A population-based study of the risk of repeat clinical chorioamnionitis in Washington State, 1989–2008

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OBJECTIVE: Chorioamnionitis can cause severe complications for the infant; therefore, characterization of the risk of recurrence and identification of the factors that modify it are clinically relevant to pregnant women and their providers.

STUDY DESIGN: The risk of recurrence was examined in a retrospective population-based cohort study with the use of birth certificate and delivery hospitalization discharge data from Washington State for the years 1989–2008.

RESULTS: Women who had chorioamnionitis in their first deliveries were 3.43 times as likely to have chorioamnionitis in their second deliveries as were women who did not have chorioamnionitis in their first deliveries (95% confidence interval [CI], 2.67–4.42; $P < .001$). Smoking status modified this association (smokers: odds ratio, 1.38 [95% CI, 0.62–3.08]; nonsmokers: odds ratio, 3.80 [95% CI, 2.88–5.00]).

CONCLUSION: These data provide strong evidence for the occurrence of repeat chorioamnionitis; the association is strongest in women who do not smoke during pregnancy.

Key words: chorioamnionitis, intraamniotic infection, pregnancy complication, smoking

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Chorioamnionitis or intraamniotic infection is an inflammation of the amniotic fluid, membranes, placenta, and/or decidua. Diagnosis can be made histologically but is generally diagnosed clinically based on the finding of fever (>100.4°F) plus 2 of the following occurrences: uterine tenderness, maternal or fetal tachycardia, elevated maternal leukocytosis (>15,000 cells/mm^3), or foul odor of the amniotic fluid.[1-5] Chorioamnionitis usually results from ascending polymicrobial infection from the lower genital tract into the amniotic cavity with subsequent invasion of the fetus[6,7]; however, transmission is also possible after invasive procedures by retrograde seeding from the peritoneal cavity or by hematogenous spread.[8-12] Although usually acute, chronic cases have been documented and associated with preterm birth.[13,14] Factors that are associated with chorioamnionitis include prolonged rupture of membranes (ROM), prolonged labor, multiple digital examinations with ROM, nulliparity, group B streptococcus colonization, bacterial vaginosis, alcohol or tobacco use, meconium-stained amniotic fluid, internal monitoring, and epidural anesthesia.[15-20]

With the use of antibiotics, severe maternal complications are rare in the United States; however, maternal bacteremia may occur in up to 10% of cases, with other potential complications that include increased risk of postpartum hemorrhage, cesarean delivery, and associated surgical complications.[21,22] In contrast, the infant faces increased risk for more severe complications that include cerebral palsy, neonatal sepsis, and pneumonia.[22-24] In term infants, intraamniotic infection increases the incidence of cerebral palsy from 3 per 1000 to 8 per 1000 live births.[25] In preterm premature rupture of membranes (PROM), chorioamnionitis increases the neonatal morbidity rate from 18-55%.[26] In light of these complications, mothers who previously have had clinical chorioamnionitis with a poor birth outcome may express hesitation about future pregnancies. Further, preventive methods are available for high-risk women; thus, characterization of the risk of recurrent chorioamnionitis and identification of factors that modify this risk are of interest.

To date, 2 hospital-based studies have shown evidence for an increased risk of repeat clinical chorioamnionitis.[27,28] The purpose of this study was to use a population-based data set to compare the risk of clinical chorioamnionitis in the second delivery among women whose first deliveries were complicated by clinical chorioamnionitis, relative to that of women whose first deliveries were not complicated by clinical chorioamnionitis. Additionally, because decreased host resistance has been associated with chorioamnionitis, we assessed whether smoking, which is a controllable cause of decreased host resistance, modified the risk of recurrence.[29] Furthermore, because preterm PROM is associated strongly with chorioamnionitis, we sought to assess whether it modified the risk.[5]

Materials and Methods

We conducted a retrospective population-based cohort study using maternally linked longitudinal birth certificate data from Washington State that were linked to

