OBSTETRICS

Infectious morbidity is higher after second-stage compared with first-stage cesareans

Methodius G. Tuuli, MD, MPH; Lucy Liu, BS; Ryan E. Longman, MD; Anthony O. Odibo, MD, MSCE; George A. Macones, MD, MSCE; Alison G. Cahill, MD, MSCI

OBJECTIVE: The objective of the study was to compare maternal and neonatal infectious morbidity following cesareans performed in the second and first stages of labor.

STUDY DESIGN: We conducted a retropective cohort study of all consecutive, singleton, term, cesarean deliveries in laboring women in a single institution from 2005 to 2012. Second-stage cesareans were defined as those performed at complete cervical dilation (10 cm), and first-stage cesareans were those performed before 10 cm cervical dilation. The primary outcome was endometritis. Rates of infectious morbidity were compared in the 2 groups. Multivariable logistic regression was used to calculate adjusted risk estimates.

RESULTS: Of 2505 cesareans meeting inclusion criteria, 400 (16.0%) were performed in the second stage, whereas 2105 (84.0%) were performed in the first stage of labor. The risk of endometritis was nearly 3-fold higher in second- compared with first-stage cesareans (4.25% vs 1.52%; crude odds ratio, 2.88; 95% confidence interval, 1.58—5.23). The risk remained significantly higher after controlling for confounders (adjusted odds ratio, 2.78; 95% confidence interval, 1.51—5.09).

CONCLUSION: Second-stage cesarean is associated with an increased risk of endometritis compared with first-stage cesarean. Further studies will determine whether different infection preventive strategies are needed at second-stage cesareans to reduce endometritis.

Key words: cesarean, first stage, infections, labor, second stage

Cite this article as: Tuuli MG, Liu L, Longman RE, et al. Infectious morbidity is higher after second-stage compared with first-stage cesareans. Am J Obstet Gynecol 2014;211:410.e1-6.

Cesarean delivery is the most common major surgical procedure performed on women in the United States. In 2012, 1.3 million of the 4 million births in the United States (32.8%) were by cesarean.[1] Infectious morbidity is one of the most common complications, affecting 2-20% of cesareans, depending on the population.[2] Although some infections are superficial, a significant proportion are more severe and involve deeper abdominal wall tissue, the peritoneal cavity, or the uterus.[3] These require prolonged hospitalization, readmissions, or additional outpatient visits. The sheer numbers of these infections represent a substantial burden for individuals and the health care system.[4] Although costs vary, depending on the location, depth, and severity, the average attributable cost for each cesarean infection is estimated to be $2800-3400.[5]

Preoperative antibiotic prophylaxis has been established as an effective preventive measure for reducing postcesarean infections. The Cochrane review of randomized trials suggests a 60% decrease in postcesarean infections when antibiotic prophylaxis is used at cesarean delivery.[2] In addition, pooled results from five randomized trials showed a further 50% reduction in the risk of endometritis and a possibly lower rate of wound infections when antibiotics are administered prior to skin incision rather than after cord clamp.[6] However, even with optimal use of preoperative antibiotic prophylaxis the rate of postcesarean infections remains high.[7]

Identifying specific subgroups at higher risk for residual infections will permit the application of tailored preventive strategies. Prior studies have compared intraoperative and postoperative complications following second-stage and first-stage cesarean with mixed results.[8-12] A number of these studies primarily compared composite maternal and neonatal outcomes, and infectious morbidity was not the primary focus.

The objective of this study was to compare the risk of infectious morbidity following cesarean performed in the second stage with those performed in the first stage of labor. We hypothesized that

From the Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, MO.

Received Jan. 21, 2014; revised Feb. 23, 2014; accepted March 14, 2014.

The views expressed herein are those of the authors and do not necessarily represent the official view of the National Institutes of Health or the Robert Wood Johnson Foundation.

M.G.T. is supported by Women's Reproductive Health Research Career Development grant 1K12HD063086-01 from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. A.G.C. is supported by *Eunice Kennedy Shriver* National Institute of Child Health and Human Development grant R01HD061619-01 and was a Robert Wood Johnson Faculty Physician Scholar, which partially supported this work.

The authors report no conflict of interest.

Reprints: Methodius Tuuli, MD, MPH, Department of Obstetrics and Gynecology, Washington University School of Medicine, Campus Box 8064, 4566 Scott Ave., St. Louis, MO 63110. methodiustuuli@yahoo.com

0002-9378/$36.00 • • http://dx.doi.org/10.1016/j.ajog.2014.03.040

women undergoing cesarean in the second stage constitute a subgroup at higher risk for postcesarean infections.

Materials and Methods

We conducted a retrospective cohort study of all consecutive, singleton, term cesarean deliveries in the setting of labor from 2005 to 2012 at Washington University in the St. Louis Medical Center. The study was approved by the Washington University School of Medicine Human Research Protection Office.

