predominantly on postpartum depression rather than specifically examining cortisol and MDA trajectories in non-depressed populations (9). In particular, evidence from longitudinal studies tracking changes in these biomarkers during the early postpartum period remains limited, especially among specific populations such as Indonesian mothers. This limitation highlights the need for targeted research to provide insights that are both culturally and biologically relevant (10,11). Furthermore, previous studies have often examined psychological stressors and physiological responses separately, limiting our understanding of the interplay between these factors during postpartum adaptation (3,12).

This study is one of the few studies that offered preliminary insight to the biological and psychological changes which occurred in the early postpartum period in non-depressed Indonesian mothers by adding to the existing body of knowledge. This study offers evidence in the population it examined that may fill a gap in the literature for postpartum biomarker research and offer culturally specific data useful for culturally responsive maternal health care. In addition, the results could serve as a foundation for future studies that investigate the stress-related and oxidative stress markers in various populations and sociocultural settings. Cortisol and MDA could be helpful markers of physiological adaption postpartum and potentially become markers of women who are at risk of adverse postpartum outcomes with further validation (13). This evidence may contribute towards the creation of more effective preventive measures and maternal health interventions in the future. In Indonesia, this is especially relevant as improving maternal and infant health continues to be an important public health problem and is aligned to the Sustainable Development Goals (SDGs) (14). Specifically, enhancing healthcare services for mothers plays a vital role in realizing Sustainable Development Goal 3, a global initiative aimed at securing lifelong health and wellness for everyone. Within this context, the present study provides preliminary evidence on early postpartum biological adaptation that may inform future research and maternal health initiatives. Findings will provide evidence for policy changes and health programs aimed at reducing health disparities, thus contributing to improved maternal and child health outcomes nationally.

However, much of the current academic attention has been directed toward clinically depressed populations or later postpartum periods, leaving a critical gap in understanding early biological trajectories among non-depressed mothers within the first 72 hours postpartum. In this context, this research was structured as a preliminary study to examine early postpartum trajectories of cortisol and malondialdehyde levels among healthy, Indonesian mothers and to explore their relationship with subclinical depressive symptom scores. By characterizing hormonal and oxidative patterns during the first 72 hours after delivery, this study aims to generate foundational evidence to inform future longitudinal and case-control studies.

2. MATERIALS AND METHODS

2.1. Study design, Setting, and Population

This pilot study employed a quantitative prospective time-series design to investigate early postpartum trajectories of stress-related and oxidative biomarkers among healthy postpartum mothers. Repeated measurements were performed at two predefined time points, namely at 24 and 72 hours post-delivery, to evaluate short-term physiological changes during the immediate postpartum period. The study was conducted in the maternity ward of Islamic Hospital of Jemursari, Surabaya, Indonesia, between August and October 2023. Participants were recruited using purposive sampling. Eligible participants were women aged 20–40 years who had delivered a live singleton infant at term (37–42 weeks of gestation), were clinically stable after delivery, and provided written informed consent. Mothers with a history of psychiatric illness, pregnancy or postpartum complications (including preeclampsia and postpartum hemorrhage), chronic diseases known to influence cortisol or oxidative stress (such as diabetes mellitus or hypertension), or current corticosteroid or antioxidant therapy were excluded.

2.2. Sample Size

As a pilot study, the sample size of 30 participants was determined based on recommendations for preliminary biomarker studies aimed at estimating variability and feasibility rather than hypothesis testing. This approach is often in preliminary biomarker studies because it helps reduce variability between participants and allows short-term physiological changes to be identified more clearly.

2.3. Data Collection Procedure

Data were collected at two time points during the early postpartum period: within 24 hours after delivery (day 1) and at 72 hours postpartum (day 3). At the first assessment, a certified medical laboratory technologist collected approximately 3 mL of venous blood from the antecubital vein using an aseptic technique. Samples of blood were drawn into tubes containing EDTA. To isolate the plasma, centrifugation was performed at 4°C for 10 minutes at a speed of 3,000 rpm. Finally, the plasma fractions were aliquoted and maintained at -20°C prior to subsequent assays. After blood sampling, each participant completed the Edinburgh Postnatal Depression Scale (EPDS) with assistance from the research team when required. On postpartum day 3, blood collection and psychological assessment were repeated following the same procedures used on day 1. To protect participant confidentiality, each participant was identified using a unique study code. Written agreement was formally collected from the individuals preceding any experimental interventions. As part of laboratory quality control, duplicate measurements were conducted on 10% of randomly selected samples.