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maternal hospital discharge data from the Birth Events Records Database. We selected "exposed" and "comparison" women from among 306,769 women who had a first pregnancy from 1989–2008 and at least 2 consecutive live singleton births. Previous studies have shown a higher incidence of chorioamnionitis in the first pregnancy, compared with the second pregnancy,[4,18,29] so we restricted our search to women who were nulliparous at first recorded birth. The exposed cohort consisted of women whose first birth resulted in clinical chorioamnionitis. For completeness, clinical chorioamnionitis was defined by maternal and infant International Classification of Diseases (ICD-9) codes (658.40, 658.41, 658.43 and 762.7). However, all but 3 women were coded with the ICD-9 code 658.41. From here on, the phrase *chorioamnionitis* will refer to this clinical diagnosis of intraamniotic infection or chorioamnionitis.

The comparison group was a subset of women who did not have chorioamnionitis in their first deliveries. Based on power calculations, we selected 4 comparison women for each exposed woman. Because of changes in the birth certificate data over time and potential temporal trends, we frequency matched on birth year but otherwise randomly selected from women with ≥2 live singleton births who did not have chorioamnionitis in their first deliveries. In both groups, we further excluded women who were reported to be either nulliparous (711 women) or multiparous (2305 women) for their second birth on record (total, 3016/34,530 women) because these indicate data-recording errors or women who had intervening births outside of Washington State. Our final sample size was 6219 exposed women and 25,294 unexposed women (N = 31,514).

The odds ratio (OR) for chorioamnionitis in the second delivery was estimated with logistic regression. Because factors from the second pregnancy are related more directly to the outcome, we present descriptive information on variables from the second pregnancy. Potential confounders included maternal and paternal age (years), maternal and paternal ethnicity (white, black, Native American, Asian, Hispanic, Pacific Islander), marital status (married, not married), maternal years of education, Medicaid enrollment, infant's sex, interpregnancy interval (months), chronic or gestational diabetes mellitus, chronic hypertension, gestational age (weeks), prolonged labor ≥20 hours, medium or heavy meconium-stained amniotic fluid, internal monitoring during labor (based on ICD-9 codes 74.32, 75.34, 75.35; yes, no), genital herpes (no, active, established), and syphilis. Observations with missing data were dropped from the multivariable analyses. Only maternal education, paternal age, and paternal ethnicity had >10% missing in either type of pregnancy; none of these characteristics were included in our final models.

We decided a priori to include maternal age, maternal ethnicity, PROM, and internal monitoring as confounders. We assessed other variables from both pregnancies and year of birth as potential confounders, with a confounder defined as altering the OR by ≥10%.[30] Because black race and decreased host resistance are risk factors for chorioamnionitis,[29,31] we also conducted a sensitivity analysis of women who self-reported as white without chronic hypertension or diabetes mellitus.

We evaluated smoking during pregnancy (self-reported on the birth certificate, any or none) and PROM (categorized as no PROM, PROM at term [≥37 weeks' gestation], and preterm PROM [<37 weeks' gestation]; based on ICD-9 codes 658.1, 658.10, 658.11, 658.13, and 761.1 and gestational age from birth certificate) as potential effect modifiers by including an interaction term in the regression model. For significant interactions, we performed stratified analysis, calculating stratum-specific ORs directly from the regression model.

All probability values were 2-sided, and the significance level was set at .05. Statistical analysis was performed with STATA software (release 11; StataCorp, College Station, TX).

The institutional review board of the University of Washington approved this study.

RESULTS

Demographic, medical, and obstetric characteristics of the cohort at time of first and second pregnancies are given in Table 1. The characteristics of exposed and unexposed women were generally similar. We observed 131 cases of chorioamnionitis in the second delivery among women with chorioamnionitis in their first deliveries (2.11%) and 139 cases of chorioamnionitis in the second delivery among women without chorioamnionitis in their first deliveries (0.59%; unadjusted OR, 3.60; 95% confidence interval [CI], 2.84–4.57). Adjustment for the a priori factors of maternal age, maternal ethnicity, PROM, internal monitoring, and year of birth to address the possibility of a temporal trend or other variables (Table 1) did not substantially alter the risk estimate, so the final model included only our a priori factors (adjusted OR, 3.43; 95% CI, 2.67–4.42).

