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Original Contribution

Induced Abortions and the Risk of Preeclampsia Among Nulliparous Women

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Induced abortion (IA) has been associated with a lower risk of preeclampsia among nulliparous women, but it remains unclear whether this association differs by method (either surgical or medical) or timing of IA. We performed a nested case-control study of 12,650 preeclampsia cases and 50,600 matched control deliveries identified in the Medical Birth Register of Finland from 1996 to 2010. Data on number, method, and timing of IAs were obtained through a linkage with the Registry of Induced Abortions. Odds ratios and 95% confidence intervals were calculated. Overall, prior IA was associated with a lower risk of preeclampsia, with odds ratios of 0.9 (95% confidence interval (CI): 0.9, 1.0) for 1 prior IA and 0.7 (95% CI: 0.5, 1.0) for 3 or more IAs. Differences in the associations between IA and preeclampsia by timing and method of IA were small, with odds ratios of 0.8 (95% CI: 0.6, 1.1) for late (≥12 gestation weeks) surgical abortion and 0.9 (95% CI: 0.7, 1.2) for late medical abortion. There was no association between IA in combination with a history of spontaneous abortion and risk of preeclampsia. In conclusion, prior IA only was associated with a slight reduction in the risk of preeclampsia.

induced abortion; medical abortion; preeclampsia; surgical abortion

Abbreviations: BMI, body mass index; CI, confidence interval; HDR, Hospital Discharge Register; IA, induced abortion; MBR, Medical Birth Register; OR, odds ratio; SAB, spontaneous abortion.

Editor's note: *An invited commentary on this article appears on page 670, and the authors' response appears on page 673.*

Preeclampsia is estimated to affect 4%–8% of first pregnancies. The prevalence in subsequent pregnancies is 2–4 times lower among women without a history of preeclampsia (1, 2). One of several hypotheses to explain this decrease in risk is that spiral artery remodeling that occurs during pregnancy creates favorable conditions for placentation in subsequent pregnancies (3). Determining whether the decrease in risk from a first to a second pregnancy is restricted to women with a prior live birth or if a prior pregnancy, regardless of outcome, confers similar protection has been the topic of several studies. In general, studies have shown a lower risk of preeclampsia associated with induced abortion (IA) (4–7) but not spontaneous abortion (SAB) (5–8), although findings have been inconsistent (4, 9, 10).

The mechanism through which IA might protect against subsequent preeclampsia remains unclear, but there is evidence to suggest that the method and timing of IA may play a role. IAs comprise a heterogeneous group of procedures conducted using surgical methods (i.e., vacuum aspiration and dilation and evacuation) or medical methods (i.e., administration of prostaglandins, mifepristone, and methotrexate). In a previous study, women with a history of cervical dilation and curettage, particularly 2 or more procedures, had a reduced risk of preeclampsia, although type of abortion (spontaneous or induced) was not noted (8). In clinical practice, women who use assisted reproductive techniques have a higher success of implantation if endometrial injury, such as biopsy or curettage, occurred in the previous cycle (11), possibly because of an induced an inflammatory response that facilitates implantation (12, 13).

In addition to the type of procedure performed, the timing of abortion is variable. To our knowledge, only 1 study to date reported a reduction in the risk of preeclampsia as the

gestational age at abortion increased, with abortions that were performed in the second and third months of gestation being associated with reductions of 50% and 70%, respectively (4). These estimates were based on small numbers, and the investigators did not distinguish between SAB and IA. The number of prior IAs might also play a role in the risk of preeclampsia; a greater reduction in risk for women with 2 or more previous IAs than for women with 1 prior IA was reported in previous studies (5, 8). The aim of the present study was to investigate the association between IA and subsequent risk of preeclampsia and to determine whether this association differs based on method, timing, or number of prior abortions.

