# Prior pregnancy outcome and the risk of intraamniotic infection in the following pregnancy

**Marijane A. Krohn, PhD,[a] Marc Germain, MD, PhD,[b] Kathrin Mühlemann, MD, PhD,[c] and Durlin Hickok, MD[d]**

*Pittsburgh, Pennsylvania, Quebec, Quebec, Canada, Bern, Switzerland, and Seattle, Washington*

**OBJECTIVE:** Our purpose was to determine whether the outcome of a prior pregnancy influenced the risk of intraamniotic infection in the following pregnancy.

**STUDY DESIGN:** A case-control study was conducted at five King County, Washington, hospitals from 1990 through 1994. Cases ($n$ = 585) of intraamniotic infection were identified by a medical record review for clinical signs of infection during labor and compared with controls ($n$ = 575). Women were classified as having a spontaneous abortion or elective termination if the pregnancy had been diagnosed by a health care professional before 20 weeks and was verified by medical record review. Adjusted odds ratios and 95% confidence intervals were estimated using logistic regression.

**RESULTS:** Women with spontaneous abortion (odds ratio = 4.3; 95% confidence interval 2.9 to 6.4) or elective termination (odds ratio = 4.0; 95% confidence interval 2.7 to 5.8) had an increased risk of intraamniotic infection. The increased risk was similar for women who did and did not have an earlier pregnancy carried beyond 20 weeks.

**CONCLUSIONS:** Women who have had a spontaneous abortion or an elective termination have an increased risk of intraamniotic infection regardless of previous successful pregnancy outcome. (Am J Obstet Gynecol 1998;178:381-5.)

**Key words:** Amnionitis, spontaneous abortion, elective termination

Intraamniotic infection (IAI) is a serious condition diagnosed during labor that affects both the mother and the neonate.[1,2] It is frequently diagnosed by clinical signs and symptoms because isolating an etiologic agent from the amniotic fluid once labor has begun and the fetal membranes have ruptured has proved unrewarding.[3] The microorganisms associated with IAI can also be isolated from vaginal specimens, which has led investigators to conclude that IAI is the result of an ascending genital infection by opportunistic genital flora.[4-6]

Among all births, the frequency of IAI is from 2% to 5%; however, the frequency is increased for women delivering preterm (5% to 15%) compared with women delivering at term.[7-9] IAI has very serious consequences for neonates born after a labor for which it is a complication. After controlling for preterm delivery, infants have a twofold increased risk of death and a greater than twofold increased risk of sepsis.[2] Women who have IAI during labor have a greater than threefold increased risk of cesarean delivery and an increased risk of postpartum endometritis.[9] The greatly increased risk of neonatal death and the increased risk of maternal morbidity associated with IAI make it an important target for intervention strategies. IAI has a number of characteristics that make successful treatment difficult when it is identified during labor: its sudden onset during labor, diagnostic signs that lack specificity, absence of rapid microbiologic diagnostic tests that lead to appropriate antimicrobial treatments, the time interval necessary for antimicrobial treatments to become effective, and the uncertain efficacy of intrapartum antimicrobial treatments in preventing neonatal sepsis. It is important to identify women at high risk of IAI before labor begins because of the ineffectiveness of intervention strategies once labor begins.

Prior studies have identified few risk factors or risk markers from the same pregnancy, known before labor begins, that are associated with an increased risk of IAI. These characteristics have been proposed by some investigators but not confirmed by others: first pregnancy, nonwhite race, and young age of mother at delivery.[4,7,8,10] Investigators have also examined the relationship of prior pregnancy outcomes with the risk of IAI. These

*From the Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh,[a] Group de recherche en épidémiologie, Hôpital du Saint-Sacrement,[b] Institute of Medical Microbiology, University of Bern,[c] and Department of Epidemiology, SC-36, University of Washington.[d]*

*Supported by grant number HD 26377 from the National Institutes of Health.*

*Received for publication April 8, 1997; revised May 27, 1997; accepted September 18, 1997.*

*Reprint requests: Marijane A. Krohn, PhD, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh, Magee-Womens Hospital, 300 Halket Street, Pittsburgh, PA 15213.*