Smoking status modified the risk of recurrence ($P_{interaction}$ = .02; Table 2), with the adjusted risk of recurrence being higher in nonsmokers than smokers (Table 3). We did not observe statistical evidence for the risk of recurrence being modified by PROM ($P_{interaction}$ = .41).

In a sensitivity analysis of low-risk women who self-reported as white without chronic hypertension or diabetes mellitus, the OR that was adjusted for maternal age, PROM, and internal monitoring was 3.38 (95% CI, 2.50–4.56; $P < .001$).

After adjustment for maternal age, maternal ethnicity, PROM, and internal monitoring, smoking increased the risk of the development of chorioamnionitis among women who had not had a previous delivery that was complicated by chorioamnionitis (OR, 1.83; 95% CI, 1.15–2.90). We investigated the levels of absolute risk for chorioamnionitis among smokers and nonsmokers (Figure 1). The incidence of chorioamnionitis during the second delivery was 51 of 10,000 unexposed women who did not smoke and 21 of 1000 exposed women who did not smoke. In contrast, the incidence was 10 of 1000 for unexposed women who did smoke and 14 of 1000 among exposed women who did smoke.

TABLE 1
Characteristics of the first and second pregnancies

	First pregnancy[b]		Second pregnancy[b]	
Characteristic	Chorioamnionitis (n = 6220)	No chorioamnionitis (n = 25,294)	Chorioamnionitis (n = 270)	No chorioamnionitis (n = 31,234)
Mean maternal age, y[c,d]	25.4 ± 5.7	24.6 ± 5.6	28.1 ± 5.9	28.0 ± 5.7
Maternal ethnicity, n (%)				
White	4360 (70.1)	19,633 (77.6)	201 (72.0)	24,100 (77.2)
Black	313 (5.0)	708 (2.8)	17 (6.1)	1039 (3.3)
Native American	159 (2.6)	601 (2.4)	9 (3.2)	739 (2.4)
Asian	663 (10.7)	1622 (6.4)	33 (11.8)	2249 (7.2)
Hispanic	556 (8.9)	2122 (8.4)	15 (5.4)	2322 (7.4)
Pacific Islander	31 (0.5)	88 (0.4)	0	126 (0.4)
Mean maternal education, y[c,e]	13.3 ± 2.7	13.3 ± 2.7	13.2 ± 2.6	13.5 ± 2.7
Mean paternal age, y[c,f]	28.4 ± 6.3	27.7 ± 6.1	31.7 ± 6.9	30.8 ± 6.2
Paternal ethnicity, n (%)				
White	3938 (66.3)	17,328 (68.5)	179 (65.2)	22,057 (70.6)
Black	329 (5.3)	810 (3.2)	23 (8.2)	1237 (4.0)
Native American	120 (1.9)	426 (1.7)	4 (1.4)	511 (1.6)
Asian	456 (7.3)	1343 (5.3)	23 (8.2)	1844 (5.9)
Hispanic	502 (8.1)	2143 (8.5)	15 (5.4)	2489 (8.0)
Pacific Islander	24 (0.4)	95 (0.4)	0	135 (0.4)
Married, n (%)	4136 (66.5)	16,898 (66.8)	193 (69.2)	24,105 (77.2)
Infant's sex, n (%)				
Female	2818 (45.3)	12,401 (49.0)	126 (45.2)	15,390 (49.3)
Male	3402 (54.7)	12,893 (51.0)	153 (54.8)	15,845 (50.7)
Smoker, n (%)	633 (10.2)	2776 (11.0)	39 (14.0)	3470 (11.1)
Medicaid, n (%)	2413 (38.8)	9489 (37.5)	100 (35.8)	10,332 (33.1)
Chronic hypertension, n (%)	65 (1.0)	214 (0.9)	1 (0.36)	331 (1.1)
Diabetes mellitus, n (%)[g]	189 (3.0)	695 (2.8)	5 (1.8)	1238 (4.0)
Mean gestational age, wk[c,h]	38.6 ± 3.4	39.2 ± 1.8	36.8 ± 4.6	39.0 ± 1.6
Premature rupture of membranes, n (%)				
None	4638 (74.6)	21,675 (85.7)	214 (76.7)	28,322 (90.7)
Term	794 (12.8)	1591 (6.3)	16 (5.7)	929 (3.0)
Preterm	351 (5.6)	397 (1.6)	29 (10.4)	345 (1.1)
Prolonged labor: >20 hr, n (%)	462 (7.4)	641 (2.5)	14 (5.0)	189 (0.6)
Meconium staining, n (%)[i]	815 (13.1)	1,575 (6.2)	17 (6.1)	1225 (3.9)
Internal monitoring, n (%)	968 (15.6)	3383 (13.4)	36 (12.9)	2902 (9.3)
Herpes, n (%)				
No	5559 (89.4)	22,977 (90.8)	246 (89.3)	23,323 (92.2)
Active	13 (0.2)	102 (0.4)	0	71 (0.2)
Established	138 (2.2)	554 (2.2)	8 (2.9)	820 (2.6)
Syphilis, n (%)	2 (0.03)	7 (0.03)	0	8 (0.03)

