# Peripartum Infectious Morbidity in Women with Preeclampsia

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## ABSTRACT

*Background:* Dysregulated maternal systemic inflammatory response is part of the pathogenesis of preeclampsia. It leads to chronic inflammation characterized by oxidative stress, pro-inflammatory cytokines, and auto-antibodies.
*Objective*: To examine the association between the diagnosis of preeclampsia and chorioamnionitis, postpartum fever, endometritis and wound infection.
*Study Design*: This was a retrospective cohort study of the Consortium on Safe Labor in women ≥ 24 weeks of gestation. Women presenting with PPROM were excluded from the analysis. The primary outcome was a composite of maternal peripartum infection including chorioamnionitis, postpartum fever, endometritis and wound infection. This outcome was compared between women with and without preeclampsia using univariable and multivariable analyses.
*Results*: A total of 102,304 women were eligible for the analysis, of these 8,235 (8.0%) were diagnosed with preeclampsia. In univariable analysis, as expected, women with preeclampsia were older (28.2 ± 6.7, vs. 27.7 ± 6.2), had higher BMI (37.0 ± 6.4 vs. 35.7 ± 5.3 ), were more likely to be non-Hispanic black (38.2% vs. 28.7%), nulliparous (50.3% vs. 35.7%), carry multifetal gestation (5.2% vs. 1.9%), and more likely to undergo induction of labor (49.0% vs. 30.3%) (all p values <0.001). The rate of tobacco use was lower among women with preeclampsia (6.1% vs. 7.0%, p=0.002). The rate of composite maternal peripartum infection was higher among women with preeclampsia (6.8% vs.4.3%, p<0.001, odds ratio of 1.64, 95% confidence interval 1.50 – 1.80). In multivariable logistic regression, adjusted for significant variables from the univariable analysis as well as risk factors for maternal peripartum infection, including pre-gestational and gestational diabetes, number of digital exams during labor, premature ROM, GBS status, presence of sexually transmitted infections during this pregnancy, IUPC use, time from ROM to delivery, and mode of delivery, the association between preeclampsia and composite maternal peripartum infection did not persist.
*Conclusion*: In this large cohort of women with a diagnosis of preeclampsia, no association was found between preeclampsia and peripartum infectious morbidity. Women with preeclampsia were not more likely to have peripartum infections after adjusting for risk factors for maternal infectious morbidity.

## BACKGROUND

- **Inflammatory dysregulation** is considered a key component of preeclampsia
  - Overproduction of inflammatory cytokines
  - Decrease in anti-inflammatory processes
  - Worsening oxidative stress
  - Increase in inflammatory T-cells
- This leads to physiologic changes such as:
  - **Endothelial damage and dysfunction**
  - Tissue edema
  - Internal organ damage/failure
- These same changes occur with infectious processes
- Additionally, factors that contribute to infection and preeclampsia overlap significantly, particularly:
  - Diabetes
  - Obesity
  - Cesarean delivery
  - Induction of labor
- **It is unknown whether there is an association between preeclampsia and maternal peripartum infection**

## OBJECTIVE

The goal of this study was to evaluate whether the heightened inflammatory state of preeclampsia predisposes women to develop peripartum infectious complications such as chorioamnionitis, postpartum fever, endometritis and/or wound infection in a large population.

We hypothesized that women with preeclampsia will have higher rates of a composite infectious morbidity.

## METHODS

- Secondary analysis of de-identified patient data from the Consortium on Safe Labor (CSL) through the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)
- Retrospective data collected during labor and delivery admissions for over 228,000 deliveries from nineteen hospitals in the United States from 2002 to 2008
- **Primary outcome: a composite infectious outcome including chorioamnionitis, endometritis, wound infection, and postpartum fever**
- Inclusion criteria:
  - Pregnant women 18 years of age or older
  - Viable singleton pregnancy
  - >= 24 weeks gestation at delivery
- Exclusion criteria:
  - Preterm premature rupture of membranes
- All tests were two-tailed and p<0.05 was used to define statistical significance
- Univariable comparisons were conducted with Chi-square, Fisher exact, or one-way ANOVA as appropriate
- Multivariable logistic regression was used to estimate the independent association between preeclampsia and infectious complications

