Journal of the American Heart Association

ORIGINAL RESEARCH

Increased Cardiac Arrhythmia After Pregnancy-Induced Hypertension: A South Korean Nationwide Database Study

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BACKGROUND: Although pregnancy-induced hypertension (PIH) is associated with an elevated cardiovascular risk, long-term studies or prepregnancy baseline data are scarce. Therefore, using a large nationwide cohort with prepregnancy periodic health screening data, we investigated whether clinically significant arrhythmia incidence increases after PIH.

METHODS AND RESULTS: Data were extracted from the Korea National Health Insurance database and combined with the National Health Screening Examination database; women who gave birth between 2007 and 2015 and underwent the national health screening test within a year before pregnancy were followed up until 2016. We excluded women who had a diagnosis of arrhythmia within 1 year before pregnancy. The primary outcome was significant arrhythmia during the year after delivery. Secondary analysis included only specific diagnostic codes of arrhythmia with clinical significance. Additionally, the risk of arrhythmia was stratified by the use of magnesium sulfate. Of 2 035 684 women (PIH; n=37 297 versus normotensive pregnancy; n=1 998 387), the PIH group had a higher prepregnancy risk profile and showed a higher incidence of arrhythmia than women with normotensive pregnancies within 1 year. Women with PIH had a significantly higher risk of atrial flutter/fibrillation and atrioventricular block, but not lethal arrhythmias. Other predictors of arrhythmia development included advanced maternal age and cesarean section. Stratified analysis showed a higher risk of arrhythmia with magnesium sulfate use.

CONCLUSIONS: PIH was significantly associated with the development of arrhythmia within 1 year after delivery. Nevertheless, the incidence of lethal arrhythmias was not increased by PIH. Arrhythmia, especially atrial fibrillation, may largely contribute to increasing the future cardiovascular risk in women with a PIH history.

Key Words: atrial fibrillation ■ cardiac arrhythmia ■ hypertensive disorders of pregnancy ■ preeclampsia

Pregnancy-induced hypertension (PIH) is characterized by the presence of hypertension with or without proteinuria or other severe features after 20 weeks of gestation.[1] It is associated with an elevated risk and an accelerated development of cardiovascular diseases (CVDs) such as hypertension; dyslipidemia; heart failure; diabetes; and coronary, cerebrovascular, and peripheral arterial diseases in later life.[2–6]

Hitherto, it was debated whether PIH is an independent risk factor of CVD or a manifestation of common cardiovascular risk factors.[7–12]

Previous studies on the long-term CVD risk of women after PIH have a few limitations. First, very few studies adjusted for baseline metabolic characteristics[7–12]; among these studies, data collected before pregnancy, rather than from recall, are scarce.[8] Therefore, it is unclear whether PIH itself or preexisting

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Supplemental Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.023013

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- From a South Korean nationwide cohort, women with pregnancy-induced hypertension had a significantly higher incidence of developing arrhythmia within 1 year of delivery, especially atrial flutter/fibrillation and premature beats.

What Are the Clinical Implications?

- Arrhythmia may be a mediator of increased future cardiovascular risk in women with a history of pregnancy-induced hypertension.

Nonstandard Abbreviations and Acronyms

$MgSO_4$	magnesium sulfate
PIH	pregnancy-induced hypertension

risk factors are the main determinants of CVD development. Second, cardiac arrhythmia has been a neglected outcome in many of the long-term studies. Some studies undertook to evaluate electrical changes in the heart during and after a preeclamptic pregnancy.[13–16] However, to our knowledge, no study has focused on arrhythmia as a long-term end point, barring the study by Ray et al,[17] who included a broad spectrum of patients with maternal placental syndromes; their study outcomes were limited to hard end points. Third, the Asian population was underrepresented in most of these studies.[2,4,6]

Additionally, magnesium sulfate ($MgSO_4$) is widely administered to women with high-risk pregnancies, including PIH[18] and preterm labor[19,20]; nonetheless, the impact of $MgSO_4$ on the development of arrhythmia after PIH is unknown.

Therefore, using a large Asian nationwide cohort and combined prepregnancy laboratory data, we aimed to investigate whether the incidence of arrhythmia increases after PIH, and whether this increase, if present, is associated with the use of $MgSO_4$.

METHODS

Study Design and Data Collection

This was a retrospective cohort study using a nationwide administrative database. Data were extracted from the Korean National Health Insurance Database by the Health Insurance Review & Assessment Service, which covers 97% of South Korean population, and the National Health Insurance Service—Health Screening Cohort databases. Anonymized data and materials have been made publicly available at the Healthcare Bigdata Hub by Health Insurance Review & Assessment Service and can be accessed at https://opendata.hira.or.kr/home.do. According to the Act on the Protection of Personal Information Maintained by Public Agencies, claims data from the Health Insurance Review & Assessment Service database do not contain individual identification information. Thus, this study was exempt from review and the requirement for informed consent was waived by the Institutional Review Board of the Korea University Medical Center (IRB No. 2018GR0403).

Study Population

Among women who gave birth between January 2007 and December 2015, those diagnosed with arrhythmia before and during pregnancy were excluded, as well as those with chronic hypertension on antihypertensive medication, previous preeclampsia, or missing data (Figure 1). Data of women who had records from the national screening test within 1 year before pregnancy were extracted from the whole data set (data set B) and analyzed as data set A to adjust for baseline characteristics. Data sets A1 and B1 included data of women who gave birth between 2007 and 2015; data from women who gave birth between 2007 and 2008 were analyzed separately as data sets A2 and B2 for long-term follow-up. Follow-up data up to December 2016 were analyzed, and the results were presented as 1-year data for groups A1 and B1, and 7-year data for groups A2 and B2. A data flowchart is depicted in Figure 1. PIH was defined as gestational hypertension, preeclampsia, or eclampsia based on diagnostic codes (O13, O14, O15). All diagnoses were based on the *International Classification of Diseases, Tenth Revision* (*ICD-10*). Women without a health care record of any end points were censored at December 2016 or termination of health insurance.

Study End Points

The primary end point was a new diagnosis of arrhythmia within 1 year of childbirth. Secondary end points included new diagnoses of clinically significant arrhythmias and predictors of arrhythmia. Significant arrhythmias were selected from rhythms associated with clear symptoms, potential of progression to high-risk diseases, or a high risk of complications and were classified into 6 categories: lethal arrhythmias, atrial flutter or fibrillation, atrioventricular block, paroxysmal tachycardia, premature beats, and right bundle-branch block. Specific codes to include in each category were selected by consulting at least 2 cardiologists (Table S1). Ambiguous or frequently misused diagnostic codes