*Copyright © 1998 by Mosby, Inc.*

*0002-9378/98 $5.00 + 0* ***6/1/86260***

**Table I.** Demographic and social characteristics of women with IAI and control subjects

| | IAI | | |
|---|---|---|---|
| | *Cases (n = 585)* | *Controls (n = 575)* | *Significance* |
| Age | | | $p = 0.2$ |
| 16-19 yr | 36 (6%) | 31 (5%) | |
| 20-25 yr | 132 (22%) | 109 (19%) | |
| 26-30 yr | 173 (30%) | 158 (28%) | |
| ≥31 yr | 244 (42%) | 277 (48%) | |
| Race | | | $p = 0.03$ |
| White | 438 (75%) | 469 (82%) | |
| Black | 52 (9%) | 37 (6%) | |
| Other | 94 (16%) | 69 (12%) | |
| Married | | | $p = 0.001$ |
| Yes | 434 (74%) | 472 (82%) | |
| No | 151 (26%) | 103 (18%) | |
| Smoking during pregnancy | | | $p = 0.7$ |
| Yes | 66 (11%) | 60 (10%) | |
| No | 519 (89%) | 515 (90%) | |
| Alcohol use during pregnancy | | | $p = 0.9$ |
| Yes | 84 (14%) | 83 (14%) | |
| No | 501 (86%) | 492 (86%) | |

**Table II.** Obstetric characteristics of women with IAI and control subjects

| | IAI | | |
|---|---|---|---|
| | *Cases (n = 585)* | *Controls (n = 575)* | *Significance* |
| Gravidity | | | $p < 0.001$ |
| 1 | 271 (46%) | 153 (27%) | |
| 2 | 150 (26%) | 199 (35%) | |
| ≥3 | 164 (28%) | 223 (39%) | |
| Preterm delivery | | | $p < 0.001$ |
| Yes | 97 (17%) | 35 (6%) | |
| No | 486 (83%) | 539 (94%) | |
| Premature rupture of membranes | | | $p < 0.001$ |
| Yes | 240 (41%) | 135 (24%) | |
| No | 343 (59%) | 440 (76%) | |
| Duration of rupture of membranes | | | $p < 0.001$ |
| ≥25 hr | 124 (22%) | 19 (3%) | |
| 13-24 hr | 194 (34%) | 77 (14%) | |
| 0-12 hr | 247 (44%) | 469 (83%) | |
| Duration of labor | | | $p < 0.001$ |
| ≥25 hr | 57 (11%) | 7 (1%) | |
| 13-24 hr | 263 (49%) | 108 (20%) | |
| 0-12 hr | 218 (40%) | 431 (79%) | |

studies have shown that abortion in a previous pregnancy may increase the risk of IAI.[10, 11] These studies were not able to separate the effect of spontaneous abortion or elective termination of pregnancy. The purpose of this study is to determine whether the outcome of prior pregnancies influences the risk of IAI. More specifically, does a shortened prior pregnancy because of spontaneous abortion or elective termination increase the risk of IAI? Furthermore, is the relationship of shortened pregnancy with IAI similar regardless of the outcome of earlier pregnancies?

## Material and methods

Women were enrolled into a case-controlled study from 1990 through 1994 at five King County, Washington, hospitals: University of Washington Medical Center, Swedish Hospital Medical Center, Group Health Cooperative of Puget Sound, Overlake Hospital Medical Center, and Valley Medical Center. The protocol was approved by the human experimentation review board at the University of Washington and at each of the hospitals. These hospitals were chosen because they had the largest number of deliveries and they represented 70% of births in King County. To identify cases, women's medical records were reviewed for signs of IAI. The medical record review categorized 1213 women as having IAI on the basis of the following criteria: intrapartum temperature of at least 37.8° C accompanied by at least two of the following signs present intrapartum: maternal (>100 beats/min) or fetal (>160 beats/min) tachycardia, uterine tenderness, purulent amniotic fluid, and peripheral leukocyte count >15,000.[12] Control subjects were selected from the same hospital and delivering in the same month as study subjects. Systematic sampling was used to select control subjects from among women who did not have the signs of IAI.

From among the 1213 case women identified, 301 were not eligible because they lived outside King County (62%), had a multiple gestation (7%), spoke no English (26%), or were <16 years old (5%). From the remaining 912 potential cases, 290 women did not enroll for the following reasons: physician refusal (5%), respondent refusal (20%), or out-of-date address information (7%). The remaining 622 women (68%) enrolled. A complete medical record review was not available on 37 case women (6%). From among 1165 eligible controls, 452 women did not enroll because of the following reasons: physician refusal (35), respondent refusal (13%), out-of-date address information (22%). The remaining 713 women enrolled (61%). A complete medical record review was not available on 138 control women (19%).

Obstetric definitions include the following: Women were categorized as having premature rupture of membranes if fetal membranes spontaneously ruptured before the onset of contractions at any gestational age. Preterm delivery was defined as gestation <37 completed weeks. Gestational age at delivery was based on the best obstetric estimate when women were admitted for delivery obtained from the medical record review.