2.4. Cortisol Measurement

Plasma cortisol was measured as an indicator of hypothalamic-pituitary-adrenal (HPA) axis activity. Measurements were performed using a Human Cortisol ELISA Kit (Elabscience, USA) according to the manufacturer's protocol. Each plasma sample was tested in duplicate, and the mean value was used for data analysis. Absorbance was measured at 450 nm using a calibrated microplate reader (Bio-Rad Laboratories, USA), and cortisol concentrations were expressed in ng/mL (15).

2.5. Malondialdehyde Measurement

Plasma MDA was used as a biomarker of oxidative stress and levels were measured using the TBARS (Thiobarbituric acid reactive substances) protocol. A unique pink complex is formed by combining MDA with TBA at high temperatures and low pH. The absorbance of the sample was then measured using a Boeco spectrophotometer (Boeco, Germany) at 532 nm. The concentration of MDA was determined by referring to a standard calibration curve and reported as nmol/mL. All laboratory analyses were made under standard conditions and reagent blanks were used for all analytical runs to reduce measurement variability.

2.6. Assessment of Depressive Symptoms

The Edinburgh Postnatal Depression Scale (EPDS) was used to assess maternal psychological status with 10 items. The participants respond to questions regarding their emotions on a scale of 0-3 with a total score of 0-30; the higher the score the more severe their state of depression. The results of this initial investigation were analyzed continuously to more closely monitor early postpartum emotional shifts as opposed to a clinical diagnosis of postpartum depression. Previous validation studies have suggested that EPDS scores ≥ 10 would be considered a threshold for postpartum depression, but no participants in the current study had a score ≥ 10 . Those with relatively higher scores were informed about the appropriate information and were informed to undertake further psychological evaluation if necessary.

2.7. Statistical Analysis

IBM SPSS version 11 (IBM Corp., Armonk, NY) was used to process data. Continuous parameters were presented as mean $\pm$ SD, while the assumptions of the parametric test, namely the normality of the data and homogeneity of variance were respectively tested using the Shapiro-Wilk and Levene's tests. The changes between postpartum day 1 and day 3 were assessed by paired-samples t-test for variables that were normal. To test the associations between cortisol, MDA and EPDS scores, Pearson's correlation coefficient was computed at each time point. All tests performed were conducted with p-value < 0.005 taken as statistically significant and the tests were two-tailed.

3. RESULTS AND DISCUSSION

3.1. Postpartum Trajectories of Cortisol, MDA, and EPDS Scores

Table 1 presents the characteristics and measured outcomes of the postpartum mothers, including maternal age, cortisol and malondialdehyde (MDA) levels, and Edinburgh Postnatal Depression Scale (EPDS) scores. Cortisol, MDA, and EPDS scores did not differ significantly between postpartum day 1 and day 3 (p-value = 0.900, p-value = 0.211, and p-value = 0.244, respectively). On day 1, cortisol showed a moderate positive correlation with EPDS scores ($r = 0.519$, p-value = 0.003); however, this association was no longer evident on day 3. MDA was not significantly correlated with EPDS scores at either measurement time point.