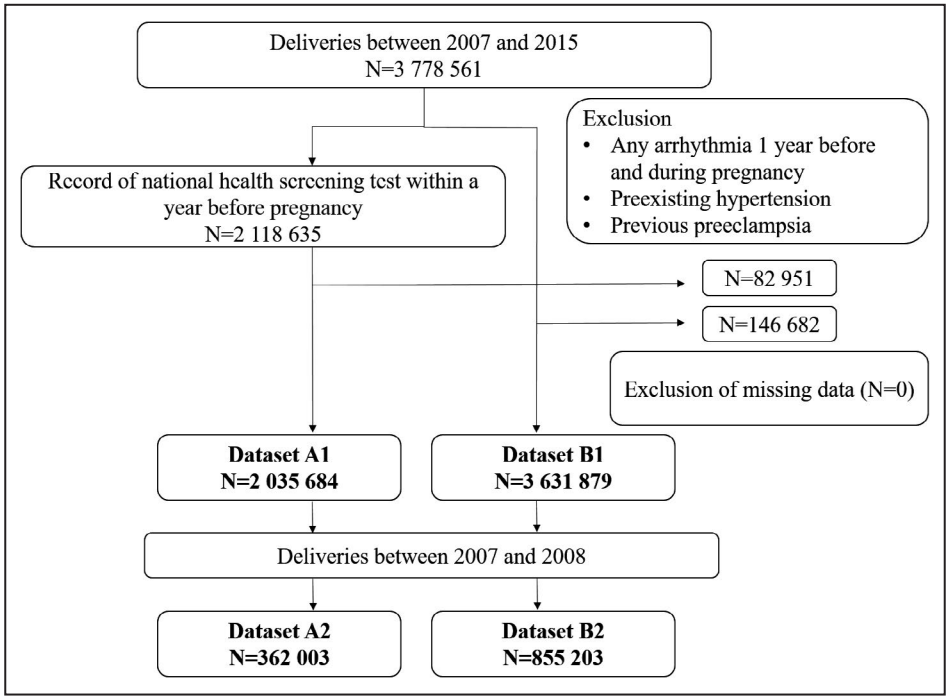


Figure 1. Study flowchart.
Data set A1: Women who gave birth between 2007 and 2015 and had health records within 1 year before pregnancy. Data set B1: Women who gave birth between 2007 and 2015. Data set A2: Women who gave birth between 2007 and 2008 and had health records within 1 year before pregnancy. Data set B2: Women who gave birth between 2007 and 2008.

were not selected. Information on the use of intravenous $MgSO_4$ was additionally collected using prescription codes. We did not differentiate between specific regimens such as bolus or continuous infusion.

Statistical Analysis

Clinical characteristics and outcomes of patients with PIH were compared with those of normotensive pregnant women. Multiple sensitivity analyses were performed in different sets of populations with different follow-up periods (Figure 1); moreover, analyses were also performed using data of women who developed versus did not develop arrhythmia after delivery. Continuous variables were presented as means with SDs, whereas categorical variables were presented as numbers and percentages. Student's *t* test and χ^2 test were used to compare continuous and categorical variables, respectively. Cox proportional hazards models were used to estimate the adjusted hazard ratios (HRs) and 95% CIs for the development of arrhythmia after delivery. Adjusted variables were selected from factors of high-risk pregnancies or traditional cardiovascular risk factors and were the following: age, primipara, cesarean section, and multiple pregnancy in all data sets; body mass index; systolic and diastolic blood pressures; fasting blood glucose; aspartate aminotransferase levels; alanine aminotransferase levels; total cholesterol levels; and current smoking in data sets A1 and A2. A *P* value <0.05 was considered statistically significant. Statistical analyses were performed using SAS for Windows version 9.4 (SAS Inc., Cary, NC). The analytic codes and processed data sets for this study are available upon request for a limited time period.

RESULTS

Of 3 778 561 women (entire cohort; B) who gave birth between 2007 and 2015, 2 118 635 women had a record of a national health screening test within a year before pregnancy (health screening cohort; A). The exclusion of women with a diagnosis of any arrhythmia resulted in 3 631 879 and 2 035 684 women in cohorts B and A, respectively (Figure 1).

Among 2 035 684 participants (normotensive pregnancy; n=1 998 386 versus PIH; n=37 297) from the primary cohort (data set A1), the primary end point was detected in 5029 (0.25%) women. Women with PIH were older at delivery, with a greater likelihood of multiparity, multiple pregnancy, and cesarean delivery (Table 1). The analysis of prepregnancy baseline characteristics showed that, compared with women

Table 1. Clinical Characteristics Before and During Pregnancy in Women With Normotension Versus Pregnancy-Induced Hypertension and New Onset of Arrhythmia Within 1 Year After Delivery (Data Set A1)

N (%) or mean (SD)	Normotensive (n=1 998 387)	PIH (n=37 297)	*P* value
Pregnancy-related factors			
Age at delivery, y	31.12 (3.48)	31.63 (3.86)	<0.0001
Age >35 y at delivery	309 484 (15.5)	7756 (20.8)	<0.0001
Primipara	892 541 (44.7)	10 427 (28.0)	<0.0001
Cesarean section	705 081 (35.3)	23 249 (62.3)	<0.0001
Multiple pregnancy	30 041 (1.5)	2244 (6.0)	<0.0001
Prepregnancy characteristics			
BMI, kg/m^2	20.88 (3.55)	22.45 (3.84)	<0.0001
BMI ≥25, N(%)	157 526 (7.9)	7784 (20.9)	<0.0001
Systolic blood pressure, mm Hg	110.4 (10.98)	118.0 (13.90)	<0.0001
Diastolic blood pressure, mm Hg	69.4 (8.24)	74.7 (10.24)	<0.0001
Aspartate aminotransferase, IU/mL	19.4 (12.45)	20.3 (11.20)	<0.0001
Alanine aminotransferase, IU/mL	15.4 (17.21)	17.7 (16.48)	<0.0001
Fasting blood glucose, mg/dL	86.8 (12.59)	89.5 (19.32)	<0.0001
Total cholesterol, mg/dL	175.8 (33.56)	181.0 (32.66)	<0.0001
Current smoker, N(%)	76 931 (3.9)	1810 (4.9)	<0.0001
Primary end point			
New onset of arrhythmia	4799 (0.24)	230 (0.62)	<0.0001

BMI indicates body mass index; and PIH, pregnancy induced hypertension.

with normotensive pregnancies, those with PIH were more obese and had higher blood pressure values, serum liver aminotransferase levels, fasting blood glucose, and total cholesterol levels; moreover, they were more likely to be smokers. These differences in baseline characteristics were consistently significant in other data sets that included larger populations (B1; Table S2) or had a longer observation period (A2 and B2; Tables S3 and S4). There was a significantly higher incidence of arrhythmia within 1 year after delivery in women with PIH (0.62% versus 0.24%; PIH versus normotensive pregnancy) (Table 1).

From sensitivity analysis using different data sets, the short- (1 year) and long-term (7 years) incidences of arrhythmia after delivery were consistently higher in women with PIH than in those with normotensive pregnancies (Table 2). The incidence of arrhythmia in the largest data set (B1) was 0.26%.

Similarly, women who subsequently developed arrhythmia were older and more likely to have had a cesarean section, multiple pregnancies, and PIH during the antecedent pregnancy compared with those who did not develop arrhythmia (Tables S5 through S8). Although not hypertensive, women who developed arrhythmia after delivery tended to have higher systolic and diastolic blood pressures, higher levels of alanine aminotransferase, and lower levels of total cholesterol before pregnancy; they were likely to have been smokers before their pregnancies.

