HHS Public Access

Author manuscript

J Midwifery Womens Health. Author manuscript; available in PMC 2016 July 01.

Published in final edited form as:

J Midwifery Womens Health. 2015 July ; 60(4): 428–436. doi:10.1111/jmwh.12294.

Perineal Injury During Childbirth Increases Risk of Postpartum Depressive Symptoms and Inflammatory Markers

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Abstract

Introduction—Perineal lacerations during childbirth affect more than 65% of women in the United States. Little attention has been given to the long-term biologic consequences associated with perineal lacerations or possible associations with postpartum mental health. In this article we describe the results of a study that explored inflammatory pathways in women who reported perineal lacerations during childbirth and the relationship with stress and depressive symptoms during the first six months postpartum.

Methods—A repeated measures design was used to explore the relationship between varying degrees of perineal lacerations, inflammatory cytokines, postpartum stress, and depressive symptoms in 153 women over six months. Depressive symptoms were measured using the Edinburg Postnatal Depression Scale (EPDS) and maternal stress via the Perceived Stress Scale (PSS). Plasma was analyzed for pro (TNF-α, IL-6, IL-1β, IFN-γ) and anti-inflammatory (IL-10) cytokines. Levels of cytokines were compared between women with or without varying degrees of injury.

Results—A relationship was identified between symptoms of depression and a 2nd degree or more severe perineal laceration starting at 1 month postpartum (P=0.04) and continuing through 3 months (P=0.03). Similarly, stress symptoms were higher at 3 months postpartum (P=0.02). Markers of inflammation were significantly higher among this group with IL-6 increased at 2 weeks postpartum (P=0.02), and remaining elevated through 2 months postpartum (P=0.003); there were also significant differences in pro to anti-inflammatory cytokine ratios out to 6 months postpartum. Regression analysis indicated that 2nd degree or more severe lacerations accounted for

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Conflicts of Interest:
The authors have no conflicts of interest to disclose.

5.9% of the variance in EPDS score at one month postpartum (*P*=0.024, F=2.865, t=2.127), increasing substantially when the 1-month stress score was included as well.

Discussion—This study suggests that perineal lacerations, inflammation, stress, and depressed mood are associated, however, more research is needed to elucidate the actual relationship between inflammation and mental health in women who experience such injuries.

Keywords

postpartum depression; stress; perineal lacerations; inflammation; postpartum complications

INTRODUCTION

Of the 4 million women giving birth annually in the United States, approximately 2.6 million deliver vaginally.[1] Although vaginal birth is the desired and best outcome for most women, the recent National Hospital Discharge Survey reported that more than 65% of women who experienced vaginal birth also experienced some degree of perineal/genital tract laceration.[2] The postpartum period for women with perineal laceration is often complicated by challenges due to persistent pain and poor sexual readjustment, and ultimately, an increased risk for postpartum depression (PPD).[3,4] Risk factors for PPD traditionally focus on psychosocial domains, however identification of specific biologic mechanisms may provide a better understanding of PPD pathogenesis in this population.

As with any tissue injury, perineal laceration following childbirth and the subsequent healing mechanisms initiate a complex immune inflammatory reaction. In non-pregnant, non-postpartum populations, inflammation is associated with depressed mood, [5-8] and indeed, recent investigations have suggested that inflammation also may be a risk factor for PPD.[9,10] Stress, commonly experienced during both pregnancy and the postpartum period, is likewise associated with perinatal depression[11,12] and inflammation.[13] These associations are also true in non-pregnant, non-postpartum populations.[6,7,14] However, to our knowledge, no previous studies have reported a relationship between perineal lacerations, inflammatory pathways, and postpartum mental health. Therefore, the purpose of this study was to explore the relationship between perineal laceration, inflammation, and the development of stress and depressive symptoms, during the first six months postpartum.

BACKGROUND

Perineal lacerations, especially those that are moderate or severe, are associated with acute and chronic postpartum perineal pain and dyspareunia.[15-19] Severe perineal lacerations can lead to long term complications including urinary stress incontinence, anal incontinence,[20] chronic pain,[21] and dyspareunia.[16,22] When comparing women with an intact perineum to women who experienced a significant perineal laceration during childbirth, Signorello[23] found those with a 2nd degree injury were 80% more likely – and those with a 3rd degree injury 270% more likely -- to report pain with intercourse at 3 months postpartum. Postpartum depression (PPD) also has been reported in women with perineal injury; however studies have limited investigations to the impact of persistent pain and/or sexual distress on PPD.[3,4]

Postpartum depression, as defined by the American Psychological Association DSM-V, is a major depressive disorder with a postpartum onset within four weeks of childbirth[24]; it affects 12-15% of women and symptoms may last up to one year postpartum.[25] Psychosocial risk factors including previous history of mood disorders, life stress, poor social support, and low socioeconomic status are consistently supported in the literature.[26] Biologic mechanisms, including thyroid dysfunction, genetic factors, and hormonal changes also have been proposed as risk factors for PPD. [27-29] More recently, in light of the recognized risk of depression related to inflammation in other populations,[5-8] the contribution of an exaggerated pro-inflammatory response to PPD has been under investigation as well.