Subjects were selected from a comprehensive database of all deliveries. Trained research nurses abstracted demographic information from patients' records including medical and surgical history, obstetric and gynecological history, and prenatal history. We also obtained detailed labor and delivery information including labor duration, medications, diagnosis of chorioamnionitis, and mode of delivery. For women who underwent cesarean delivery we obtained information on the stage of labor in which the cesarean was performed, indication for cesarean delivery, antibiotic administration, and postoperative complications including maternal fever, endometritis, and suspected or proven neonatal sepsis.

Our institutional protocol for prophylactic antibiotics at a cesarean calls for the administration of a single dose of antibiotics within 60 minutes prior to the skin incision. However, in emergent situations these antibiotics are administered as soon as practical after skin incision. One or two grams of cefazolin are generally used, except in women who are allergic to cephalosporins in which case clindamycin is given.

Women were eligible if they carried a term singleton fetus and underwent cesarean during labor. We excluded women who underwent prelabor cesarean and those carrying multiple gestations or anomalous fetuses. Term pregnancy was defined as gestational age of 37 weeks or longer. Pregnancies were dated by a woman's last menstrual period and confirmed with a first- or second-trimester ultrasonography using standard criteria.[13] The timing of the cesarean in the first or second stage defined the comparison groups. First-stage cesareans were defined as cesareans performed any time during labor but prior to complete (10 cm) cervical dilation, whereas second-stage cesareans were those performed after complete cervical dilation.

The primary outcome was endometritis as diagnosed clinically by the attending physician from delivery until 6 weeks' postpartum. An institutional standard protocol guides this clinical diagnosis, specifying the following: (1) maternal fever (temperature >38.0°C on 2 occasions, 4 hours apart or >39.0°C on 1 occasion) more than 12 hours after delivery; (2) uterine tenderness; and (3) no evidence of another infection.

Secondary outcomes were wound infection (defined clinically from delivery until 6 weeks postpartum), maternal fever (defined as maternal temperature >38.0°C after 24 hours' postpartum), and suspected or confirmed neonatal sepsis. Suspected neonatal sepsis was defined as neonatal clinical signs and symptoms indicative of possible sepsis and requiring laboratory workup (complete blood count, blood cultures, chest x-ray, and spinal puncture) or the administration of antibiotics. Proven sepsis was defined as bacteria isolation from blood, cerebrospinal fluid, or urine cultures in addition to clinical, radiographic, or laboratory findings consistent with the diagnosis of sepsis.

We compared baseline characteristics of women who underwent first-stage and second-stage cesareans. Continuous variables were compared using the independent Student t test, whereas categorical variables were compared using the χ^2 or Fisher exact test as appropriate. Normality of distribution of the continuous variables was confirmed using the Kolmogorov-Smirnov test. We calculated rates and unadjusted odds ratios with 95% confidence intervals (CIs) for endometritis and the secondary outcomes.

Multivariable logistic regression was used to adjust for confounders and calculate adjusted odds ratios. Candidate variables for the logistic regression models were selected on the basis of biological plausibility, risk factors that have been identified in prior studies for the various outcomes, and results of our univariable and stratified analyses. The number of variables in each model was reduced using backward elimination. Differences between hierarchical explanatory models were assessed using the Wald test. Model fit for the final models was assessed with the Hosmer-Lemeshow goodness-of-fit test.[14]

Because chorioamnionitis may be more common in women undergoing second-stage cesarean and is also a risk factor for postpartum infectious morbidity, we repeated the analysis excluding women with chorioamnionitis. To explore whether latent or active labor influenced the risk of infectious morbidity following first-stage cesarean we compared the rates of endometritis in the latent (cervical dilation <6 cm) and active (6 to <10 cm) phases of labor.

Finally, to explore whether time in labor explained the increased risk of infectious morbidity associated with second-stage cesarean, we used a time-to-event analysis to account for the length of labor. The Cox proportional hazard model was fitted, adjusting for potentially confounding factors. The proportional hazards assumption was tested using the Schoenfeld's global test.[15]

We included all consecutive subjects meeting inclusion criteria; no a priori sample size estimation was performed. Statistical tests were all 2 tailed and $P < .05$ was considered significant. All statistical analyses were completed using the STATA software package, version 11, special edition (StataCorp, College Station, TX).

Results

Of 2505 women meeting inclusion criteria who underwent cesarean during labor, 2105 (84.0%) were performed during the first stage and 400 (16.0%) during the second stage (Figure 1). Maternal age, prevalence of diabetes, use of epidural anesthesia, and preoperative antibiotics prior to the cord clamp were not significantly different between the 2 groups. Women undergoing second-stage cesarean were more likely to be African American, have a higher body