Women with PIH had an increased risk of arrhythmia within 1 year before and after adjustment for multiple potential risk factors (HRs, 2.58 and 2.39, respectively) (Table 3). Women with PIH had a significantly increased incidence of arrhythmia than normotensive women starting from early after delivery, as shown in Figure 2 (log-rank *P*<0.001). Other significant predictors of arrhythmia were older age and delivery by cesarean section. Subcategorical analysis revealed that PIH was a significant predictor of atrioventricular block, atrial flutter or fibrillation, premature beats, and paroxysmal tachycardia in descending order of HR. PIH was not associated with

Table 2. Arrhythmia After Delivery in Multiple Data Sets–Sensitivity Analysis

N (%)	Total	Normotensive	PIH	*P* value
Data set A1 (2007–2015)	2 035 684	1 998 387	37 297	
Data set B1 (2007–2015)	3 631 879	3 561 426	70 453	
Data set A2 (2007–2008)	362 003	355 224	6779	
Data set B2 (2007–2008)	855 203	838 206	16 997	
Arrhythmia within 1 year of delivery				
Data set A1	5029 (0.25)	4799 (0.24)	230 (0.62)	<0.0001
Data set B1 (sensitivity analysis)	9580 (0.26)	9136 (0.26)	444 (0.63)	<0.0001
Arrhythmia any time after delivery				
Data set A2	12 295 (3.40)	11 973 (3.37)	322 (4.75)	<0.0001
Data set B2 (sensitivity analysis)	30 961 (3.62)	30 065 (3.59)	896 (5.27)	<0.0001

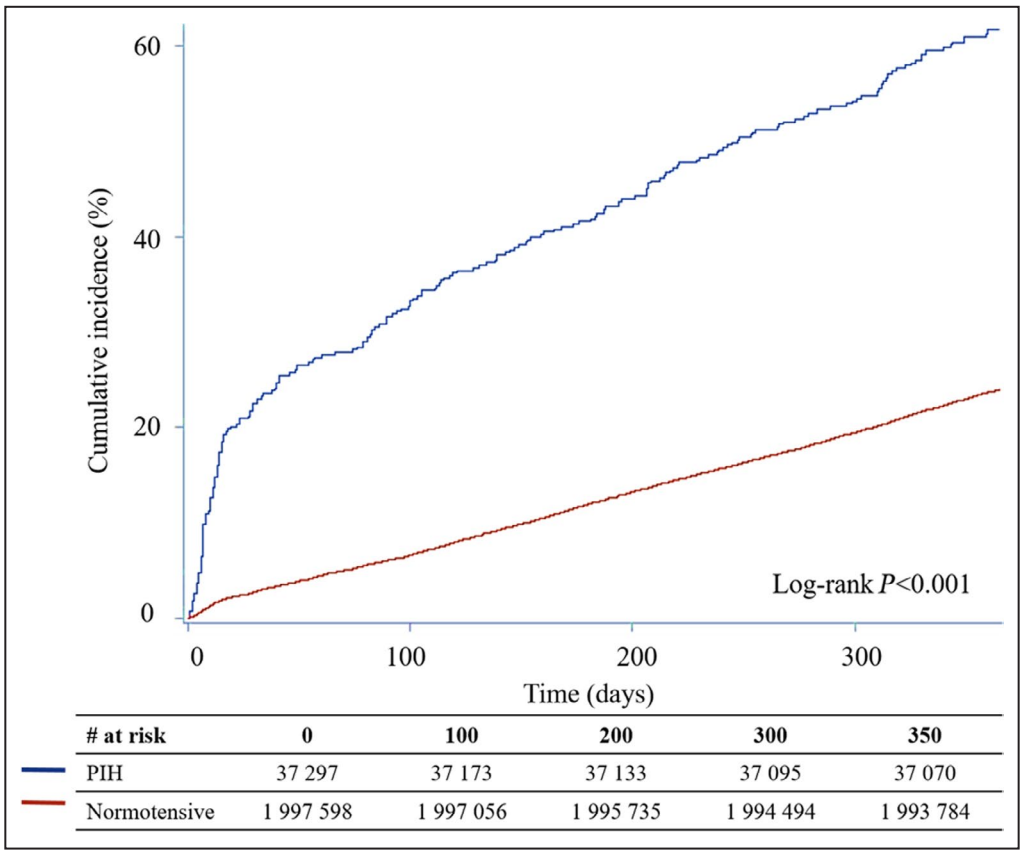
Data sets A1 and A2 include women with health records within 1 year before pregnancy, while B1 and B2 consist of the entire study population. Data sets A2 and B2 include deliveries between 2007 and 2008 and show the incidence of arrhythmia any time after delivery during long-term follow up.

Table 3. Predictors of Arrhythmia During 1 Year After Delivery and Subcategorical Analysis Including Only Significant Arrhythmias

HR (95% CI)	Arrhythmia	Lethal arrhythmias	Atrial flutter or fibrillation	Atrioventricular block	Paroxysmal tachycardia	Premature beats	Right bundle branch block
Unadjusted							
PIH	2.58 (2.25–2.95)	1.25 (0.70–2.21)	2.45 (2.07–2.90)	2.22 (1.22–4.06)	1.45 (1.14–1.84)	1.49 (1.37–1.62)	2.45 (0.33–18.17)
Adjusted*							
PIH	2.39 (2.08–2.75)	1.14 (0.64–2.03)	2.27 (1.91–2.69)	2.33 (1.27–4.31)	1.43 (1.12–1.82)	1.43 (1.31–1.55)	2.18 (0.28–16.91)
Age	1.15 (1.06–1.24)	1.41 (1.11–1.78)	1.33 (1.20–1.46)	1.04 (0.72–1.50)	1.45 (1.30–1.61)	1.18 (1.13–1.22)	1.92 (0.69–5.37)
Primipara	1.01 (0.95–1.07)	1.12 (0.94–1.34)	1.06 (0.99–1.14)	1.08 (0.85–1.38)	1.03 (0.95–1.11)	1.01 (0.98–1.04)	0.91 (0.39–2.12)
Cesarean section	1.27 (1.20–1.35)	1.42 (1.19–1.70)	1.16 (1.07–1.24)	1.02 (0.79–1.32)	1.15 (1.06–1.25)	1.14 (1.10–1.17)	0.77 (0.31–1.89)
Multiple pregnancy	1.11 (0.91–1.36)	0.84 (0.42–1.70)	1.11 (0.86–1.44)	0.67 (0.21–2.13)	1.08 (0.81–1.45)	0.94 (0.84–1.05)	…
BMI	0.99 (0.98–1.00)	0.98 (0.95–1.01)	1.00 (1.00–1.01)	1.00 (0.99–1.01)	0.96 (0.95–0.98)	1.00 (0.99–1.00)	1.00 (0.99–1.02)
SBP	1.00 (1.00–1.00)	1.01 (1.00–1.03)	1.00 (1.00–1.01)	1.00 (0.99–1.02)	1.00 (1.00–1.01)	1.00 (1.00–1.00)	1.05 (1.02–1.08)
DBP	1.00 (1.00–1.01)	0.99 (0.97–1.00)	1.00 (1.00–1.01)	1.00 (0.98–1.02)	1.00 (0.99–1.01)	1.00 (1.00–1.00)	0.97 (0.92–1.03)
FBG	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (1.00–1.00)	1.00 (0.99–1.02)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	0.97 (0.93–1.01)
AST	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (1.00–1.00)	0.99 (0.97–1.01)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	0.93 (0.84–1.02)
ALT	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (0.98–1.02)
Total cholesterol	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (0.99–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.01)
Current smoker	1.03 (0.89–1.19)	0.83 (0.50–1.39)	1.16 (0.97–1.38)	0.76 (0.36–1.61)	1.23 (1.01–1.50)	1.20 (1.12–1.28)	2.56 (0.60–10.96)

After adjustment, PIH, age, and cesarean section remained as arrhythmia predictors in most of the subcategories. PIH did not increase lethal arrhythmia incidence. ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HR, hazard ratio; PIH, pregnancy-induced hypertension; and SBP, systolic blood pressure.