Trauma to any tissue initiates an inflammatory response, characterized by increased blood flow to the site and migration of white blood cells into the surrounding tissue space. Pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), interferon gamma (IFN-γ), interleukin-1 beta (IL-1β), and interleukin 6 (IL-6) coordinate these non-specific responses, whereas anti-inflammatory cytokines such as interleukin 10 (IL-10) and interleukin-4 (IL-4) provide negative feedback to limit inflammation and instead direct the immune response towards the production of antibodies.[5,30] Since reciprocal interactions between pro- and anti-inflammatory cytokines finely tune and ultimately balance the immune response, evaluating pro- and anti-inflammatory cytokine ratios is a highly sensitive means by which to identify cytokine equilibrium or disequilibrium.[7,30]

Although some level of inflammation is expected following perineal injury, little is known about the inflammatory balance or the long term physiologic or behavioral consequences triggered by this process. However, increased circulating levels of pro-inflammatory cytokines, including IL-1β, IL-6, and TNF-α, have been reported elevated in non-pregnant populations suffering from depression.[6] Similarly, therapeutic administration of IFN-γ to persons suffering from cancer or hepatitis is well-recognized to increase the risk of depressive symptoms while the addition of anti-inflammatory medication to patients with treatment-resistant depression has demonstrated efficacy in those with high baseline inflammatory markers.[31]

The mechanisms by which circulating pro-inflammatory cytokines exert their effects on the central nervous system (CNS) are still under investigation,[6] but may include leakage or transport of cytokines across the blood brain barrier, or activation of vagal afferent nerve fibers that exert effects in the CNS. Once in the brain, pro-inflammatory cytokines appear to affect the availability or metabolism of serotonin or dopamine, and/or alter the release of corticotrophin releasing hormone (CRH), thereby altering mood.[32] Given these and additional studies, we [33,34] and others [35-38] have proposed that women experiencing exaggerated inflammation after childbirth may also be at increased risk for developing postpartum depressive symptoms. And finally, stress -- also commonly reported during the postpartum period -- triggers a complex neuroendocrine immune response that promotes the release of pro-inflammatory cytokines associated with depressed mood [33,39] and, likewise, is identified as an independent risk factor for PPD.[11,12]

To our knowledge, a direct examination of the underlying biologic consequences of perineal laceration has not been reported, and not in regard to the risk of PPD. In this longitudinal study, we tested two hypotheses; first, that women experiencing more severe perineal lacerations would report more stress and depressive symptoms compared to women with no or mild perineal injury, and second, that women with more severe perineal lacerations would demonstrate an exaggerated postpartum pro-inflammatory response as indicated by: higher plasma levels of pro-inflammatory cytokines (e.g., IL-1β, IL-6, and TNF-α, and/or IFN-γ); lower plasma levels of the anti-inflammatory cytokine (e.g., IL-10); or a shift in the ratio of pro- to anti-inflammatory cytokines such that the new equilibrium favors a pro-inflammatory milieu.

METHODS

A secondary analysis was conducted using data from a prospective 5-year study investigating the psychoneuroimmunology of PPD. As described previously,[13] pregnant women residing in Ohio and Colorado were recruited during their 2nd and early 3rd trimesters between September 2008 and February 2014 via outreach to prenatal classes and placement of advertisements on billboards in prenatal clinics at The Ohio State University and the University of Colorado.