## RESULTS

- A total of 102,304 women were eligible for the analysis. 8,235 women (8.0%) were diagnosed with preeclampsia

## RESULTS

**Table 1. Maternal characteristics**

| | Preeclampsia (n=8,235) | Controls (n=94,069) | P-value |
|---|---|---|---|
| Maternal age (years ± SD) | 28.2 ± 6.7 | 27.7 ± 6.2 | p < 0.001 |
| Maternal race/ethnicity | | | |
| Non Hispanic white | 3,190 (40.9) | 42,587 (47.7) | |
| Non Hispanic black | 2,881 (38.2) | 25,593 (28.7) | p < 0.001 |
| Hispanic | 1,191 (15.3) | 14,752 (16.5) | |
| Other | 446 (5.7) | 6,272 (7.0) | |
| BMI (kg/m$^2$ ± SD) | 37.0 ± 6.4 | 35.7 ± 5.3 | p < 0.001 |
| Nulliparity | 4,143 (50.3) | 33,573 (35.7) | p < 0.001 |
| Tobacco use | 499 (6.1) | 6,565 (7.0) | p = 0.002 |
| Chronic hypertension | 1,440 (17.5) | 2,251 (2.4) | p < 0.001 |
| Pre-gestational diabetes | 419 (5.1) | 1,680 (1.8) | p < 0.001 |
| Induction of labor | 4,034 (49.0) | 28,484 (30.3) | p < 0.001 |
| Gestational diabetes | 852 (10.4) | 6,081 (6.5) | p < 0.001 |

**Table 2. Pregnancy outcomes**

| | Preeclampsia (n=8,235) | Controls (n=94,069) | P-value |
|---|---|---|---|
| Gestational age at delivery (wks) | 36.5 ± 3.5 | 38.6 ± 2.3 | p < 0.001 |
| Cesarean Delivery | 4,195 (50.9) | 28,907 (30.7) | p < 0.001 |
| Composite infectious morbidity | 563 (6.8) | 4,026 (4.3) | p < 0.001 |
| Chorioamnionitis | 171 (2.1) | 2,212 (2.4) | p = 0.113 |
| Endometritis (n=70,732) | 58/6,220 (0.9) | 288/64,512 (0.4) | p < 0.001 |
| Wound infection (n=64,122) | 46/5,090 (0.9) | 241/59,032 (0.4) | p < 0.001 |
| Postpartum fever (n=68,308) | 442/5,896 (7.5) | 2,696/62,412 (4.3) | p < 0.001 |

**Table 3. Multivariable analysis***

| Composite Infectious Morbidity | aOR | 95% Confidence Interval | P-value |
|---|---|---|---|
| Pre-eclampsia this pregnancy | 0.89 | 0.61-1.30 | p = 0.548 |
| **Cesarean Delivery** | **4.22** | **3.34-5.34** | **p < 0.001** |
| Pre-pregnancy BMI (kg/m2) | 1.00 | 0.98-1.02 | p = 0.807 |
| **Hispanic ethnicity** | **2.27** | **1.75-2.96** | **p < 0.001** |
| **Nulliparity** | **2.73** | **2.11-3.53** | **p < 0.001** |
| **IUPC placement** | **2.05** | **1.58-2.67** | **p < 0.001** |
| Pre-gestational diabetes mellitus | 1.63 | 0.94-2.93 | p = 0.082 |
| Gestational diabetes mellitus | 0.92 | 0.63-1.33 | p = 0.650 |
| Chronic hypertension | 0.93 | 0.48-1.79 | p = 0.827 |

*Adjusted for pre-gestational and gestational diabetes, number of digital exams during labor, premature ROM, GBS status, presence of sexually transmitted infections during pregnancy, IUPC use, time from ROM to delivery, and mode of delivery

## CONCLUSION

Women with preeclampsia were not more likely to experience infectious morbidity than women without preeclampsia.