*Adjusted for age, primipara, cesarean section, and multiple pregnancy, body mass index, systolic and diastolic blood pressures, fasting blood glucose, aspartate aminotransferase levels, alanine aminotransferase levels, total cholesterol levels, and current smoking.



# at risk	0	100	200	300	350
PIH	37 297	37 173	37 133	37 095	37 070
Normotensive	1 997 598	1 997 056	1 995 735	1 994 494	1 993 784

Figure 2. Risk of arrhythmia during 1 year after delivery in pregnancy-induced hypertension (PIH) and normotensive pregnancy.
Cumulative incidence of arrhythmia over a year after delivery was higher in the PIH group compared with normotensive pregnancies.

the occurrence of potentially lethal arrhythmias such as ventricular tachycardia or fibrillation. Sensitivity analyses showed that while the incidence of paroxysmal tachycardia increased only within a year after PIH, atrial flutter/fibrillation and premature beats were the types of arrhythmias that showed the most persistent increase in incidence after PIH (Figure 3 and Tables S9 through S11). Kaplan-Meier curves showed increased incidence of atrial flutter/fibrillation, paroxysmal tachycardia and premature beats in the PIH group (Figure S1).

The use of $MgSO_4$ infusion during pregnancy was associated with an increased risk of arrhythmia regardless of the presence of PIH (Table 4). Accordingly, the highest-risk group after multivariate analysis was the group of women that had PIH and received $MgSO_4$ infusion concurrently. The arrythmogenic risk at 1 year was higher in women with PIH who did not receive $MgSO_4$ compared with that in women with normotensive pregnancies who received $MgSO_4$; however, this risk was lower at 7 years in the former group of women.

Although baseline laboratory data did not affect the risk of arrhythmia, maternal age and cesarean section remained significant short- and long-term predictors of arrhythmia. Cigarette smoking within a year before pregnancy was associated with a higher long-term risk of arrhythmia after delivery.

DISCUSSION

We investigated whether the incidence of significant arrhythmia increased after PIH and found that previously healthy women with PIH had a higher risk of developing an arrhythmia after delivery compared with those with normotensive pregnancies. Atrial arrhythmia and premature beats were the most significantly associated arrhythmias in women with a history of PIH, and the use of $MgSO_4$ was associated with an additional risk of arrhythmia.

We demonstrated for the first time that, compared with women with normotensive pregnancies, those with PIH have a higher risk of developing various types of arrhythmias, especially atrial arrhythmia and premature beats, after pregnancy. In our study, women with PIH had a >2-fold risk of developing an arrhythmia than those with normotensive pregnancies. The incidences of arrhythmias in the general

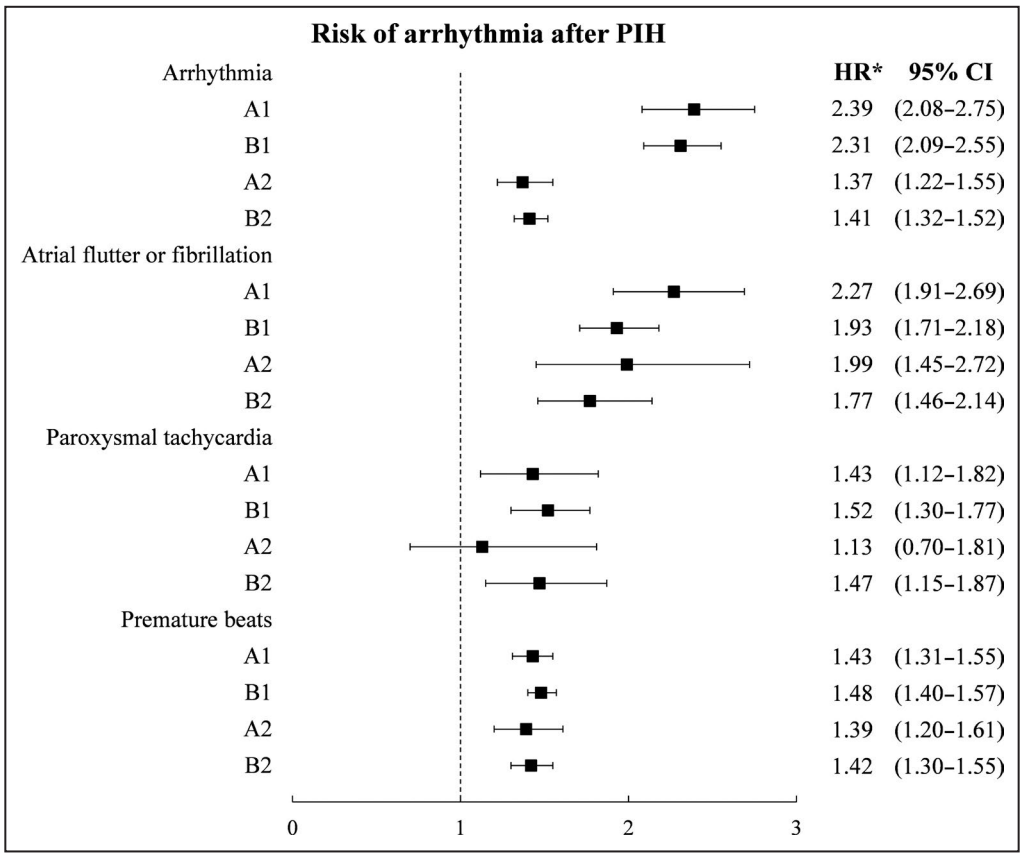


Figure 3. Risk of overall and specific arrhythmia after pregnancy-induced hypertension.
The 1-year and 7-year risk of arrhythmia are shown in data sets A1 and B1 and data sets A2 and B2, respectively. Atrial flutter/fibrillation and premature beats were the categories with the most persistently increased incidences in different data sets (A1–B2). HR indicates hazard ratio. *Adjusted for age, primipara, cesarean section, and multiple pregnancy in all data sets; body mass index, systolic and diastolic blood pressures, fasting blood glucose, aspartate aminotransferase levels, alanine aminotransferase levels, total cholesterol levels, and current smoking in data sets A1 and A2.