After an initial screening, women meeting basic inclusion criteria were visited at home by a registered nurse 8 times. The first visit was conducted to review the protocol and obtain informed consent, ensuring all procedures were carried out with the understanding and written consent of participants, and to gather information on: age, marital status, race/ethnicity, receipt of government assistance through the Women, Infants, and Children (WIC) assistance program, and personal or family history of depression. Self-report of height and pre-pregnancy weight was obtained for determination of body mass index (BMI). All subsequent home visits conducted for the purpose of data collection occurred: between 32-36 weeks of pregnancy and again at 1-week, 2-weeks, 1-month, 2-months, 3-months, and 6-months after birth. At each of these visits, women first completed questionnaires on; symptoms of infection, use of over-the-counter or prescribed medications or herbs, smoking behaviors, the presence of depressive symptoms via completion of the Edinburgh Postnatal Depression Scale (EPDS),[40] and the Perceived Stress Scale.[41] Next, venous blood was drawn into EDTA (anticoagulant)-containing tubes for later measurement of plasma pro-inflammatory cytokines IL-6, IL-1β, TNF-α and IFN-γ, and anti-inflammatory cytokine IL-10. At the week 1 home visit, women were additionally asked to provide information about their labor and birth including: hours of labor and whether or not they experienced a perineal laceration and, if so, to what degree. Clinical records were later retrieved to verify the self-reports. Home visits typically lasted approximately 30-minutes. At the end of each visit, women were compensated up to $35 for their participation (depending upon if they had responded to pre-visit phone calls) and the next home visit was arranged. All study procedures were approved by the institutional review boards at The Ohio State University and the University of Colorado, and were reviewed annually by a research data safety advisory committee.

Inclusion/Exclusion Criteria

Prenatal inclusion criteria were that all women were between 18-40 years of age, less than 36-weeks pregnant, non-smokers, and anticipating the vaginal birth of a singleton infant. Additionally, women were required to be free of any medically-required pregnancy restrictions, any known chronic illness, and, with the exception of prenatal vitamins, not taking any over-the-counter or prescribed medications including anti-inflammatory or anti-depressant agents. Postnatal criteria for continued inclusion were that women had given birth vaginally to a live singleton infant without experiencing hemorrhage or transfusion, and that both the woman and her newborn left the hospital within 72-hours after the birth. These inclusion/exclusion criteria were established to reduce to the extent possible prenatal or postnatal conditions that might themselves be associated with inflammation and/or depressed mood. Women also were required to be without symptoms of infection at the time of each home visit and to live within 20 miles of the laboratory, to minimize the time biologic samples were in transport, preserving the validity of the biomarkers.

Measures

Depressive Symptoms—The 10-item EPDS was used for self-report of symptoms of depression. It is an easy to administer and effective screening tool, validated for both antepartum and postpartum use. Answers to questions such as “I have looked forward with enjoyment to things” are scored from 0 (“As much as I ever did”) to 4 (“Hardly at all”). After completion, a woman’s score is summed to provide information on the likelihood of clinical depression. Scores range from 0-30 with scores of 10 or higher suggestive of more depressive symptoms and increased risk for PPD. Validation of the EPDS against a diagnostic clinical interview identified a specificity of 78%, a sensitivity of 86%, and a positive predictive value of 73% for women scoring higher than 10.[40]

To protect the health of all participants, any woman scoring 10 or higher on the EPDS was provided information on accessing mental health counseling and the research nurse offered to assist her in seeking help. A follow-up call was made within 7-days to see if she had sought help. Moreover, if any woman answered other than “never” on question 10, further steps were implemented as this question asks about suicidal ideation. Steps included contacting the family member identified by the woman in her Informed Consent form for this purpose and contacting one of the mental health specialists on the research team (psychiatrist or psychiatric nurse practitioner) who then evaluated the woman. As outlined in the Informed Consent, if after speaking with the mental health specialist the woman was deemed at serious risk, a plan was activated to call the woman’s health care provider and remain with her until that individual and/or her family member arrived, or, if necessary, to take her immediately to the Emergency Department for further evaluation; these steps were never required during the study and no serious adverse event of any kind occurred.

Perceived Stress—The 14-item Perceived Stress Scale (PSS) was used to measure maternal stress.[41] The PSS is well validated, including during pregnancy and the postpartum period.[42] Responses are based on a Likert-scale from 0 to 4, or from “never” to “very often.” Each question asks how the individual has felt during the past month, addressing seven negative and seven positive items. Scores range from 0-56 with higher scores indicative of

greater perceived stress. In Cohen's original report, reliability was high (alphas ranged from .84-.86) as was test-retest correlation (.85). Evidence for concurrent and predictive validity was significant at $P < .05$ (r = .49).