METHODS

Source population

We conducted a nested case-control study using data from the Medical Birth Register (MBR) of Finland. The MBR is a population-based registry that was established in 1987 and collects data on all live births and stillbirths at 22 weeks' gestation or later and on infants who weigh 500 g or more. The MBR captures data on 99.9% of newborns in Finland, which improves to 100% after linkages with the Central Population Register and Cause of Death Register. The source population for the present study was restricted to singleton deliveries among women who were nulliparous or who had no prior pregnancy resulting in a delivery at 22 weeks or later from 1996 to 2010. Pregnant women for whom parity data were missing were excluded (0.1%). Approval for this study was obtained from the National Institute of Health and Welfare.

Preeclampsia

Both preeclampsia and eclampsia were included in the case definition. Superimposed preeclampsia and HELLP syndrome, a variant of preeclampsia named for its characteristic hemolysis, elevated liver enzyme levels, and low platelet count, were also included (14).

Cases were identified using *International Classification of Diseases, Tenth Revision*, codes (O11, O14, and O15, which includes eclampsia with seizures) in the Hospital Discharge Register (HDR) (1996–2010) and the MBR (2004–2010). The MBR also includes data on hospitalizations due to hypertension during pregnancy. Although hypertension may indicate the presence of preeclampsia, women who had hypertension were not included if diagnosis codes did not confirm the condition. Four control women whose deliveries were unaffected by preeclampsia, as confirmed by the absence of a diagnosis code, were randomly selected from the MBR and frequency-matched to each case on year of delivery.

Induced abortions

Data on IAs were obtained from the Registry of Induced Abortions. All hospitals and clinics that perform abortions at any gestational age are required to report to the registry, which captures data on an estimated 99% of all procedures performed (15). Data on gestational age and procedure method are reported. Cases and all selected control deliveries were linked to the Registry of Induced Abortions using a maternal personal identification number. Data on IAs (1987–2010) before the women's last menstrual periods were collected. The number of prior IAs was categorized as 0, 1, 2, or ≥3. Gestational age at the time of abortion was categorized as <12 weeks or ≥12 weeks. The method of abortion was categorized as either surgical or medical. In addition, the interpregnancy interval between most recent IA and the study pregnancy was calculated by subtracting the date of abortion procedure from the last menstrual period of the study pregnancy.

Covariates

Data on maternal age, smoking during pregnancy, number of antenatal visits, marital status, and socioeconomic correlates were obtained from the MBR. These data are recorded at the time of birth and include information from the prenatal care record. Prepregnancy height and weight, as measured by health-care personnel, were included in the MBR beginning in 2004. Prepregnancy body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) was categorized as underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), or obese (≥30). Diagnoses of chronic hypertension and preexisting diabetes from 1987 to 2010 were ascertained from the HDR.

Data on SABs were collected from maternal self-report of prior SAB in the MBR and procedure codes in the HDR. The HDR only includes data on inpatient care (1987–2010) and outpatient visits in public hospitals (1998–2010); therefore, we combined HDR data with maternal self-reported data to capture information on prior SABs that would have been missed by the HDR.

Statistical analyses

The distributions of covariates by case and control status were examined. Odds ratios and 95% confidence intervals were calculated using unconditional logistic regression to measure the association between prior IAs and the risk of preeclampsia in the study pregnancies. Potential confounders were identified a priori based on reported associations with IA and preeclampsia and included maternal age (<20, 20–24, 25–29, 30–34, or ≥35 years), smoking during pregnancy (yes, no, or unknown), and history of SAB. Year of delivery was also considered because of the matched study design. Data on prepregnancy height and weight were not ascertained in the MBR until 2004. Therefore, we were missing data on BMI for approximately half of the study population. We used multiple imputation methods with 10 imputed data sets to impute missing BMI values. Variables that were associated with BMI or the probability of having a missing BMI were used as predictor variables. These included delivery year, maternal age, number of antenatal visits, marital status, smoking during pregnancy, chronic hypertension, preexisting diabetes, and SAB. Preeclampsia and history of IA were also included as predictor variables. Confounders were defined as those variables that altered the crude odds ratio by at least 10% upon adjustment. Using this change in estimate approach, none of the variables assessed met the definition of a confounder; therefore, crude odds ratios are presented.