study population were ≈0.25% and 3.62% within 1 and 7 years, respectively. Most previous studies that evaluated the long-term cardiovascular risk in women after hypertensive pregnancies did not consider arrhythmia.[2–6] To the best of our knowledge, only a few studies have reported arrhythmia in patients with a history of pregnancy-related hypertension.[9,17,21] Most recently, Garovic et al[21] reported increased cardiac arrhythmia in women with hypertensive disorders of pregnancy (adjusted HR, 1.33; 95% CI, 1.11–1.60) and preeclampsia (adjusted HR, 1.38; 95% CI, 1.07–1.77) in a 40-year long-term outcomes study. Lin et al[9] reported a malignant arrhythmia incidence among women with preeclampsia/eclampsia of 70/100 000 per year (1.57%) with an adjusted HR of 7.7 (95% CI, 5.5–10.8; P<0.0001). They adjusted for chronic hypertension, PIH, diabetes, and other high-risk pregnancy–related factors, but not for other metabolic factors. Medical history was obtained from recall, and no information was collected before pregnancy in their study. They reported a higher HR than that in our study probably because their study population and end point definition were different from those in our study. We excluded only patients with chronic hypertension and previous arrhythmia, whereas Lin et al excluded patients with extreme ranges of pregnancy outcomes or previous major adverse cardiac events from the study group. This may have resulted in a study population with a lower risk profile, and hence an accentuated HR. In addition, their definition of malignant arrhythmia was broad, including nonspecific codes such as “unspecified cardiac arrest” (*International Classification of Diseases, Ninth Revision* [*ICD-9*] code 427.5).[22–24] On the other hand, Ray et al[17] investigated atrial and ventricular arrhythmias separately for secondary end points in a population of women with maternal placental syndromes, including paroxysmal tachycardia (*ICD-9*, 427.2; *ICD-10*, I47.9), which is also a broad and nonspecific code. However, narrowing the end point definition to

Table 4. Risk Stratified by the Presence of PIH and the Use of $MgSO_4$ Infusion and Predictors of Arrhythmia

HR (95% CI)	Data set A1	Data set A2	Data set B1	Data set B2
Unadjusted				
Normotensive and no $MgSO_4$ infusion	1	1	1	1
Normotensive and $MgSO_4$ infusion	1.59 (1.21–2.09)	1.40 (1.11–1.77)	1.72 (1.42–2.08)	1.41 (1.22–1.62)
PIH and no $MgSO_4$ infusion	2.56 (2.21–2.97)	1.39 (1.22–1.59)	2.49 (2.24–2.77)	1.38 (1.27–1.50)
PIH and $MgSO_4$ infusion	2.72 (1.97–3.76)	1.64 (1.28–2.10)	2.62 (2.08–3.29)	1.92 (1.67–2.21)
Adjusted*				
Normotensive and no $MgSO_4$ infusion	1	1	1	1
Normotensive and $MgSO_4$ infusion	1.53 (1.16–2.01)	1.36 (1.08–1.73)	1.64 (1.36–1.99)	1.38 (1.20–1.59)
PIH and no $MgSO_4$ infusion	2.39 (2.05–2.78)	1.33 (1.17–1.52)	2.31 (2.08–2.57)	1.32 (1.22–1.43)
PIH and $MgSO_4$ infusion	2.51 (1.82–3.48)	1.56 (1.22–2.00)	2.41 (1.91–3.03)	1.83 (1.59–2.11)
Age	1.14 (1.06–1.24)	1.18 (1.11–1.26)	1.10 (1.04–1.16)	1.15 (1.11–1.19)
Primipara	1.01 (0.95–1.07)	0.96 (0.92–0.99)	1.01 (0.96–1.05)	0.95 (0.93–0.97)
Cesarean section	1.27 (1.20–1.35)	1.09 (1.05–1.14)	1.28 (1.23–1.34)	1.11 (1.08–1.14)
Multiple pregnancy	1.08 (0.88–1.32)	1.04 (0.89–1.22)	1.15 (1.00–1.33)	1.00 (0.91–1.10)
BMI	0.99 (0.98–1.00)	0.99 (0.98–1.00)	…	…
Systolic blood pressure	1.00 (1.00–1.00)	1.00 (1.00–1.00)	…	…
Diastolic blood pressure	1.00 (1.00–1.01)	1.00 (1.00–1.01)	…	…
Fasting blood glucose, mg/dL	1.00 (1.00–1.00)	1.00 (1.00–1.00)	…	…
Aspartate aminotransferase, IU/mL	1.00 (1.00–1.00)	1.00 (1.00–1.00)	…	…
Alanine aminotransferase, IU/mL	1.00 (1.00–1.00)	1.00 (1.00–1.00)	…	…
Total cholesterol, mg/dL	1.00 (1.00–1.00)	1.00 (1.00–1.00)	…	…
Current smoker	1.03 (0.89–1.19)	1.17 (1.05–1.30)	…	…

Before and after adjustment for multiple potential risk factors, PIH and the use of magnesium sulfate infusion were associated with a higher risk of arrhythmia. Age and cesarean section remained as arrhythmia predictors in all data sets. BMI indicates body mass index; $MgSO_4$, magnesium sulfate; and PIH, pregnancy induced hypertension.

*Adjusted for age, primipara, cesarean section, and multiple pregnancy in all data sets; body mass index, systolic and diastolic blood pressures, fasting blood glucose, aspartate aminotransferase levels, alanine aminotransferase levels, total cholesterol levels, and current smoking in data sets A1 and A2.

admission for arrhythmias may have increased the specificity for diagnosis. In concordance with our results, Ray et al concluded that atrial but not ventricular arrhythmias were associated with prior maternal placental syndromes (atrial dysrhythmia: adjusted HR, 1.48; 95% CI 1.10–1.98; ventricular dysrhythmia: adjusted HR, 1.41; 95% CI, 0.96–2.07).

Most importantly, we found that women with PIH had more than a 2-fold risk of developing atrial flutter or fibrillation compared with those with normotensive pregnancies. The diagnosis of atrial arrhythmia is unambiguous and is rarely falsely given, as it requires electrocardiographic analysis; atrial fibrillation is of clinical importance because it is associated with critical complications such as stroke and heart failure.[25,26]

Stroke is the most debilitating complication of atrial fibrillation. It is well established that preeclampsia is a major contributor to maternal stroke occurrence.[27,28] Although the pathophysiology underlying stroke and the thrombotic tendency in preeclampsia is unclear,[29,30] the increased incidence of atrial arrhythmias may provide a clue to this pathophysiology.

The reason for the increased arrhythmia incidence after PIH is unclear. A few studies based on echocardiography during pregnancy or the peripartal period have demonstrated diastolic dysfunction in women with PIH,[31] which has a close relationship with atrial function[32] and left atrial dilation.[33,34] However, some of these parameters are preload-dependent and large studies with concrete evidence are lacking. Larger prospective studies using electrocardiographic and echocardiographic data, with prepregnancy baseline evaluation, are necessary to further elucidate the relationship between PIH and arrhythmia incidence.