Figure 1A presents the mean values ($\pm$ SD) of each variable at both measurement time points. Mean cortisol levels were 28.25 ± 3.16 ng/mL on postpartum day 1 and 28.44 ± 3.90 ng/mL on postpartum day 3, showing only a minimal change between the two assessments. The error bars also showed considerable overlap. Serum malondialdehyde (MDA) showed a similarly small rise from 8.70 ± 0.14 to 8.78 ± 0.14 nmol/mL. EPDS scores decreased from 9.80 ± 3.21 on postpartum day 1 to 8.00 ± 4.46 on day 3, although considerable variability was observed among participants. Consistent with the patterns shown in the figure, paired-samples t-tests indicated no significant differences between day 1 and day 3 in cortisol ($t = -0.128$, p-value = 0.900), MDA ($t = -1.310$, p-value = 0.211), or EPDS scores ($t = 1.216$, p-value = 0.244). Thus, cortisol and MDA levels remained relatively stable during the first three postpartum days, while EPDS scores showed a numerical decrease that did not reach statistical significance. Figure 1B illustrates the changes in mean values between the two measurement points. Cortisol levels remained nearly unchanged, consistent with the absence of a significant short-term difference between postpartum days 1 and 3. MDA showed only a small increase of less than 0.1 nmol/mL, which was also not statistically significant. In comparison, the mean EPDS score was lower on day 3, although the wider variation in scores indicates that changes were not uniform across participants. In general, the graphical patterns confirm the statistical results, with few differences in cortisol, MDA and EPDS scores in the early postpartum period, which were not significant. The results could be a physiological and/or psychological adaptation of the mother's body to post-childbirth, but the brief period of observation and the small sample size must be taken into account when interpreting these patterns.

This is a preliminary study that gives insight into the biological and psychological changes that occur in the first 72 hours after childbirth for healthy mothers in Indonesia. There was no significant increase or decrease in cortisol, and there was only a slight decrease in EPDS scores, between postpartum days 1 and 3. Levels of cortisol and malondialdehyde (MDA) did not significantly change between postpartum days 1 and 3, and EPDS scores did not significantly decrease between the same time period. This was the opposite situation for the correlation analysis. There was moderate and positive correlation between cortisol and EPDS scores on day 1 ($r = 0.519$, p-value = 0.003) and none on day 3 ($r = -0.164$, p-value = 0.387). The study results indicate that the association between cortisol and depressive symptoms might be stronger shortly after giving birth, and may vary as the early postpartum adaptation takes place. This, however, is considered a preliminary finding and should not be interpreted as a sustained or dysregulated HPA-axis activity, due to the small sample-size and the relatively short time frame of observation.

3.2. Association Between Cortisol and Depressive Symptoms

There were moderate and positive correlations between cortisol and EPDS on postpartum day 1 ($r = 0.519$, p-value = 0.003) as seen in Figure 1B. Higher cortisol levels were thus associated with higher scores of depressive symptoms during the first 24 hours postpartum, but not the participants met the study criterion for clinical postpartum depression. This finding may indicate a relationship between the physiological stress response and early emotional adjustment immediately after delivery. By postpartum day 3 (Figure 1C), the correlation between cortisol and EPDS scores was weak and not statistically significant ($r = -0.164$, p-value = 0.387). Thus, an association observed on day 1 was not evident at the later assessment. This might be because within the first days following childbirth physiological and psychological changes take place quickly. These data, however, do not provide direct evidence of changes in the activity of the HPA-axis or emotional regulation, and this needs to be investigated further. Overall, the results indicate that cortisol and depressive symptoms might not be correlated throughout the early postpartum period. The strong correlation on day 1 and the lack of correlation on day 3 suggests that there may be a window of opportunity for the cortisol-EPDS association to be most evident immediately following childbirth. However, both the correlation coefficients were not formally tested

for difference, so it does not necessarily mean that this is a significant temporal change. More studies with larger sample sizes at more time points need to be done to understand the trajectory of cortisol and psychological adjustment in postpartum recovery.