The associations of gestational age and method of abortion with the risk of preeclampsia were investigated among women with 1 prior abortion to separate the associations of timing and method with preeclampsia from those of number of abortions. The joint association of gestational age and method was assessed by investigating combinations of gestational age and method using women with no prior IAs as the reference group. Lastly, interpregnancy interval was explored in relation to preeclampsia as a continuous variable using restricted cubic spline regression transformation (16). We also performed an analysis using women without a history of either an IA or SAB as the reference group to assess the independent associations of IA only, SAB only, and both IA and SAB with preeclampsia risk.

We conducted a sensitivity analysis in which we separated early-onset preeclampsia, defined as preeclampsia in a woman who delivered before 34 weeks' gestation, and late-onset preeclampsia, because these have been suggested to be conditions with different underlying pathologies (17). Other sensitivity analyses were conducted after excluding controls who were hospitalized during pregnancy due to hypertension and excluding women with chronic hypertension and preexisting diabetes.

RESULTS

Among the 349,861 singleton deliveries to nulliparous women from 1996 to 2010, there were 12,650 cases of preeclampsia, yielding an overall prevalence of 3.6%. Compared with the 50,600 controls with the same distribution of delivery year, cases were more likely to be 35 years of age or older and overweight or obese and to have chronic hypertension or preexisting diabetes. Controls were more likely to smoke during pregnancy (17.4% of controls vs. 14.2% of cases) (Table 1). Distributions of demographic variables with respect to prior IA are presented in Table 2.

A prior IA was more common among controls, with 13.1% of controls having a prior IA compared with 11.7% of cases. The unadjusted odds ratio for the association between any prior IA and preeclampsia was 0.9 (95% confidence interval (CI): 0.8, 0.9). Higher numbers of IAs were associated with corresponding greater reductions in the risk of preeclampsia. Women with 1, 2, and 3 or more IAs had unadjusted odds ratios of 0.9 (95% CI: 0.9, 1.0), 0.8 (95% CI: 0.7, 0.9), and 0.7 (95% CI: 0.5, 1.0), respectively, compared with women without any prior IA (Table 3).

After excluding women with more than 1 IA, we investigated the associations between gestational age at the time of abortion and procedure method in relation to preeclampsia (Table 4). When compared with women without a prior IA, women who had abortions performed at 12 gestational weeks or later (odds ratio (OR) = 0.8, 95% CI: 0.7, 1.0) had a greater reduction in risk of preeclampsia than did women with abortions performed at less than 12 gestational weeks (OR = 0.9, 95% CI: 0.8, 1.0), although the difference was small and the confidence intervals overlapped. There was little difference in the risk of preeclampsia by method of abortion. In the evaluation of the combination of timing and method, surgical abortions at 12 weeks or later were associated with a greater reduction in risk of preeclampsia (OR = 0.8, 95% CI: 0.6, 1.1)

Table 1. Distribution of Selected Characteristics of Cases With Preeclampsia and Controls, Medical Birth Register of Finland, 1996–2010