Other PIH-associated arrhythmias included atrioventricular block, premature beats, and paroxysmal tachycardia. Although not always requiring treatment, new-onset atrioventricular block disturbs cardiac conduction and can potentially evolve into other high-risk conditions.[35,36] However, in our study, the risk of atrioventricular block was present only within 1 year after PIH and became insignificant in the long run. This may be attributable to our broad definition of atrioventricular block; discriminating between low-grade and

high-grade atrioventricular block may result in different outcomes. The diagnostic codes of premature beats and paroxysmal tachycardia are frequently used for nonspecific palpitations and have less diagnostic accuracy. Nonetheless, the persistently high risk of these arrhythmias after 7 years following PIH implies that some patients continue to have cardiac symptoms years after delivery, for which they seek medical advice; some of these patients may be experiencing subclinical stages of significant arrhythmia.

In our study, women with PIH had higher prepregnancy risk profiles than those with normotensive pregnancies. This strengthens the suggestion that the higher cardiovascular risk after PIH may be largely attributable to shared risk factors. Whether PIH causes or results from common risk factors of future CVD remains a strongly debated issue.[7,8,11,12] The key to the answer of this question is whether CVD risk factors are present before pregnancy. Preeclampsia itself seems to, in part, contribute to future CVD risk as the severity and recurrence of preeclampsia were shown to have a linear relationship with long-term cardiovascular admissions.[11] Notwithstanding, most of the other studies that reported independent or common risk were based on adjustments for baseline data from early pregnancy or limited information.[7,12] However, different hemodynamic responses were observed in early pregnancies from 6 weeks of gestation on echocardiography in women with preeclampsia and fetal growth retardation compared with those with normal pregnancy.[37] Therefore, strictly speaking, data from early pregnancy may not reflect the true baseline characteristics.

We identified very few studies that evaluated future cardiovascular risk in women with PIH using prepregnancy data. Grandi et al[8] collected clinical but not laboratory information based on diagnostic codes and medications from 2 years before childbirth. Their study was inconclusive with respect to the independent CVD risk. On the other hand, Romundstad et al[12] showed from the Nord-Trøndelag Health Studies 1 and 2 that the worse metabolic profile of women with PIH was attenuated after adjustment for prepregnancy blood pressure and body mass index. Our study adds valuable information to the literature by further adjusting for baseline laboratory values, which were significantly different between the 2 groups. Women with a history of PIH are more likely to have CVD risk factors before the actual diagnosis of CVD while they are still in their 40s, which may be an important window for preventive interventions.[38] Therefore, this population should be educated for CVD prevention and actively screened for early diagnosis and treatment.

Furthermore, we found that the risk of arrhythmia significantly increased with the use of intravenous $MgSO_4$. Although $MgSO_4$ is widely used in high-risk pregnancies such as preterm labor and for neurologic complication prevention in preeclampsia, the exact treatment protocol has not been established.[1,20] Recently, there have been attempts to explore regimens with shorter infusion time, which have shown similar effects in eclampsia prevention.[39,40] Although it is unclear whether the higher risk of arrhythmia is related to the innate higher risk of these pregnancies or $MgSO_4$ related, our results forewarn the unguarded use of $MgSO_4$ in clinical practice, advocating a more selective approach.

Limitations

First, health administrative data may not detect gaps in health care services or subclinical and mild forms of the disease; however, we used a prepregnancy washout period of 1 year. We also used only discrete and specific end points. Second, women who experienced complicated pregnancies may have increased health awareness, which may lead to increased health care use by these women; thus, CVD risks might have been overestimated. Third, since the follow-up period was relatively short and the study population consisted of young women, we did not assess mortality. Fourth, we may have not adjusted for some potential confounding factors. For example, we do not have information on underlying cardiovascular diseases such as structural heart disease or specific medication other than MgSO4 during or after pregnancy. However, since we have excluded chronic hypertension taking antihypertensive medication at enrollment, the impact of beta blockers on arrhythmia was not considered in our analysis. We do assume that the PIH group may have been treated with beta blockers during delivery. Despite this, they resulted in having increased arrhythmias. Finally, although we used a database representative of the South Korean population, the results may not be directly applicable to other countries.

CONCLUSIONS

Based on data from a large nationwide database, PIH was significantly associated with the development of an arrhythmia within 1 year after delivery. The most salient finding of our study was that the risk of developing atrial flutter and fibrillation is 2-fold higher in women with PIH than in those with normotensive pregnancies. However, the incidence of lethal arrhythmias did not increase. Arrhythmias may largely contribute to increasing the future cardiovascular risk in women with a PIH history.

Our study is unique in that it is the first to formally evaluate the long-term risk of arrhythmias in women with a PIH history; we adjusted for prepregnancy baseline clinical and laboratory data, and additionally stratified the risk related to $MgSO_4$ use. Our results

add to the previously scarce data on the relationship between PIH and CVD risk in the Asian population. Future research should focus on uncovering high-risk features after a complicated pregnancy, such as echocardiographic or electrocardiographic parameters that precede cardiovascular disorders, as well as the prevention of these disorders.

ARTICLE INFORMATION

Received June 27, 2021; accepted November 22, 2021.

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Acknowledgments

We thank the Korea National Health Insurance Corporation for providing access to the claims database.

Author Contributions: Drs Park, Na, and Cho conceived this project. Dr Cho had full access to the primary data and conducted all analyses with inputs from Drs Park and Roh. Dr Park wrote the first draft of the manuscript. All authors contributed to the interpretation of the results and the final manuscript.

Sources of Funding

This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HI19C0502).

Disclosures

None.

Supplemental Material

Tables S1–S11
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Categories of significant arrhythmias and ICD-10 codes.

Categories for significant arrhythmias and ICD-10 codes	
Lethal arrhythmias	
I47.2	Ventricular tachycardia
I49.0	Ventricular fibrillation and flutter
I49.01	Ventricular fibrillation
I49.02	Ventricular flutter
Atrial flutter or fibrillation	
I48	Atrial fibrillation and flutter
I48.0	Paroxysmal atrial fibrillation
I48.1	Persistent atrial fibrillation
I48.2	Chronic atrial fibrillation
I48.3	Typical atrial flutter
I48.4	Atypical atrial flutter
I48.9	Atrial fibrillation and atrial flutter, unspecified
I48.91	Unspecified atrial fibrillation
I48.92	Unspecified atrial flutter
Atrioventricular block	
I44.0	Atrioventricular block, first degree
I44.1	Atrioventricular block, second degree
I44.2	Atrioventricular block, complete
I44.7	Left bundle-branch block, unspecified
Paroxysmal tachycardia	
I47	Paroxysmal tachycardia
I47.0	Re-entry ventricular arrhythmia
I47.1	Supraventricular tachycardia
Premature beats	
I49.1	Atrial premature depolarization
I49.2	Junctional premature depolarization
I49.3	Ventricular premature depolarization
I49.40	Other and unspecified premature depolarization
I49.49	Other premature depolarization
I49.9	Cardiac arrhythmia, unspecified
Right bundle branch block	
I45	Right fascicular block

Specific codes to be included in each category were selected after consulting a cardiac electrophysiologist. ICD-10, International Classification of Diseases, 10th Revision.