Case and control subjects provided demographic,

**Table III.** Risk of IAI associated with shortened prior pregnancy regardless of gravidity

| | *IAI* | | | |
|---|---|---|---|---|
| | *Cases (n = 585)* | *Controls (n = 575)* | *OR** | *CI** |
| Outcome of prior pregnancy† | | | | |
| Birth >20 wk | 85 (15%) | 254 (44%) | 1.0 | — |
| No prior pregnancy | 261 (45%) | 148 (26%) | 5.5 | 4.0-7.8 |
| Spontaneous abortion | 100 (17%) | 70 (12%) | 4.3 | 2.9-6.4 |
| Elective termination | 127 (22%) | 90 (16%) | 4.0 | 2.7-5.8 |
| No information | 12 (2%) | 13 (2%) | Not estimated | |

*OR*, Odds ratio; *CI*, 95% confidence interval.
*Adjusted for age, race, marital status, and hospital of delivery.
†Pregnancy immediately preceding the study pregnancy in which case-control status was determined.

lifestyle, and reproductive history information during a structured, personal interview (displayed in Tables I and II). The interview was conducted for case and control subjects by one interviewer between 3 and 6 months after delivery. The interviewer traveled to the respondent's home to conduct the interviews for both case and control subjects. Information concerning the characteristics of labor and delivery were obtained from a structured medical record review conducted by trained study personnel.

Information on spontaneous abortion and elective termination was obtained during a structured personal interview and was verified with medical record review. During the interview, women were asked which of their prior pregnancies had been diagnosed by health care professionals and whether the pregnancy had ended before 20 weeks' gestational age. Pregnancies were classified as spontaneous abortion if they had been diagnosed by a health care professional, had ended spontaneously before 20 weeks' gestation, and were verified by medical record review. Pregnancies were classified as elective terminations if they fit the same criteria but were electively terminated by a health care professional. (The outcome of the pregnancy immediately preceding the study pregnancy in which case-control status was determined is displayed in Tables III to V.)

Unconditional logistic regression was used to estimate unadjusted and adjusted odds ratios. Confidence intervals of 95% were used for tests of statistical significance and confirmed by likelihood ratio tests.[13] Maternal age, race, and marital status were included in logistic regression models to control for their confounding effect. Hospital of delivery was included in the first model to account for the potential differences in labor management among practice groups and sociodemographic differences represented by choice of hospital.

## Results

During the months the study was enrolling respondents, the participating hospitals had 34,193 deliveries from which 1213 cases (3.5%) were identified. Cases of IAI occurred more frequently among black and other nonwhite races. Unmarried women were at a higher risk of IAI compared with married women regardless of whether women were currently unmarried or never married. Tobacco and alcohol use of any amount during pregnancy was not associated with an increased risk of IAI (Table I). Further analysis categorizing women on the amount of tobacco or alcohol use did not reveal any increased risk for women who were heavy users (alcohol use 2 to 4 days per week or tobacco use of more than one pack per day).

Women with IAI were more likely to be having their first pregnancy compared with control subjects. Other obstetric characteristics of the women were evaluated because of their well-established association with IAI. The following obstetric characteristics were more frequent among women with IAI compared with controls: preterm delivery, membrane rupture before the onset of contractions, and prolonged membrane rupture and prolonged labor (Table II). Women whose labor was complicated by IAI were more likely to be managed with a surgical delivery (relative risk = 3.0; 95% confidence interval 2.4 to 3.8) and intrapartum antimicrobial agents (relative risk = 8.7; 95% confidence interval 6.5 to 11.7). Women with IAI were more likely to have postpartum endometritis develop (8%) than those without IAI (0.2%) ($p < 0.00001$). The number of women with IAI who went on to have endometritis develop were few (44 of 585), and endometritis may represent a continuation of their antepartum infection.

Women with IAI and the control group were assessed for the outcome of their immediately preceding pregnancy. Women with IAI had higher frequencies of no prior pregnancy, a spontaneous abortion, or an elective termination than the control group. After adjustment for age, race, marital status, and hospital of delivery, women with no prior pregnancy (odds ratio = 5.5; 95% confidence interval 4.0 to 7.8), spontaneous abortion (odds ratio = 4.3; 95% confidence interval 2.9 to 6.4), or elec-

**Table IV.** Risk of IAI associated with shortened prior pregnancy for women of gravidity 1 or 2

| | IAI | | | |
|---|---|---|---|---|
| | *Cases (n = 414)* | *Controls (n = 342)* | *OR** | *CI** |
| Outcome of prior pregnancy | | | | |
| Birth >20 wk | 41 (10%) | 125 (37%) | 1.0 | — |
| No prior pregnancy | 261 (63%) | 148 (43%) | 6.2 | 4.0-9.5 |
| Spontaneous abortion | 35 (8%) | 21 (6%) | 7.0 | 3.5-14.3 |
| Elective termination | 77 (19%) | 48 (14%) | 4.9 | 2.9-8.4 |

*OR*, Odds ratio; *CI*, 95% confidence interval.
*Adjusted for age, race, and marital status.