Characteristic	Cases With Preeclampsia (n = 12,650)		Controls (n = 50,600)	
	No.	%[a]	No.	%[a]
Maternal age, years				
<20	631	5.0	3,105	6.1
20–24	2,912	23.0	12,467	24.6
25–29	4,401	34.8	18,478	36.5
30–34	3,024	23.9	11,857	23.4
≥35	1,682	13.3	4,693	9.3
Mean (SD)	28.0 (5.5)		27.3 (5.2)	
Body mass index[b]				
Underweight (<18.5)	190	2.7	1,234	4.4
Normal (18.5–24.9)	3,509	50.3	17,320	62.0
Overweight (25.0–29.9)	1,485	21.3	4,903	17.6
Obese (≥30.0)	1,167	16.7	2,362	8.5
Missing	629	9.0	2,101	7.5
Mean (SD)	25.37 (5.4)		23.71 (4.5)	
Socioeconomic status based on maternal occupation during pregnancy				
Upper white collar	2,131	16.8	8,934	17.7
Lower white collar	4,632	36.6	16,936	33.5
Blue collar	1,839	14.5	7,120	14.1
Student	1,552	12.3	7,151	14.1
Other[c]	382	3.0	1,521	3.0
Unknown	2,114	16.7	8,938	17.7
Marital status				
Married	5,969	47.2	23,451	46.3
Cohabiting	4,865	38.5	19,547	38.6
Single	1,785	14.1	7,471	14.8
Unknown	31	0.2	131	0.3
Smoked during pregnancy				
Yes	1,790	14.2	8,801	17.4
Unknown	294	2.3	1,003	2.0
No. of antenatal visits				
<15	3,188	25.2	15,184	30.0
15–19	4,585	36.2	22,800	45.1
≥20	4,593	36.3	11,819	23.4
Unknown	284	2.2	797	1.6
History of spontaneous abortion[d]	1,897	15.0	7,307	14.4
Chronic hypertension[d]	84	0.7	73	0.1
Pre-existing diabetes[d]	334	2.6	276	0.5

Abbreviation: SD, standard deviation.

[a] Values may not add to exactly 100% because of rounding.

[b] Weight (kg)/height (m)^2. Data were available beginning in 2004.

[c] This category includes entrepreneurs, farmers, unemployed women, self-employed women, and stay-at-home mothers.

[d] Data were ascertained from 1987 to 2010.

Table 2. Distribution of Selected Characteristics of Nulliparous Women, by History of Induced Abortion, Medical Birth Register of Finland, 1996–2010

Characteristic	Prior Induced Abortion ($n = 6,604$)		No Prior Abortion ($n = 43,996$)	
	No.	%	No.	%
Maternal age, years				
<20	399	6.0	2,706	6.2
20–24	1,722	26.1	10,745	24.4
25–29	2,118	32.1	16,360	37.2
30–34	1,545	23.4	10,312	23.4
≥35	820	12.4	3,873	8.8
Body mass index[a]				
Underweight (<18.5)	154	4.3	1,080	4.4
Normal (18.5–24.9)	2,124	58.9	15,196	62.5
Overweight (25.0–29.9)	653	18.1	4,250	17.5
Obese (≥30.0)	339	9.4	2,023	8.3
Missing	337	9.3	1,764	7.3
Socioeconomic status based on maternal occupation during pregnancy				
Upper white collar	794	12.0	8,140	18.5
Lower white collar	2,237	33.9	14,699	33.4
Blue collar	1,312	19.9	5,808	13.2
Student	891	13.5	6,260	14.2
Other[b]	203	3.1	1,318	3.0
Unknown	1,167	17.7	7,771	17.7
Marital status				
Married	1,948	29.5	21,503	48.9
Cohabiting	3,205	48.5	16,342	37.1
Single	1,430	21.7	6,041	13.7
Unknown	21	0.3	110	0.3
Smoked during pregnancy				
Yes	2,114	32.0	6,687	15.2
Unknown	130	2.0	873	2.0
No. of antenatal visits				
<15	1,926	29.2	13,258	30.1
15–19	3,026	45.8	19,774	44.9
≥20	1,547	23.4	10,272	23.3
Unknown	105	1.6	692	1.6
History of spontaneous abortion[c]	1,330	20.1	5,977	13.6
Chronic hypertension[c]	12	0.2	60	0.1
Pre-existing diabetes[c]	39	0.6	237	0.5

[a] Values may not add to exactly 100% because of rounding.
[b] Weight (kg)/height (m)^2. Data were available beginning in 2004.
[c] This category includes entrepreneurs, farmers, unemployed women, self-employed women, and stay-at-home mothers.
[d] Data were ascertained from 1987 to 2010.