Table S2. Clinical characteristics before and during pregnancy in women with normotension vs. pregnancy-induced hypertension and new-onset arrhythmia within 1 year after delivery (Dataset B1).

N (%) or mean (SD)	Normotensive (n=3,561,426)	PIH (n=70,453)	*P*-value
Pregnancy-related factors			
Age at delivery, years	30.98 (3.91)	31.66 (4.31)	<0.0001
Age >35 at delivery	617,430 (17.3)	17,037 (24.2)	<0.0001
Primipara	1,738,256 (48.8)	23,807 (33.8)	<0.0001
Cesarean section	1,305,670 (36.7)	44,591 (63.3)	<0.0001
Multiple pregnancy	50,521 (1.4)	3,841 (5.5)	<0.0001
Primary endpoint			
New onset of arrhythmia	9,136 (0.26)	444 (0.63)	<0.0001

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation.

Table S3. Clinical characteristics before and during pregnancy in women with normotension vs. pregnancy-induced hypertension and new-onset arrhythmia within 7 years after delivery (Dataset A2).

N (%) or mean (SD)	Normotensive (n=355,224)	PIH (n=6,779)	*P*-value
Pregnancy-related factors			
Age at delivery, years	29.97 (3.28)	30.35 (3.67)	<0.0001
Age >35 at delivery	30,902 (8.7)	868 (12.8)	<0.0001
Primipara	142,582 (40.1)	1,616 (23.8)	<0.0001
Cesarean section	117,757 (33.2)	3,964 (58.5)	<0.0001
Multiple pregnancy	4,555 (1.28)	389 (5.7)	<0.0001
Pre-pregnancy characteristics			
BMI, kg/m2	20.78 (5.84)	21.96 (3.39)	<0.0001
BMI ≥ 25, N(%)	23,929 (6.7)	1,074 (15.8)	<0.0001
Systolic blood pressure, mmHg	110.9 (11.20)	117.3 (13.87)	<0.0001
Diastolic blood pressure, mmHg	70.0 (8.45)	74.3 (10.46)	<0.0001
Aspartate Aminotransferase, IU/mL	19.56 (11.49)	20.05 (10.20)	<0.0001
Alanine Aminotransferase, IU/mL	15.45 (15.71)	16.97 (14.22)	<0.0001
Fasting blood glucose, mg/dL	85.97 (14.37)	88.19 (21.67)	<0.0001
Total cholesterol, mg/dL	174.1 (34.60)	178.0 (31.79)	<0.0001
Current smoker, N(%)	9,824 (2.8)	212 (3.1)	<0.0001
Primary endpoint			
New onset of arrhythmia	11,973 (3.37)	322 (4.75)	<0.0001

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation.

Table S4. Clinical characteristics before and during pregnancy in normotensive vs. pregnancy-induced hypertension and new-onset arrhythmia within 7 years after delivery (Dataset B2).

N (%) or mean (SD)	Normotensive (n=838,206)	PIH (n=16,997)	*P*-value
Pregnancy-related factors			
Age at delivery, years	30.23 (3.80)	30.92 (4.25)	<0.0001
Age >35 at delivery	107,805 (12.9)	3,305 (19.4)	<0.0001
Primipara	405,494 (48.4)	5,732 (33.7)	<0.0001
Cesarean section	300,799 (35.9)	10,434 (61.4)	<0.0001
Multiple pregnancy	10,792 (1.3)	974 (5.7)	<0.0001
Primary endpoint			
New onset of arrhythmia	30,065 (3.59)	896 (5.27)	<0.0001

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation.

Table S5. Clinical characteristics before and during pregnancy in control group women vs. women with new-onset arrhythmia within 1 year after delivery (Dataset A1).

N (%) or mean (SD)	Control (n=2,030,655)	New arrhythmia (n=5,029)	*P*-value
Pregnancy-related factors			
Age at delivery, years	31.13 (3.48)	31.28 (3.65)	0.002
Age >35 at delivery	316,351 (15.6)	889 (17.7)	<0.0001
Primipara	900,749 (44.4)	2,219 (44.1)	0.739
Cesarean section	726,215 (35.8)	2,115 (42.1)	<0.0001
Multiple pregnancy	32,175 (1.6)	110 (2.2)	0.001
Pregnancy induced hypertension	37,067 (1.8)	230 (4.6)	<0.0001
Pre-pregnancy characteristics			
BMI, kg/m2	20.91 (3.56)	20.93 (2.95)	0.616
BMI ≥ 25, N(%)	164,878 (8.1)	432 (8.6)	0.222
Systolic blood pressure, mmHg	110.6 (11.08)	111.0 (11.50)	0.005
Diastolic blood pressure, mmHg	69.5 (8.31)	69.9 (8.63)	0.001
AST, IU/mL	19.39 (12.44)	19.49 (8.64)	0.569
AST > 31 mg/dL, N(%)	70,567 (3.5)	193 (3.8)	0.161
ALT, IU/mL	15.42 (17.21)	15.83 (12.53)	0.091
ALT > 31 mg/dL, N(%)	81,835 (4.0)	240 (4.8)	0.008
AST or ALT > 31 mg/dL, N(%)	89,589 (4.4)	265 (5.3)	0.003
FBG, mg/dL	86.90 (12.74)	87.13 (13.25)	0.201
FBG ≥ 125 mg/dL	11,493 (0.6)	34 (0.7)	0.299
TC, mg/dL	175.9 (33.56)	174.8 (31.30)	0.026
TC ≥ 200 mg/dL	391,079 (19.3)	928 (18.5)	0.148
Current smoker, N(%)	78,533 (3.9)	208 (4.1)	0.324

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; TC, total cholesterol.

Table S6. Clinical characteristics before and during pregnancy in control group women vs. women with new-onset arrhythmia within 1 year after delivery (Dataset B1).

N (%) or mean (SD)	Control (n=3,622,299)	New arrhythmia (n=9,580)	*P*-value
Pregnancy-related factors			
Age at delivery, years	30.99 (3.92)	31.07 (4.12)	0.044
Age >35 at delivery	632,589 (17.5)	1,878 (19.6)	<0.0001
Primipara	1,757,419 (48.5)	4,644 (48.5)	0.937
Cesarean section	1,346,049 (37.2)	4,212 (44.0)	<0.0001
Multiple pregnancy	54,154 (1.5)	208 (2.2)	<0.0001
Pregnancy induced hypertension	70,009 (1.9)	444 (4.6)	<0.0001

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation.

Table S7. Clinical characteristics before and during pregnancy in control group women vs. women with new-onset arrhythmia within 7 years after delivery (Dataset A2).