Biomarkers

Upon reaching the laboratory, blood samples were centrifuged at 4°C for 8 minutes at 2000 rpm. Plasma aliquots were placed into 1.5 cc polypropylene microtubes and stored at −70°C, until assayed using a Human Pro-inflammatory Ultra-Sensitive assay and quantitative multiplex array technology (Meso Scale Discovery, Gaithersburg, Maryland). Intra-assay coefficient of variation was <5% and inter-assay coefficient of variation was <10%. The plasma level of each cytokine was determined as well as the ratio of each pro- to anti-inflammatory cytokine (e.g., IL-6/IL-10). Identical procedures for sample collection and processing were followed in Ohio and Colorado and all assays were conducted at The Ohio State University.

Statistical Analysis

Descriptive statistics (eg, mean, standard deviation and percentages) were computed for baseline demographic (eg, age, BMI, hours in labor, race, income level, marital status) and psychosocial variables (eg, prenatal PSS, EPDS, personal and family history of depression) and tested for statistically significant differences between women with and without perineal laceration. Continuous variables were compared using independent sample Student t-tests whereas Chi-square tests or Fisher's exact tests were used for categorical variables when appropriate. Similar comparisons were also performed between women with and without severe perineal laceration (defined as a 2nd degree or a more severe laceration).

To evaluate associations between varying degrees of perineal lacerations and the risk of developing depressive and stress symptoms, multiple linear regression was used to assess differences in the raw EPDS and PSS scores for women with and without a 2nd degree or more severe laceration. Demographic and psychosocial variables that were significantly different between the two groups were controlled for in the regression analysis. Analyses were performed for outcomes at the prenatal time point as well as all six-time points postpartum to assess any differences over time.

A second set of multiple linear regressions were used to assess whether plasma levels of inflammatory cytokines (e.g. IL1β, IL6, IL10, IFN-γ, TNF-α) and pro- to anti-inflammatory cytokine ratios (IL1β/IL10, IL6/IL10, IFN-γ/IL10 and TNF-α/IL10) prenatally (32-36wks) or postpartum (weeks 1 and 2, months 1, 2, 3 and 6) were significantly higher in women with a 2nd degree or more severe perineal laceration compared to those with lesser degrees of injury after controlling for baseline characteristics that were significantly different between the two groups.

Additional exploratory linear regression analyses were performed to test whether elevated plasma levels of inflammatory cytokines were associated with a higher risk of PPD symptoms (higher EPDS scores) prenatally and postpartum week 1, 2, and Month 1, 2, 3, and 6.

Because the cytokine data were skewed, natural log transformations were performed prior to the analysis and results were reported based on back transformation of the log values to the original scale. Statistical analysis was performed using SAS (version 9.2; SAS Institute, Cary, NC) and SPSS 20. All statistical tests were two-sided and a p value of <0.05 was considered statistically significant.

RESULTS

A total of 201 women enrolled in the study; 17 discontinued participation prior to giving birth, leaving 184 women for whom the birth outcome was known. One hundred and fifty-eight women gave birth vaginally (86%), and information about perineal injury was available for 155 participants. The primary method for identification of women with perineal injury was self-report; clinical records were later retrieved to verify the degree of the perineal laceration. Of this group, 64% had a perineal laceration of any degree (Table 1), and 32% had a 2nd degree or more severe perineal laceration (Table 2).

There were significant baseline demographic differences, including age (*P*=0.03) and income (*P*=.01), between women who did and did not experience any perineal laceration (Table 1). Additionally there were significant baseline demographic differences including age (*P*=.04), personal and family history of depression (*P*=.004), and hours in labor (*P*=.03) between women who did or did not experience a 2nd degree or more severe perineal laceration (Table 2). All subsequent analyses controlled for these variables.

Women who experienced any degree of perineal injury had higher EPDS scores than did women with no injury only at week 1 postpartum (mean =4.6 vs 3.12 respectively, *P*=0.02). In contrast, persistent and significant relationships existed between experiencing a 2nd degree or more severe perineal laceration and symptoms of depression, starting at 1-month postpartum (*P*=0.04) and continuing through at least 3-months postpartum (*P*=0.03) (Table 3). Perceived stress was not significantly different between women with any vs no injury, however in women who had a 2nd degree or more severe laceration, perceived stress was higher compared to women with less severe injury at 3-months postpartum (mean =20.8 vs 17.2 respectively, *P* = 0.02).