Table 3. Odds Ratios for the Associations of Any Prior and Number of Prior Induced Abortions With Preeclampsia, Medical Birth Register of Finland, 1996–2010

Abortion Category	Preeclampsia Cases ($n = 12,650$)		Controls ($n = 50,600$)		OR	95% CI
	No.	%	No.	%		
Prior induced abortion						
No	11,164	88.3	43,996	86.9	1.0	Referent
Yes	1,486	11.7	6,604	13.1	0.9	0.8, 0.9
No. of prior induced abortions[a]						
1	1,283	10.1	5,557	11.0	0.9	0.9, 1.0
2	161	1.3	821	1.6	0.8	0.7, 0.9
≥3	42	0.3	226	0.4	0.7	0.5, 1.0

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Test for trend: $P < 0.01$.

than were other combinations of timing and method. A subsequent analysis of second trimester IAs using more detailed gestational age categories indicated that the association with preeclampsia was strongest for surgical abortions at 14–15 weeks and at 16 weeks or later, with odds ratios of 0.4 (95% CI: 0.1, 1.2) and 0.5 (95% CI: 0.3, 1.2), respectively. Associations for medical abortions at these same gestational ages were weaker, with odds ratios of 0.8 (95% CI: 0.5, 1.3) and 1.0 (95% CI: 0.7, 1.4).

The association between interpregnancy interval and risk of preeclampsia among women with a prior IA was investigated using spline regression models. The test for curvature of the spline plot was nonsignificant ($P = 0.3$). The linear plot demonstrated a reduced risk of preeclampsia with interpregnancy intervals of less than 1 year. Longer intervals were associated with an increase in the odds ratio for preeclampsia from the referent value at 1 year (OR = 1) to the value at 10 years (OR = 1.13).

Compared with no history of either IA or SAB, SAB was not associated with a reduced risk of preeclampsia either alone (OR = 1.0, 95% CI: 1.0, 1.1) or in combination with a history of IA (OR = 1.0, 95% CI: 0.9, 1.1) (Table 5). Nearly 10% of cases were classified as early-onset preeclampsia (<34 weeks). Associations with early-onset preeclampsia (OR = 0.9; 95% CI: 0.7, 1.0) were similar to those with late-onset preeclampsia (OR = 0.9; 95% CI: 0.8, 1.0). Removing controls who were hospitalized for hypertension during pregnancy (3%) and women with chronic hypertension and preexisting diabetes (3.3% of cases, 0.7% of controls) from the sensitivity analyses did not materially change results (data not shown).

DISCUSSION

A history of IA was associated with a decreased risk of preeclampsia among nulliparous women. This risk further declined with an increasing number of prior IAs. The risk of preeclampsia among nulliparous women with an IA was 3.3%, which decreased to 2.7% for women with 3 or more prior IAs. This risk was still approximately 2-fold higher

Table 4. Odds Ratios for the Associations of Timing and Method of Abortion With Preeclampsia, Restricted to Women With No or 1 Prior Induced Abortion, Medical Birth Register of Finland, 1996–2010

Abortion Characteristic	Preeclampsia Cases ($n = 12,447$)		Controls ($n = 49,553$)		OR	95% CI
	No.	%	No.	%		
Timing of abortion, gestational weeks						
<12	1,141	9.2	4,903	9.9	0.9	0.8, 1.0
≥12	142	1.1	654	1.3	0.8	0.7, 1.0
Method						
Surgical	1,012	8.1	4,388	8.9	0.9	0.9, 1.0
Medical	271	2.2	1,161	2.3	0.9	0.8, 1.1
Timing in gestational weeks and method						
<12, Surgical	944	7.6	4,059	8.2	0.9	0.9, 1.0
<12, Medical	197	1.6	841	1.7	0.9	0.8, 1.2
≥12, Surgical	68	0.5	329	0.7	0.8	0.6, 1.1
≥12, Medical	74	0.6	320	0.6	0.9	0.7, 1.2
No induced abortion	11,164	89.7	43,996	88.8	1.0	Referent

Abbreviations: CI, confidence interval; OR, odds ratio.

than the risk of 1.3% among multiparous women in Finland. The reduction in risk of preeclampsia associated with a prior IA did not equate to that of a previous birth. Our findings are consistent with those from other studies, which reported a lower risk of preeclampsia after an IA (4, 5, 7) and a greater reduction in risk after multiple IAs (5). In another study, investigators reported an increasing risk of preeclampsia with an increasing number of abortions, but this discrepancy may be explained by their inclusion of both SABs and IAs (18).