**Table V.** Risk of IAI associated with shortened prior pregnancy for women of gravidity ≥3

| | IAI | | | |
|---|---|---|---|---|
| | *Cases (n = 159)* | *Controls (n = 220)* | *OR** | *CI** |
| Outcome of prior pregnancy† | | | | |
| Birth >20 wk | 44 (28%) | 129 (59%) | 1.0 | — |
| Spontaneous abortion | 65 (41%) | 49 (22%) | 4.5 | 2.6-7.8 |
| Elective termination | 50 (31%) | 42 (19%) | 3.0 | 1.7-5.4 |

*OR*, Odds ratio; *CI*, 95% confidence interval.
*Adjusted for age, race, and marital status.
†No prior pregnancy was excluded because everyone had a least one prior pregnancy.

tive termination (odds ratio = 4.0; 95% confidence interval 2.7 to 5.8), had an increased risk of IAI using women with a birth at >20 weeks' gestation as the reference group (Table III).

To determine whether the risk of IAI associated with a spontaneous abortion or elective termination was influenced by previous successful pregnancies, women were divided into two subgroups: (1) those whose study pregnancy was gravidity 1 or 2 and (2) those whose study pregnancy was gravidity ≥3. This stratification was performed to answer the question whether earlier pregnancies carried beyond 20 weeks' gestation would reduce the risk of IAI associated with a spontaneous abortion or elective termination in the immediately preceding pregnancy. Among women of gravidity 2, a spontaneous abortion (odds ratio = 7.0; 95% confidence interval 3.5 to 14.3) or elective termination (odds ratio = 4.9; 95% confidence interval 2.9 to 8.4) in their first pregnancy was associated with an increased risk of IAI. Similarly, women with a successful earlier pregnancy also had an increased risk of IAI associated with spontaneous abortion (odds ratio = 4.5; 95% confidence interval 2.6 to 7.8) or elective termination (odds ratio = 3.0; 95% confidence interval 1.7 to 5.4) in the immediately preceding pregnancy. The odds ratios for women with and without prior successful pregnancies were not statistically significantly different.

In a further attempt to understand factors that may account for this association, we stratified women by the duration of labor in their study pregnancy. Women who had no preceding pregnancy or who had a spontaneous abortion or elective termination in their preceding pregnancy may have had prolonged labor in the following pregnancy. Prolonged labor is a risk factor for IAI and may account for its association with spontaneous abortion or elective termination. No difference was found in the risk of IAI associated with spontaneous abortion or elective termination among women with a prolonged labor (>12 hours) compared with women whose labor lasted ≤12 hours. Among women with prolonged labor, there was an increased risk of IAI associated with spontaneous abortion (odds ratio = 4.9; 95% confidence interval 1.9 to 12.9) and with elective termination (odds ratio = 2.5; 95% confidence interval 1.2 to 5.2). Women with a shorter duration of labor also had an increased risk of IAI associated with spontaneous abortion (odds ratio = 3.0; 95% confidence interval 1.7 to 5.2) and with elective termination (odds ratio = 3.6; 95% confidence interval 2.1 to 6.2).

## Comment

The frequency of IAI (3.5%) from this report agrees well with other large studies that included a complete, structured medical record review to determine the presence of IAI.[4, 7] The frequency of IAI presented here is lower than that found in a study from one hospital offering care to women with high-risk pregnancies.[8] This

study, as well as studies conducted by other investigators, found the risk marker of unmarried status and nonwhite race to be associated with IAI.[10] However, this study failed to confirm the findings of other investigators that young maternal age was associated with IAI.[10] Other investigators have found a constellation of obstetric characteristics associated with an increased risk of IAI: first pregnancy, preterm delivery, prolonged rupture of membranes, and prolonged labor.[4, 7, 8, 10] The findings from this study support the findings of these other investigators (Table II).