[a] Because this is a descriptive summary, we did not include probability values; [b] Percentages include missing data; [c] Data are given as mean ± SD; [d] 6/31,514 records were missing maternal age at first pregnancy; 9/31,514 records were missing maternal age at second pregnancy; [e] 6,295/31,514 records were missing maternal education at first pregnancy; 2077/31,514 records were missing maternal education at second pregnancy; [f] 3,465/31,514 records were missing paternal age at first pregnancy; 2,381/31,514 records were missing paternal age at second pregnancy; [g] Chronic or gestational; [h] 589/31,514 records were missing gestational age at first delivery; 386/31,514 records were missing gestational age at second delivery; [i] Moderate, heavy.

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TABLE 2
Logistic model of the risk of repeat chorioamnionitis

Variable	Model A[a,b] Odds ratio	95% CI	*P* value	Model B[a,c] Odds ratio	95% CI	*P* value
Chorioamnionitis	3.43	2.67–4.42	< .001	3.80	2.88–5.00	< .001
Maternal age	1.00	0.98–1.02	.956	1.00	0.98–1.03	.793
Maternal ethnicity	1.01	0.92–1.11	.844	1.01	0.92–1.11	.850
White	Reference			Reference		
Black	1.52	0.88–2.61	.133	1.39	0.78–2.47	.267
Native American	1.40	0.71–2.79	.333	1.12	0.52–2.42	.771
Asian	1.59	1.08–2.32	.018	1.57	1.07–2.32	.023
Hispanic	0.62	0.34–1.12	.116	0.65	0.36–1.19	.163
Pacific Islander	—	—	—	—	—	—
Premature rupture of membranes	2.92	2.39–3.58	< .001	2.83	2.30–3.50	< .001
Internal monitoring	1.56	1.08–2.25	.018	1.59	1.10–2.32	.015
Maternal smoking status	—	—	—	1.74	1.12–2.72	.015
Chorioamnionitis × smoker[d]	—	—	—	0.36	0.16–0.85	.019

CI, confidence interval.

[a] Adjusted for maternal age (y), ethnicity (white, black, Native American, Asian, Hispanic, Pacific Islander), premature rupture of membranes (none, term, preterm), and internal monitoring (yes, no); [b] n = 29,102 women; [c] n = 28,657 women; [d] The coefficient for this interaction term should not be considered an odds ratio.

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We further assessed the joint effects of smoking and chorioamnionitis. Among women who did not smoke during their second pregnancy, the risk of recurrent chorioamnionitis was 3.80 (95% CI, 2.88–5.00). Among women who did smoke during their second pregnancy, the risk of recurrent chorioamnionitis was 1.74 (95% CI, 1.12–2.72). Finally, women who both smoked during their second pregnancies and had chorioamnionitis during their first deliveries were 2.41 (95% CI, 1.15–5.03) times as likely to experience chorioamnionitis in their second deliveries as women who neither smoked during their second pregnancies nor had chorioamnionitis during their first deliveries (Table 4).