No differences in markers of inflammation were found between women reporting any versus no perineal laceration. However, various indicators of inflammation were significantly different among women who experienced a 2nd degree or more severe laceration compared to those with no laceration or a laceration that was less severe (Table 4). The pro-inflammatory cytokine IL-6 plasma levels increased at 2-weeks postpartum (*P*=0.02) and remained elevated through 2-months postpartum (*P*=0.002) among women who experienced a 2nd degree or more severe laceration but there were no differences at 3 and 6 months postpartum. TNF-α, IL-1β, and IFN-γ plasma levels were not significantly different between the groups. Most notably, was the significant and prolonged increase in anti-inflammatory IL-10 in women who experienced a 2nd degree or more severe laceration, that was apparent in the first week after birth (*P*=0.008) and remained at 3-months postpartum (*P*=0.04). The differences in IL-10 plasma levels between groups is striking, suggesting a strong specific (T helper 2) immune response focused on repair and healing after birth injury that continues

well into the postpartum period (Table 4). In table 5, we report the balance between the various pro and anti-inflammatory cytokines. The IL-6/IL-10 ratio was not significantly different between the groups. However, as shown in the table, there were significant decreases in the pro- to anti-inflammatory ratios of TNF-α/IL10, IL-1β/IL-10, and IFN-γ/IL 10 in women with 2nd degree or more severe lacerations, some as far out as 6 months postpartum.

In regard to depressive symptoms, the plasma levels of week 1 TNF-α and IL-10 were shown in regression analyses to be significant contributors to week 1 EPDS scores among women who had a 2nd degree or more severe laceration (*P*=0.003 and *P*=0.035 respectively). No other relationships were identified between any pro- or anti-inflammatory marker and symptoms of stress or depression at any time.

Considering all pertinent variables, linear regression analyses indicated that a 2nd degree or more severe perineal laceration accounted for 5.9% of the variance in EPDS score at 1-month postpartum, the time frame defined by the American Psychological Association DSM-V as consistent with postpartum mood disorder.[30] The overall model was significant at *P*=0.024 (F=2.865), with the independent variable of 2nd degree or more severe laceration significant at *P*=0.035 (t=2.127). No demographic or clinical variable entered (age, length of labor, or personal or family history of depression) remained significant. Although perceived stress level at 1-month postpartum was not significantly different between groups, including the 1-month PSS score increased the significance of the model to *P*<0.001 (F=26.645), explaining 57.7% of the variance in depressive symptoms. The contribution of a 2nd degree or more severe perineal laceration remained significant at *P*=0.042 (F=2.055).

DISCUSSION

While moderate to severe perineal laceration sustained during childbirth has long been recognized as a risk for longterm debilitating symptoms such as chronic pain, dyspareunia, and bowel and bladder incontinence,[16,18,22] the biologic consequences and mechanisms by which such injury may initiate psychological distress have been less a focus of scientific investigation. In this study, a 2nd degree or more severe laceration was associated with postpartum depressive symptoms. The presence of depressive symptoms postpartum can pose a significant threat to maternal and infant health. For women with frank PPD, symptoms may interfere with maternal-infant bonding, maternal adherence to safety practices, breastfeeding, and the cognitive and behavioral development of offspring.[26,43]

Perineal Laceration and inflammation

The experience of perineal laceration during childbirth is common,[16] and many times viewed as an expected outcome of vaginal birth by both women and healthcare providers. In this study, a 2nd degree or more severe perineal laceration was not only associated with postpartum depressive symptoms, but also with immune marker elevations in both pro and anti-inflammatory cytokine plasma levels.

A relationship between depressive symptoms and pro-inflammatory cytokines in postpartum women has been considered by a number of researchers over the last 20 years.[44] Briefly,

over a decade ago, Maes et al.,[9] identified a correlation between serum IL-6 levels and depression in women on postpartum days 1 and 3, however, no samplings at later dates occurred and there was no mention of perineal injury. In a later cross-sectional study by Groer et al,[35] a decrease in IFN-γ/IL-10 ratio in women with depressive symptoms at 4-6 weeks postpartum was reported. Depression, however, was determined using a non-specific measure (the Profile of Mood States [POMS]). Furthermore, women who delivered vaginally or surgically were included, and no information was provided on perineal injury in the women delivering vaginally. In a previous study by our group,[33] women reporting significant symptoms of depression at one month postpartum were found to have higher levels of urinary IL-1β 2-weeks earlier, compared to women who did not report symptoms of depression at one month, suggesting that a pro-inflammatory milieu early in the postpartum period might contribute to the subsequent development of depressive symptoms. Although all of the women included gave birth vaginally, the presence or absence of perineal injury was not evaluated. The lack of consensus regarding the association between inflammation and perinatal depressive symptoms was the subject of a recent review that included in its recommendations the need to consider potentially confounding variables.[44]