We found slight differences in risk based on timing of IA, with those performed at 12 weeks or later being associated with a greater decrease in subsequent risk of preeclampsia than those performed at less than 12 weeks. Later timing of abortion has previously been associated with a decreased risk of preeclampsia (4), but not consistently (19). Distinctions between SAB and IA were not made in those studies. To our knowledge, the present study is the first study in which the association between timing of IA, specifically, and risk of preeclampsia has been described. Differences between methods of abortion were less apparent in the present study, which is consistent with a study that reported no difference in the incidence of preeclampsia between women with a prior mifepristone abortion and a prior surgical abortion (20). In a meta-analysis of subsequent pregnancy outcomes after medical abortion compared with surgical abortion, Gan et al. (21) reported an odds ratio of 0.74 (95% CI: 0.50, 1.01) for pregnancy-induced hypertension. In Finland, medical abortions have been available since 2000, and as of 2010 they accounted for 87% of all IAs performed, making surgical abortions increasingly rare (22).

In the evaluation of timing and method combined, surgical abortions at 12 weeks or later were associated with a greater decrease in the risk of preeclampsia than were other combinations of method and timing, although differences were small and estimates were imprecise. Analyses of finer gestational age categories within the second trimester demonstrated a null association for medical abortion at 16 weeks later and an odds ratio of 0.5 (95% CI: 0.3, 1.2) for surgical abortions at 16 weeks or later, possibly indicating that method, not timing, plays a more important role in the subsequent development of preeclampsia. Having 2 or more procedures of cervical dilation and curettage has been associated with a reduced risk of preeclampsia, although in that study, distinction between types of abortion was not made (8). Surgical abortions may be associated with higher degree of endometrial injury and subsequent spiral artery remodeling, which may be in the pathogenic pathway for preeclampsia. Decidual injury has been observed to increase the invasion potential of trophoblastic cells (23), which are frequently impaired in cases of preeclampsia, leading to the characteristic placental underperfusion. Vacuum aspiration has been associated with endomyometrial injury, but other surgical and medical procedures haven't been studied (24). We speculated that the endometrial injury caused by an IA induces an inflammatory response that improves placentation and consequently reduces the risk of preeclampsia. Furthermore, the reduction in preeclampsia risk was greatest among women whose IA occurred within a year of their last menstrual period before the study pregnancy. It is possible that as repair processes occur, the immune response subsides, and the benefit of endometrial injury lessens over time.

An immunologic rationale for the development of preeclampsia would also be consistent with a decreased risk of preeclampsia among women with a prior IA and a shorter interpregnancy interval. Longer interpregnancy intervals have previously been associated with increased risks of preeclampsia (25, 26). Maternal immune recognition of trophoblasts is likely improved among women with a prior IA and a shorter interpregnancy interval, which is expected to facilitate placental growth and uteroplacental perfusion (27). Women with shorter interpregnancy intervals may also be less likely to change partners, which has been shown to attenuate associations of IA (5) or any prior loss (28) with preeclampsia.

The associations between history of SAB either alone or in combination with IA and preeclampsia were null, which is

Table 5. Odds Ratios for the Associations of Prior Induced Abortion Only, Prior Spontaneous Abortion Only, and Both Induced and Spontaneous Abortion With Preeclampsia, Medical Birth Register of Finland, 1996–2010

	Cases With Preeclampsia		Controls		OR	95% CI
	No.	%	No.	%		
Total	12,650	100.0	50,600	100.0		
IA and SAB	338	2.7	1,330	2.6	1.0	0.9, 1.1
IA only	1,148	9.1	5,274	10.4	0.9	0.8, 0.9
SAB only	1,559	12.3	5,977	11.8	1.0	1.0, 1.1
No SAB or IA	9,605	75.9	38,019	75.1	1.0	Referent