Table 1. Research results

Category	Day 1 st (Mean $\pm$ SD)	Day 3 rd (Mean $\pm$ SD)	p-value
Mother's age	28.97 $\pm$ 4.73		
Cortisol levels	28.35 $\pm$ 3.49	28.44 $\pm$ 3.9	0.900
Malondialdehyde levels	8.78 $\pm$ 0.14	8.78 $\pm$ 0.14	0.211
EPDS	9.8 $\pm$ 3.21	8.00 $\pm$ 4.46	0.244

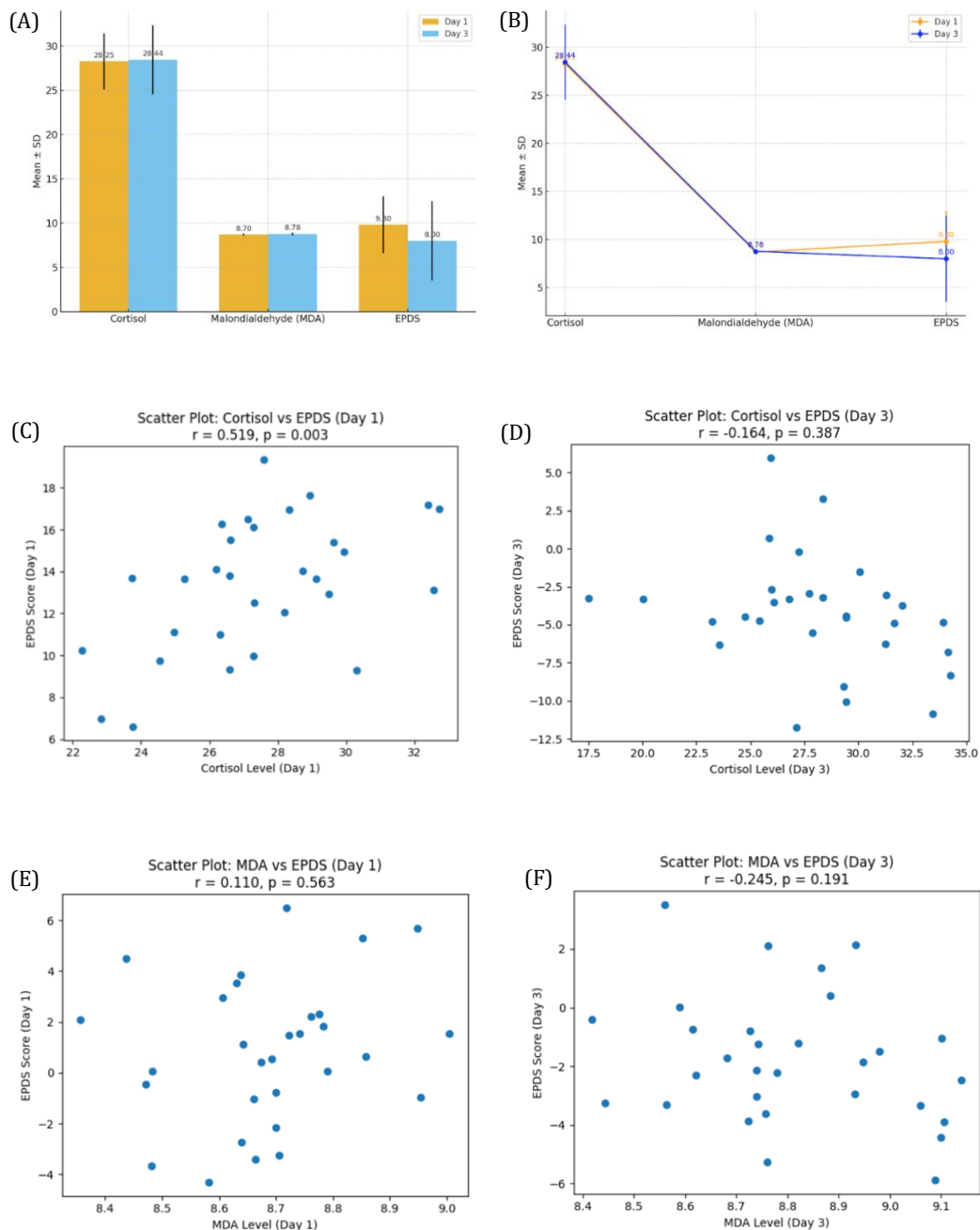


Figure 1. Postpartum trajectories of cortisol, MDA, and EPDS scores. (A) Differences in cortisol levels on day 1 and day 3 in postpartum mothers. (B) Changes in biomarker and EPDS scores on day 1 and day 3 post partum. (C) Scatter plot cortisol vs EPDS on day 1 (D) Scatter plot cortisol vs EPDS on day 3. (D) Scatter plot MDA vs EPDS on day 1. (E) Scatter plot MDA vs EPDS on day 3.