Other studies have proposed a relationship between a shortened prior pregnancy and the risk of IAI in the following pregnancy[10, 11] and have noted the difference in risk depending on the reference group used.[14-16] These studies by other investigators suggest that an extremely short prior pregnancy does not decrease the risk of IAI in a woman's following pregnancy in the same way as does a prior pregnancy that goes beyond 20 weeks' gestation. The findings from this study suggest that an increased risk of IAI is associated with a shortened prior pregnancy from spontaneous abortion or elective termination regardless whether the woman has had earlier successful pregnancies. This study provides a valuable extension to previous work because the diagnosis of IAI was systematically determined for each case from a complete medical record review, and the risks associated with spontaneous abortion and elective termination were determined separately. The risks associated with spontaneous abortion and elective termination were found to be similar for women who did and did not have earlier pregnancies carried more than 20 weeks before the spontaneous abortion or elective termination.

We may speculate that women who choose to terminate a pregnancy, who have a spontaneous abortion, or who have a high risk of IAI during labor may have some underlying characteristics in common. This study has controlled for demographic and lifestyle characteristics, such as maternal age, race, and marital status, that may have confounded the risk of IAI associated with spontaneous abortion or elective termination. However, this study because of its case-control design was not able to examine other factors such as genital infections that may have persisted from pregnancy to pregnancy and accounted for the association. Other investigators have found that bacterial vaginosis is a risk factor for second trimester spontaneous abortion[17] and for IAI.[4] Future studies may need to delineate the factors that explain why women with a spontaneous abortion or elective termination are at a high risk of IAI in their following pregnancy. Determining the reasons for this relationship may be an important first step in preventing IAI and the severe consequences to the neonate.

## REFERENCES

1. Watts DH, Krohn MA, Hillier SL, Eschenbach DA. Bacterial vaginosis as a risk factor for post-cesarean endometritis. Obstet Gynecol 1990;75:52-8.
2. Seo K, McGregor JA, French JI. Preterm birth is associated with increased risk of maternal and neonatal infection. Obstet Gynecol 1992;79:75-80.
3. Yoder PR, Gibbs RS, Blanco JD, Castaneda YS, St. Clair, PJ. A prospective, controlled study of maternal and perinatal outcome after intraamniotic infection at term. Am J Obstet Gynecol 1983;145:695-701.
4. Krohn MA, Hillier SL, Nugent RP, Cotch MF, Carey JC, Gibbs RS, et al. for the Vaginal Infection and Prematurity Study Group. The genital flora of women with intra-amniotic infection. J Infect Dis 1995;171:1475-80.
5. Gravett MG, Nelson HP, DeRouen T, Critchlow C, Eschenbach DA, Holmes KK. Independent association of bacterial vaginosis and *Chlamydia trachomatis* infection with adverse pregnancy outcome. JAMA 1986;256:1899-903.
6. Silver HM, Sperling RS, St. Clair PJ, Gibbs RS. Evidence relating bacterial vaginosis to intraamniotic infection. Am J Obstet Gynecol 1989;161:808-12.
7. Johnson JWC, Daikoku NH, Niebyl RJ, Johnson TRB, Khouzami VA, Witter FR. Premature rupture of the membranes and prolonged latency. Obstet Gynecol 1981;57:547-56.
8. Soper DR, Mayhall CG, Dalton HP. Risk factors for intraamniotic infection: a prospective epidemiologic study. Am J Obstet Gynecol 1989;161:562-8.
9. Daikoku NH, Kaltreider F, Khouzami VA, Spence M, Johnson JWC. Premature rupture of the membranes and spontaneous preterm labor: maternal endometritis risks. Obstet Gynecol 1982;59:13-20.
10. Sturchler D, Menegoz F, Daling J. Reproductive history and intra-partum fever. Gynecol Obstet Invest 1986;21:182-6.
11. Mühlemann K, Germain M, Krohn MA. Does an abortion increase the risk of an intra-partum infection in the following pregnancy. Epidemiology 1996;7:194-8.
12. Gibbs RS, Duff P. Progress in pathogenesis and management of clinical intraamniotic infection. Am J Obstet Gynecol 1991;64:1317-26.
13. Breslow NE, Day NE. Statistical methods in cancer research. Vol. 1. The analysis of case-control studies. Lyon: IARC Scientific Publications; 1980. IARC Scientific Publications No.: 32.
14. Poole C. Exposure opportunity in case-control studies. Am J Epidemiol 1986;123:352-8.
15. Schlesslemann J, Stadel B. Exposure opportunity in epidemiologic studies. Am J Epidemiol 1987;125:174-8.
16. Hogue CJ, Cates W, Tietze C. The effect of induced abortion on subsequent reproduction. Epidemiol Rev 1982;4:66-94.
17. Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonization of the genital tract and subsequent preterm delivery and late spontaneous abortion. BMJ 1994;308:295-8.