Abbreviations: CI, confidence interval; IA, induced abortion; OR, odds ratio; SAB, spontaneous abortion.

consistent with studies in which no association between SAB and preeclampsia was reported (5, 7) and 1 study in which no association between a history of both IA and SAB and preeclampsia was reported, although abortion data was self-reported and findings were based on just 2 exposed cases (4). Our findings suggest that contributions to gravidity by SAB alone are not associated with a reduced risk of preeclampsia and that history of SAB negates the protective association between IA and preeclampsia. The mechanisms by which IA would reduce the risk of subsequent preeclampsia in the absence of SAB may include subfecundity or poor placentation. In studies of time to pregnancy, increased risks of preeclampsia were associated with longer times to pregnancy (29, 30). Poor placentation may underlie particular SAB phenotypes and preeclampsia (27, 30, 31); therefore, IA may have no effect in the presence of a common etiology of SAB and preeclampsia.

The present study is not without limitations. Medical abortions that required subsequent (or post-IA) surgical evacuation procedures were not captured. Although the proportion of women who required a surgical procedure after a medical IA was estimated to be low (6%) in another Finnish study (32), the dual procedures may have resulted in misclassification of abortion method. Incomplete information on gravidity due to lack of data on ectopic pregnancies and number of SABs may have resulted in confounding. We reported no association between SAB and preeclampsia, yet misclassification of SAB history is likely, and detailed information on number of SABs is lacking. The overall null finding for an association between SAB and preeclampsia may be obscuring any gravidity-specific associations. Recurrent SAB has previously been associated with an increased risk of preeclampsia (31), although the proportion of multiple SABs in our study is expected to be small. Although Finland lacks a registry for SABs, information on prior SABs was captured using 2 sources: procedure codes from the HDR and maternal self-report at the time of delivery of the index pregnancy recorded in the MBR. When we combined data from both sources, we found that 14.6% of nulliparous women had a prior SAB. This results is similar to that from another observational study in which a rate of 15.2% was reported (5). Early losses, specifically those that occurred before clinical recognition, would not have been captured in the present study. Preeclampsia case ascertainment relied on recorded diagnostic codes in the HDR and MBR. The prevalence of preeclampsia among nulliparous in Finland from 1996 to 2010 was 3.6%, which is similar to the prevalence of 4.1% reported in Sweden from 1987 to 2004 (3). Although the specificity of diagnostic codes for preeclampsia in the registries is expected to be high, the sensitivity of preeclampsia diagnoses in other hospital discharge data sets is reported to range from 70% to 88% (33, 34). We assessed the possibility that true cases were included as controls by conducting a sensitivity analysis in which we removed controls who had hypertension during pregnancy. The results of that analysis did not alter our conclusions. Lastly, lack of information on partner changes and subfecundity are limitations of the present study, because both may confound the association between IA and preeclampsia.

Strengths of the present study include the large sample size, the use of nation-wide registers, and the inclusion of detailed information on the timing and method of IA. Cases and controls were ascertained from a nation-wide registry that captures all births in the country, thereby reducing the potential for selection bias. The Finnish Registry of Induced Abortions has collected information from medical providers since 1950 and is estimated to be 99% complete (15). The validity of several variables recorded in the Registry of Induced Abortions has been demonstrated to be high. The use of the registry for information on IAs in our study offers a major improvement over previous studies that have relied on self-reported data, thereby reducing the likelihood of exposure misclassification.

A prior IA was associated with a reduced risk of preeclampsia. Although we hypothesized that endometrial injury associated with IAs might decrease the subsequent risk of preeclampsia, the role of endometrial injury in influencing the immunology of preeclampsia remains to be understood. Studies designed to disentangle the effects of timing and method of IA, in addition to gravidity, are needed to further our understanding of the pathogenesis of preeclampsia.

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