TABLE 3
Risk of repeat chorioamnionitis by smoking status

Smoked in second pregnancy[a]	Total, n	Second deliveries complicated by chorioamnionitis, n	Odds ratio[b]	95% CI	*P* value
Yes	3509	40	1.38	0.62–3.08	.428
No	27,388	229	3.80	2.88–5.00	< .001

CI, confidence interval.

[a] Smoking status for the second pregnancy was missing for 617 women; [b] Adjusted for maternal age, maternal ethnicity (white, black, Native American, Asian, Hispanic, Pacific Islander), premature rupture of membranes (none, term, preterm), and internal monitoring (yes, no).

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Comment

The results of this population-based study indicate that the risk of chorioamnionitis in the second delivery is >3-fold higher for women who had a diagnosis of chorioamnionitis in their first deliveries compared with women who did not. We examined effect modification by smoking and defined a factor to be an effect modifier if it was an "effect-measure modifier," with the OR of recurrence differing in different strata of the factor.[32] Our results indicate that smoking status modifies the risk of recurrent chorioamnionitis, with the risk being higher in nonsmokers.

There are a number of strengths to this study. As a population-based study, the risk estimates may be more reflective of the underlying risk of recurrence in the population than those of previous hospital-based studies. Our large sample size allowed us to calculate stable risk estimates in substrata. By restricting our research to nulliparous women, we avoided possible confounding by parity. Finally, the use of ICD-9 codes increased the accuracy of the diagnosis; a previous assessment of the accuracy of data for medical conditions and pregnancy complications in Washington State indicated that discharge data were superior to live birth certificate data.[33]

This study also had limitations. Because we were relying mostly on vari-

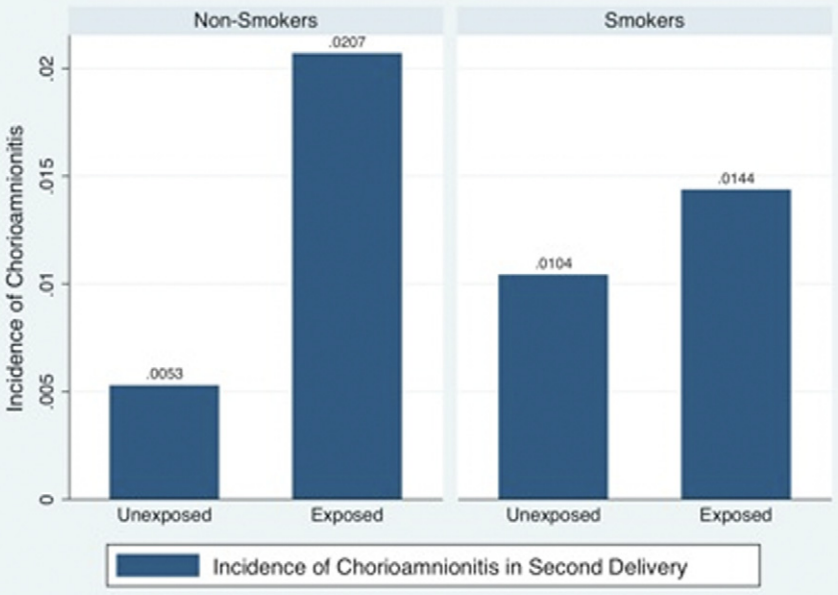
ables from birth certificate records, we could not control for all possible confounders. For example, we did not have consistent data on gestational hypertension and preeclampsia for all women, so we were not able to investigate these variables as potential confounders. Additionally, there is the possibility of recall bias in self-reported variables. In particular, because smoking status is known to be associated with poor birth outcomes, women whose deliveries were complicated by chorioamnionitis may recall or report their previous smoking status differently. This might influence the observed effect modification by smoking.