Cortisol is a key downstream output of the HPA axis and is strongly responsive to childbirth-related stressors, including labor physiology, sleep disruption, pain, and rapid withdrawal of reproductive hormones (16). The significant Day-1 cortisol-EPDS association observed here is consistent with the concept that acute HPA activation in the immediate postpartum window may coincide with transient emotional vulnerability, even when symptoms remain subclinical. Notably, the absence of a significant association on Day 3 aligns with early recalibration of stress physiology in non-depressed mothers. Recent studies (2020-2025) have highlighted the dynamic role of cortisol variability and diurnal patterns in postpartum emotional regulation has been linked to both hypercortisolemia (more often reflecting transient or acute stress states) and hypocortisolemia (more often observed in chronic or persistent depressive states), indicating that cortisol alterations in PPD are heterogeneous and likely dependent on symptom chronicity, timing, and measurement approach (17). Within this framework, the stable, mid-range cortisol profile in the current cohort together with diminishing cortisol EPDS coupling by Day 3 may reflect an adaptive, non-pathological postpartum state rather than the sustained HPA-axis dysregulation more typical of clinically depressed groups. A key methodological consideration is that cortisol has a pronounced diurnal rhythm and is highly sensitive to sampling time, sleep timing, breastfeeding, and acute stress exposures. Therefore, single time-point measurements (or limited time-point designs) may underestimate dynamic HPA-axis features relevant to PPD risk, such as diurnal slope or the cortisol awakening response (17,18). In the present study two time points were used (24 and 72 hours postpartum), but these still do not provide a diurnal profile. This constraint needs to be specifically noted, and diurnal sampling (or a standardized sampling window) should be used in future studies in order to enhance comparability and interpretability between studies.

3.3. Association Between Malondialdehyde and Depressive Symptoms

The scatter plots showed no statistically significant correlation between malondialdehyde (MDA) levels and EPDS scores at either postpartum assessment. On day 1 (Figure 1B), MDA was weakly and positively correlated with EPDS scores ($r = 0.110$, $p\text{-value} = 0.563$). The scattered distribution of data points was consistent with the absence of a clear linear relationship between the two measures. On postpartum day 3 (Figure 1D), the correlation was weak and negative ($r = -0.245$, $p\text{-value} = 0.191$) and remained statistically non-significant. These findings indicate that MDA concentrations were not significantly associated with depressive symptom scores during the first three days after childbirth in this sample of non-depressed mothers. Unlike cortisol, which was significantly correlated with EPDS scores on day 1, MDA showed no significant relationship with EPDS scores at either time point. This finding suggest that MDA may not closely correspond with short-term variations in depressive symptoms during the immediate postpartum period. However, the absence of a significant association in this small pilot sample does not exclude a possible role of oxidative stress in postpartum psychological adjustment. Future research utilizing more extensive cohorts, extended observation durations, and repeated biomarker measurements are needed to determine whether the relationship between oxidative stress and depressive symptoms becomes more apparent at later stages of postpartum recovery or among women with greater depressive symptom severity.

The correlations between the postpartum day 1 and day 3 mean with MDA were not significantly different from zero ($r = -0.245$, $p\text{-value} = 0.191$; $r = 0.110$, $p\text{-value} = 0.563$, respectively). The results suggest that the concentrations of MDA were not strongly correlated with the changes in the symptom scores of depressions in the sample of healthy postpartum mothers in the first 72 hours after delivery. This finding is in line with the reported literature, which also indicates that oxidative stress is among the various mechanisms involved in the pathophysiology of postpartum depression, along with inflammatory, mitochondrial and neuroendocrine mechanisms. The findings of previous research also indicate that oxidative disturbances could be more pronounced in women who have more depressive symptoms or vulnerability than in women with uncomplicated early postpartum adaptation (19,20). Thus, the relationship between oxidative stress and depressive symptoms may be more apparent with chronic psychosocial stress and/or chronic biological vulnerability or concurrent inflammation (21). But longer follow-up times and larger samples are required to explore the options.