In the current study, we evaluated the contribution of one potentially confounding variable, a perineal laceration, on the development of postpartum inflammation and depressive symptoms, finding that women with a second degree or more extensive laceration exhibited increases in IL-6 plasma levels early in the postpartum period, and significant increases in levels of IL-10 at nearly every time point after controlling for age, labor length, and personal and family history of depression. The magnitude of the increase in IL-10 among this group was particularly striking and suggests that a 2nd degree or more severe laceration is a strong immune stimulus, primarily favoring the specific immune response that fights infection and promotes tissue repair and healing rather than frank inflammation.[45] In addition, while it is not surprising that this type of injury initially influenced both pro and anti-inflammatory markers, it is interesting that women with a second degree or more severe laceration demonstrated significantly lower pro to anti- inflammatory cytokine ratios, given our hypothesis. This may be due to the overwhelming influence of IL-10 and other confounders that shift the inflammatory response towards a T helper 2 direction. Thus, perineal laceration, although initially an acute inflammatory event, appears to be a trigger for immune system activation geared towards the production of antibodies, in some cases as far out as six months postpartum.

Inflammation and Depression

Chronic inflammation and depression are associated in non-pregnant populations,[5-8] therefore understanding these pathways may be key to understanding perinatal triggers for depression as well. In our analyses, only an early relationship between depressive symptoms and cytokine plasma levels was identified. The depression scores prenatally were insignificant between the groups. However, findings from the exploratory regression analysis indicates a potential mediation effect of the pro-inflammatory cytokine TNF-α and thus calls for a formal analysis to test the underlying causal relationship between perineal injury and the risk of developing PPD symptoms via the inflammatory pathways. Future studies should also consider other mechanisms by which elevated inflammatory cytokines

such as IL-6 may affect mood, for example through perturbations in sleep or by heightening a woman's perception of stress.

Limitations

The primary method for identification of women with perineal injury was self-report; clinical records were later retrieved to verify the degree of the laceration, however documentation of injury and/or its degree was not always present in the chart. Additionally, data outlining the specific type of laceration (eg, labial, vaginal) or whether there was other genital tract injury (eg, cervical laceration) was not extracted from the medical chart. For the cases that were available to confirm with chart review, however, the verification with self-report showed 84% accuracy for 1st degree and 89% for 2nd degree.

This study is also limited by the relatively small sample size and limited sample diversity. Furthermore, it may be that the inflammatory pathways to depressive symptoms in this population are limited due to other factors obscuring the pro-inflammatory response, such as the use of anti-inflammatory agents for post-partum pain. Future studies would benefit in obtaining a larger sample size of women from a variety of racial, ethnic and cultural backgrounds, and controlling for additional factors such as medication usage.

CLINICAL IMPLICATIONS

Healthcare practitioners might consider close monitoring and additional education prenatally about behaviors that may affect tissue integrity, such as adequate nutrition and hydration, to decrease the risk of severe lacerations during birth. Additionally, women with previous personal and/or family history of depression may benefit from additional education prenatally regarding risk factors for perineal injury. It is plausible that a history of depression may increase the likelihood of engaging in poor health behaviors such as poor sleep and nutrition, which may promote poor tissue health and slow recovery following injury.[46,47] In addition, providers should protect the perineum as much as possible during childbirth by carefully controlling the delivery of the fetal head,[48] and limiting episiotomy use except in necessary situations.[48] Some practitioners may incorporate perineal massage to promote tissue pliability in hopes of preventing injury, however findings from recent studies are inconsistent [49,50] and more research is needed to determine the timing and usefulness of perineal massage.

After giving birth, depressed mood typically starts within the first 4 weeks postpartum, therefore women with a perineal laceration that is more severe than a second degree laceration should perhaps be seen sooner than the standard 6-week follow up visit. This will allow for early screening and intervention. Subjective questions about the degree of perineal laceration might be added to routine postpartum screening tools as well, in hopes of identifying women at risk for chronic inflammation and/or depression, especially in cases where chart review is not available. Women in our study appeared to be accurate historians of their degree of injury; therefore if a woman reports a second degree or more severe laceration this may serve as a red flag to assess for symptoms of depression.

Future research targeting inflammation may prove beneficial in improving the mental health of women with significant tissue injury during childbirth. Although the current study suggests that inflammation and depressed mood may be associated, more research is essential. It may be that the relationship between PPD and chronic inflammation is bidirectional, and that women with PPD are at increased risk for chronic inflammation and poor healing. If further studies confirm a relationship, examining therapeutic and wellness related anti-inflammatory therapies might be warranted.