Our primary exposure and outcome were taken from ICD-9 codes and are not susceptible to recall bias. However, we were unable to review the hospital records, so they are potentially susceptible to misclassification. The chorioamnionitis cases in this study may represent a heterogeneous population, with some forms being more prone to high risk of recurrence. Future work ideally would incorporate information from microbiologic studies and pathologic examinations to identify this outcome more narrowly. Additionally, a diagnosis of chorioamnionitis that is based on clinical findings may lead to over-diagnosis because the symptoms that are used to diagnose chorioamnionitis can also be caused by extrauterine infections such as pyelonephritis or appendicitis. Underdiagnosis is possible if less severe cases of chorioamnionitis are missed.

Furthermore, women with a previous diagnosis of chorioamnionitis may be more likely to be diagnosed in subsequent deliveries because of increased vigilance. Similarly, if there is a hospital-specific tendency to over- or under-diagnose chorioamnionitis and if women deliver at the same hospital in successive pregnancies, then our exposure and outcome variables would be susceptible to information bias. However, it is unlikely that such differential misclassification or information bias would account fully for the risk estimate that we observed. We used bias analysis methods to assess the potential magnitude of these biases.[34] We assumed that women without chorioamnionitis in their first pregnancies were diagnosed properly in their second pregnancies but that there was an over-diagnosis of chorioamnionitis in the second pregnancies among women who had chorioamnionitis in their first pregnancies. We ascertained that, if the true OR was 1.0, then approximately 75% of the women with chorioamnionitis in both pregnancies would need to have been misclassified as false-positive in their second pregnancy for our observed data to be likely. Further, if there was 25% false-positive results among this group, then our data would still be consistent with a true OR of nearly 3 (OR, 2.90; 95% CI, 2.53–3.16), which shows that, although the true OR may be lower than what is reported here, it is still likely to be substantially >1.

Two hospital-based studies have assessed the risk of repeat chorioamnionitis. Dinsmoor and Gibbs[27] observed a small, nonsignificant difference in the risk of recurrence, with a higher rate of chorioamnionitis in the second preg-

FIGURE
Incidence of chorioamnionitis by smoking status



Incidence of clinical chorioamnionitis in the second delivery for women in Washington State with clinical chorioamnionitis at first delivery compared with women without clinical chorioamnionitis at first delivery, stratified by smoking, 1989–2008.

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TABLE 4
Joint effects of smoking and chorioamnionitis

Smoked in second pregnancy	Chorioamnionitis in first delivery odds ratio[a] (95% CI)	
	No	Yes
No	1.00	3.80 (2.88–5.00)
Yes	1.74 (1.12–2.72)	2.41 (1.15–5.03)

CI, confidence interval.

[a] Adjusted for maternal age, maternal ethnicity (white, black, Native American, Asian, Hispanic, Pacific Islander), premature rupture of membranes (none, term, preterm), and internal monitoring (yes, no).

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nancy among women with previous chorioamnionitis (5/76; 6.58%) compared with women without previous chorioamnionitis (22/500; 4.0%).

Laibl et al[28] performed a larger, retrospective cohort study. They adjusted for age, ethnicity, ROM of >24 hours, length of labor, epidural anesthesia, use of internal monitors, oxytocin use, gestational age, and PROM and found an approximate 2-fold risk of chorioamnionitis (OR, 1.85; 95% CI, 1.49–2.30). Although the Laibl et al study also showed statistical evidence for an association, the magnitude of our risk estimate was larger (3.43 compared with 1.85). We adjusted for as many of their confounders as were available in our dataset and still observed a much larger risk estimate (OR, 3.19; 95% CI, 2.46–4.13). We did not have data on ROM of >24 hours, length of labor, epidural anesthesia, and oxytocin use; therefore, our risk estimate may be inflated because of residual confounding. However, their study was hospital-based and may have included more high-risk women with a higher prevalence of risk factors that included smoking. Our results indicate that such high-risk women have a lower risk of recurrence of chorioamnionitis, which may have resulted in their observed lower OR.