Dietary variation among mothers before and after birth, including differences in antioxidant intake and diet quality, have been proposed to impact on postpartum MDA levels (19). This evidence will be used to explain the current results. The relatively stable MDA concentrations in the first three days after birth could be partly because of the uncomplicated clinical status of the study participants; however, the role of antioxidant status remains unknown from the available data. The variability in dietary intake also may contribute to individual differences in oxidative stress, but it was not evaluated in the present study and should be taken into consideration in future studies (22). Although there is an increasing interest in the study of oxidative stress in the postpartum period, so far, there is not much evidence that describes the changes of stress markers such as cortisol and MDA in Indonesian non-depressed mothers in the short time postpartum.

3.4. Clinical and Methodological Implications

Overall, these results indicate a biological difference in the early postpartum adaptation process, with cortisol seemingly more sensitive to changes in immediate emotional processes and MDA to longer-term or context-dependent oxidative processes that are not as apparent in the early postpartum recovery phase for low risk mothers (23). From a clinical perspective, early cortisol levels may complement psychosocial screening in identifying transient vulnerability

within the first 24 hours postpartum stages or among high-risk populations. Establishing typical biomarker patterns in low-risk populations is important for interpreting deviations in future case-control studies or longer-term longitudinal research on postpartum depression. These findings also emphasize the importance of considering the timing of biomarker assessment in postpartum research, as relationship identified immediately after childbirth may change even within a relatively short period of recovery.

3.5. Limitations and Future Directions

There are a number of limitations in this study that should be taken into consideration when interpreting the findings. Some methodological limitations should be considered for these results. Most important, our conclusions must be limited to this small sample size, and the lack of sensitivity to small relationships is due to the small sample. Secondly, the lack of a clinically verified postpartum depression (PPD) group made direct case-control comparisons impossible, which restricted conclusions about differences between the normative and pathological patterns. Thirdly, the 72-hour observation period only included the short-term changes in physiology and emotions after childbirth and may not have captured the adaptation to childbirth over time.

These current shortcomings could be resolved in upcoming literature through the execution of more extensive case-control research that include mothers with clinically diagnosed postpartum depression (PPD). Extending biomarker assessment to later postpartum time points, such as six weeks or beyond, would allow further evaluation of delayed or persistent biological changes. In addition, incorporating dynamic measures of HPA-axis function, including the cortisol awakening response and diurnal cortisol patterns, may provide deeper insight into the mechanisms of stress regulation associated with postpartum mood disorders.

4. CONCLUSIONS

This pilot study offers a first glimpse into the different biological functions of HPA-axis activity and oxidative stress in the first postpartum months of non-depressed Indonesian mothers. Early HPA-axis activity was significantly related to postpartum day 1 depressive symptom scores, suggesting that postpartum transient emotional vulnerability may be linked to early HPA-axis activity. This association was no longer statistically significant by day 3, possibly because of physiological adjustments during the early postpartum period. However, at both time points, malondialdehyde (MDA) levels were not significantly correlated with depressive symptoms, indicating that the relationship between oxidative stress and postpartum mood may be influenced by the time of assessment or other circumstances. This study provides baseline biological data and presents some preliminary evidence that may be representative of a low-risk population for postpartum depression and inform future longitudinal and case-control studies of postpartum depression. The results could be used in future studies of biologically-informed interventions for maternal mental health, which is part of Sustainable Development Goal 3 (Good Health and Well-Being) and could help improve women's health in the postpartum transition which is part of Sustainable Development Goal 5 (gender Equality).

Author contributions: HN, NMH: Conceptualization, supervision. HN: methodology, resources, project administration, investigation, writing original draft preparation, project administration. AA: software, data curation, visualization. HN, NMH, UL: validation. UL: formal analysis. NHM was responsible for reviewing and editing the manuscript. The final manuscript has been read and approved by all contributing authors.

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Conflict of interest: None.

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