CONCLUSION

In summary, although identification of psychosocial factors that confer increased risk of PPD has contributed significantly to understanding of its etiology, considering psychosocial risk factors alone leaves substantial variance in PPD unexplained. Likewise, although psychosocial interventions to improve postpartum mood can be successful, their efficacy remains limited for many women. As a result, over the last decade, the study of depressed mood postpartum has shifted to include a deeper exploration of underlying biologic mechanisms that may play a fundamental role in its genesis; the data presented in this study support the need for continuing this avenue of exploration.

Acknowledgements

This study was funded by a grant to Dr. Elizabeth J. Corwin (R01NR011278) from the National Institutes of Health, National Institute of Nursing Research (NINR). Without their generous contribution to all aspects of this study (subject recruitment and compensation, data collection, bioassays, etc.) this study could not have been accomplished. The content of this paper is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

This work was supported by a grant from the National Institutes of Health, National Institute of Nursing Research (1R01NR011278).

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Quick Points

- 2nd degree or more severe lacerations are associated with the development of postpartum depressive symptoms through 3 months postpartum
- 2nd degree or more severe lacerations exert significant effects on inflammatory markers even at 6 months postpartum.
- More research is needed to elucidate the relationship between inflammation and postpartum depressive symptoms in women who experience 2nd degree or more severe lacerations during birth.

Table 1

Demographic and Clinical Characteristics of Women Without ("No") or With ("Yes") Any Perineal Laceration (N=155[a])

Demographic and Clinical Characteristics	No Perineal Laceration[b] (N=56)	Yes Perineal Laceration (N=99)	*P*-Value
Age, mean (SD)	27.6 (5.2)	29.5 (5.1)	0.03
BMI, mean (SD), kg	24.5 (4.5)	23.7 (4.1)	0.24
Marital, n (%)	40 (71)	85 (86)	0.10
Caucasian, n (%)	38 (68)	81 (82)	0.05
Not receiving WIC, n (%)	35 (63)	81 (82)	0.01
Hours in Labor, mean (SD)	9.5 (6.4)	12.4 (11.2)	0.07
Personal History of Depression, n (%)	10 (18)	24 (24)	0.36
Family History of Depression, n (%)	17 (30)	44 (44)	0.09

Abbreviations: BMI, Body Mass Index; WIC, Women, Infants, and Children

[a]Data are presented as the mean +/− standard deviation (SD).

[b]Perineal Laceration is defined as report of any injury, yes/no

Table 2

Demographic and Clinical Characteristics of Women Without (No) or With (Yes) a 2nd Degree or More Severe Perineal Laceration (N=153[a])

Demographic and Clinical Characteristics	Less than 2nd Degree Laceration (N=103)	2nd Degree or >[b] Laceration (N=50)	*P*-Value
Age, mean (SD)	28.2 (5.1)	30.0 (5.1)	0.04
BMI, mean (SD), kg	23.9 (4.0)	24.1 (4.5)	0.75
Marital (%)	82 (80)	41 (82)	0.55
Caucasian, n (%)	77 (75)	40 (80)	0.47
Not receiving WIC	73 (71)	42 (84)	0.08
Hours in Labor, mean (SD)	10.1 (7.6)	14.0 (13.1)	0.03
Personal Hx of Depression, n (%)	16 (16)	18 (36)	0.004
Family Hx of Depression, n (%)	31 (30)	27 (54)	0.004

Abbreviations: BMI, Body Mass Index; Hx, history; WIC, Women, Infants, and Children

[a] The sample size is different between tables one and two as 2 women reported they experienced a perineal laceration, however were not able to report the degree, which also was not identified in their charts; these women were excluded from the +/- 2nd degree group. Data are presented as the mean +/− standard deviation (SD).

[b] 2nd degree or > is defined as perineal laceration reported as second degree or more severe, yes/no

Table 3

Edinburgh Postnatal Depression Scores for Women Without (No) or With (Yes) 2nd Degree or More Severe Perineal Laceration[a]

Time Point	Less than 2nd Degree Laceration	2nd Degree or >[b] Laceration	P-Value
	EPDS Score[c]	EPDS Score	
Prenatal	4.30 (3.7)	4.83 (3.6)	0.29
Week 1	3.61 (3.5)	4.98 (3.5)	0.08
Week 2	3.24 (3.1)	3.78 (3.1)	0.45
Month 1	3.05 (3.5)	4.55 (3.1)	0.04
Month 2	2.81 (3.0)	4.18 (3.0)	0.02
Month 3	2.81 (2.9)	4.15 (3.9)	0.03
Month 6	2.88 (3.2)	4.33 (3.4)	0.06

Abbreviations: EPDS, Edinburgh Postnatal Depression Score; PSS, Perceived Stress Score.