We had anticipated that women who smoked during pregnancy would have a higher risk for recurrence than women who did not smoke. The observed pattern of effect modification is therefore in the opposite direction and may represent a chance finding. However, the magnitude of the interaction and the strong statistical support for our smoking interaction term lead us to consider other potential explanations for this finding.

First, a fixed increase in absolute risk will yield a lower OR within the strata with the higher background rate. Smokers have a higher background rate of chorioamnionitis than nonsmokers; therefore, a fixed increase in absolute risk would lead to a lower OR for smokers. We investigated this hypothesis by looking at the absolute levels of risk of chorioamnionitis in the second pregnancy that was stratified by smoking and chorioamnionitis in the first pregnancy (Figure). Women who smoked had a higher background rate of chorioamnionitis than women who did not smoke, but the absolute risk difference was not fixed. Like the OR, the absolute risk difference was higher in nonsmoking women.

An alternative explanation is that women who smoke in their second pregnancies are already at increased risk of chorioamnionitis, so previous chorioamnionitis does not substantially increase their risk above and beyond the risk that is conferred by this factor. However, women who do not smoke in their second pregnancies are more susceptible to the biologic impact of having a previous episode of chorioamnionitis.

Because of clinicopathologic differences in acute clinical chorioamnionitis between preterm and term birth,[35] we explored the rates of repeat preterm chorioamnionitis. There were 855 women who had preterm chorioamnionitis in their first birth; 22 women (2.57%) had preterm chorioamnionitis in their second birth, and 9 women (1.05%) had term chorioamnionitis in their second birth. In contrast, there were 5232 women who had term chorioamnionitis in their first birth; 13 women (0.24%) had preterm chorioamnionitis in their second birth, and 75 women (1.43%) had term chorioamnionitis in their second birth. If we restrict our results to the 2419 women who had a preterm delivery in their first birth, the risk of repeat chorioamnionitis (either term or preterm) was 5.31 (95% CI, 2.65–10.66), and the risk of repeat preterm chorioamnionitis was 5.94 (95% CI, 2.52–14.01). Although this analysis is based on small numbers, these findings indicate that the risk of repeat chorioamnionitis may be higher for women with preterm chorioamnionitis and merit follow-up investigation in studies that more carefully focus on the impact of gestational age.

A possible explanation for the elevated risk of repeat chorioamnionitis is genetics. In a retrospective cohort study of 149 women, Simhan et al[36] found that carriage of the tumor necrosis factor α gene allelic form, which causes a more robust inflammatory response to host infection, was associated with a 3-fold increase in the risk of chorioamnionitis (relative risk, 3.3; 95% CI, 1.3–7.1). Thus, this allele could lead to a predisposition to chorioamnionitis. Future follow-up investigation into potential genetic effects should examine whether women with a first-degree relative with chorioamnionitis are at increased risk of experiencing chorioamnionitis themselves. If familial aggregation is observed, then candidate genes and/or genome-wide association studies could be performed to identify additional genetic susceptibility loci.

Alternatively, experiencing chorioamnionitis in the first pregnancy may cause a woman to undergo biologic changes that predispose her to experiencing chorioamnionitis in subsequent pregnancies, or there may be other environmental or biologic factors that predispose a woman to chorioamnionitis. For example, bacterial vaginosis has been shown to be associated with acute chorioamnionitis during pregnancy.[37] Additionally, aerobic vaginitis has been linked to multiple adverse pregnancy outcomes that include chorioamnionitis.[38] If these factors remain constant over time, this would result in an increased risk of recurrent chorioamnionitis. Further studies could assess whether the vaginal flora remains constant over time and whether these types of flora are responsible for increased risk for recurrent chorioamnionitis.

This study provides strong evidence for the occurrence of repeat chorioamnionitis. Given that under-diagnosis is possible, providers should be more vigilant about diagnosing and treating chorioamnionitis in these women in subsequent pregnancies. We also observed that smoking was an effect modifier, with the OR being strongest in women who do not smoke during pregnancy. Future research should assess whether other controllable risk factors, such as alcohol use and epidural anesthesia, also modify the risk of repeat chorioamnionitis.

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