[a] Data are presented as mean +/− the standard deviation (SD). P values are corrected for significant demographic variables.

[b] 2nd degree or > is defined as perineal laceration reported as second degree or more severe, yes/no

[c] Minimum score is 0 Maximum Score is 30

Table 4

Pro and Anti Inflammatory Cytokine Levels (pg/mL) for Women Without (No) or With (Yes) 2nd Degree or More Severe Perineal Laceration (N=136[a])

Cytokine	Time Point	Less than 2nd Degree Laceration	2nd degree or >[b] Laceration	P-Value
IL-6				
	Prenatal	1.65 (.15)	2.35 (.74)	0.18
	Postpartum Week 1	2.78 (.21)	3.49 (.70)	0.09
	Postpartum Week 2	1.58 (.11)	2.38 (.54)	0.02
	Postpartum Month 1	1.69 (.15)	2.44 (.58)	0.05
	Postpartum Month 2	1.39 (.14)	2.66 (.79)	0.002
	Postpartum Month 3	1.66 (.34)	2.70 (1.34)	0.16
	Postpartum Month 6	1.70 (.23)	1.73 (.31)	0.23
IL-10				
	Prenatal	3.35 (.29)	19.65 (7.65)	0.15
	Postpartum Week 1	3.71 (.35)	22.18 (8.84)	0.01
	Postpartum Week 2	3.85 (.82)	23.39 (12.47)	0.02
	Postpartum Month 1	4.27 (.72)	24.12 (9.79)	0.01
	Postpartum Month 2	3.47 (.51)	28.91 (14.34)	0.003
	Postpartum Month 3	4.08 (.57)	24.59 (10.88)	0.04
	Postpartum Month 6	8.01 (3.57)	20.53 (9.69)	0.09

Abbreviations: IL-6, Interleukin-6; IL-10, Interleukin-10;

Serum Cytokines were determined as described in Methods.

[a] Blood collections were unsuccessful at various times, leading to fewer cytokine assays. Data are presented as mean +/− standard error (SE). Although actual plasma levels (pg/mL) are reported, log transformed values were used for all statistical analyses.

[b] denotes perineal lacerations that are second degree or more severe

Table 5

Comparison of the Pro to Anti Inflammatory Cytokine Ratio for Women Without (No) or With (Yes) 2nd Degree or More Severe Perineal Laceration (N=136[a]).

Cytokine Ratio	Time Point	Less than 2nd Degree Laceration	2nd degree or >[b] Laceration	P-Value
TNF-α/IL-10				
	Prenatal	2.47 (.21)	1.63 (.16)	0.002
	Postpartum Week 1	2.27 (0.24)	1.78 (.31)	0.02
	Postpartum Week 2	13.49 (10.99)	1.71 (.22)	0.002
	Postpartum Month 1	5.03 (2.34)	2.05 (.33)	0.005
	Postpartum Month 2	3.45 (.45)	2.04 (.27)	0.001
	Postpartum Month 3	3.40 (.68)	2.49 (.57)	0.02
	Postpartum Month 6	2.92 (.35)	2.35 (.60)	0.04
IL-1β/IL-10				
	Prenatal	0.18 (.02)	0.24 (.12)	0.04
	Postpartum Week 1	0.59 (.30)	0.19 (.08)	0.004
	Postpartum Month 1	0.56 (0.27)	0.37 (.20)	0.04
	Postpartum Month 2	0.40 (.13)	0.15 (.03)	0.01
	Postpartum Month 6	0.27 (.06)	0.13 (.03)	0.001
IFN-γ/IL-10				
	Prenatal	0.75 (.11)	0.63 (.19)	0.004
	Postpartum Week 1	0.97 (.13)	0.64 (.12)	0.02

Abbreviations: IL-6, Interleukin-6; TNF-α, Tumor Necrosis Factor Alpha; IL-10, Interleukin-10; IFN-γ, Interferon Gamma.

[a] Blood collections were unsuccessful at various times, leading to fewer cytokine assays. Data are presented as mean ratios +/− standard error (SE). Although actual ratios are reported, log transformed values were used for all statistical analyses.

[b] > denotes perineal lacerations that are second degree or more severe