N (%) or mean (SD)	Control (n=349,708)	New arrhythmia (n=12,295)	*P*-value
Pregnancy-related factors			
Age at delivery, years	29.97 (3.28)	30.12 (3.43)	<0.0001
Age >35 at delivery	30,538 (8.7)	1,232 (10.0)	<0.0001
Primipara	139,393 (39.9)	4,805 (39.1)	0.083
Cesarean section	117,285 (33.5)	4,436 (36.1)	<0.0001
Multiple pregnancy	4,749 (1.4)	195 (1.6)	0.032
Pregnancy induced hypertension	6,457 (1.9)	322 (2.6)	<0.0001
Pre-pregnancy characteristics			
BMI, kg/m2	20.80 (5.88)	20.77 (2.75)	0.610
BMI ≥ 25, N(%)	24,089 (6.9)	914 (7.4)	0.019
Systolic blood pressure, mmHg	111.0 (11.28)	111.4 (11.55)	0.0001
Diastolic blood pressure, mmHg	70.1 (8.50)	70.4 (8.71)	<0.0001
AST, IU/mL	19.57 (11.54)	19.70 (9.14)	0.200
AST > 31 mg/dL, N(%)	12,770 (3.7)	489 (4.0)	0.059
ALT, IU/mL	15.47 (15.75)	15.77 (13.80)	0.038
ALT > 31 mg/dL, N(%)	13,541 (3.9)	516 (4.2)	0.067
AST or ALT > 31 mg/dL, N(%)	14,986 (4.3)	564 (4.6)	0.105
FBG, mg/dL	86.02 (14.63)	85.89 (11.97)	0.358
FBG ≥ 125 mg/dL	1,960 (0.6)	67 (0.5)	0.821
TC, mg/dL	174.2 (34.63)	173.9 (32.33)	0.272
TC ≥ 200 mg/dL	62,728 (17.9)	2,176 (17.7)	0.497
Current smoker, N(%)	9,640 (2.8)	396 (3.2)	0.002

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; TC, total cholesterol.

Table S8. Clinical characteristics before and during pregnancy in control group women vs. women with new-onset arrhythmia within 7 years after delivery (Dataset B2).

N (%) or mean (SD)	Control (n=824,242)	New arrhythmia (n=30,961)	*P*-value
Pregnancy-related factors			
Age at delivery, years	30.23 (3.80)	30.40 (3.97)	<0.0001
Age >35 at delivery	106,541 (12.93)	4,569 (14.76)	<0.0001
Primipara	396,515 (48.11)	14,711 (47.5)	0.041
Cesarean section	299,033 (36.28)	12,200 (39.4)	<0.0001
Multiple pregnancy	11,292 (1.37)	474 (1.5)	0.017
Pregnancy induced hypertension	16,101 (1.95)	896 (2.9)	<0.0001

PIH, pregnancy-induced hypertension; BMI, body mass index; SD, standard deviation.

Table S9. Predictors of arrhythmia during 1 year after delivery and subcategorical analysis including only women with significant arrhythmias (Dataset B1).

HR (95% CI)	**Arrhythmia**	**Lethal arrhythmias**	**Atrial flutter or fibrillation**	**AV block**	**Paroxysmal tachycardia**	**Premature beats**	**Right bundle branch block**
Unadjusted							
PIH	2.50 (2.27-2.75)	1.50 (1.06-2.12)	2.04 (1.81-2.30)	1.39 (0.83-2.32)	1.59 (1.37-1.85)	1.55 (1.47-1.64)	2.07 (0.50-8.52)
Adjusted*							
PIH	2.31 (2.09-2.55)	1.38 (0.97-1.96)	1.93 (1.71-2.18)	1.37 (0.82-2.30)	1.52 (1.30-1.77)	1.48 (1.40-1.57)	2.13 (0.51-8.83)
Age	1.10 (1.04-1.16)	1.32 (1.14-1.53)	1.25 (1.17-1.32)	1.27 (1.02-1.58)	1.24 (1.16-1.33)	1.14 (1.11-1.17)	1.31 (0.62-2.76)
Primipara	1.00 (0.96-1.05)	1.01 (0.89-1.13)	1.02 (0.97-1.07)	1.12 (0.94-1.32)	0.99 (0.94-1.05)	1.00 (0.98-1.02)	0.65 (0.37-1.16)
Cesarean section	1.28 (1.23-1.34)	1.29 (1.15-1.46)	1.18 (1.13-1.24)	1.10 (0.93-1.31)	1.12 (1.06-1.19)	1.15 (1.13-1.17)	0.78 (0.43-1.43)
Multiple pregnancy	1.19 (1.03-1.37)	0.97 (0.62-1.54)	1.03 (0.85-1.23)	0.66 (0.29-1.49)	1.04 (0.85-1.29)	0.99 (0.91-1.07)	-

After adjustment, PIH, age, and cesarean section remained as arrhythmia predictors in most of the subcategories. PIH did not increase the incidence of lethal arrhythmias. PIH, pregnancy-induced hypertension; AV, atrioventricular; HR, hazard ratio; CI, confidence interval.

*Adjusted for age, primipara, cesarean section, and multiple pregnancy.

Table S10. Predictors of arrhythmia within 7 years after delivery and subcategorical analysis including only women with significant arrhythmias (Dataset A2).

HR (95% CI)	**Arrhythmia**	**Lethal arrhythmias**	**Atrial flutter or fibrillation**	**AV block**	**Paroxysmal tachycardia**	**Premature beats**	**Right bundle branch block**
Unadjusted							
PIH	1.44 (1.28-1.62)	1.44 (0.59-3.49)	2.11 (1.55-2.88)	2.45 (1.00-6.00)	1.13 (0.71-1.81)	1.44 (1.24-1.67)	6.65 (0.83-53.10)
Adjusted*							
PIH	1.37 (1.22-1.55)	1.42 (0.58-3.49)	1.99 (1.45-2.72)	2.47 (0.99-6.15)	1.13 (0.70-1.81)	1.39 (1.20-1.61)	7.27 (0.85-62.59)
Age	1.18 (1.11-1.26)	1.40 (0.90-2.18)	1.44 (1.19-1.74)	0.82 (0.39-1.70)	1.19 (0.94-1.50)	1.17 (1.08-1.27)	1.99 (0.24-16.74)
Primipara	0.96 (0.92-0.99)	1.48 (1.10-1.98)	0.99 (0.88-1.13)	1.31 (0.89-1.91)	0.96 (0.83-1.10)	1.02 (0.97-1.07)	0.44 (0.09-2.18)
Cesarean section	1.09 (1.05-1.14)	1.30 (0.96-1.76)	1.06 (0.93-1.20)	1.02 (0.68-1.52)	1.13 (0.98-1.30)	1.14 (1.08-1.19)	0.56 (0.11-2.79)
Multiple pregnancy	1.06 (0.90-1.23)	1.01 (0.32-3.20)	1.26 (0.81-1.95)	1.15 (0.28-4.80)	1.42 (0.90-2.23)	0.95 (0.77-1.16)	-
BMI	0.99 (0.98-1.00)	0.938(0.88-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	0.97 (0.94-1.00)	1.00 (0.99-1.01)	0.90 (0.66-1.22)
SBP	1.00 (1.00-1.00)	1.01 (0.99-1.03)	1.00 (1.00-1.01)	0.99 (0.97-1.02)	1.00 (0.99-1.01)	1.00 (1.00-1.01)	1.07 (1.01-1.14)
DBP	1.00 (1.00-1.01)	1.00 (0.98-1.03)	1.00 (0.99-1.01)	1.02 (0.99-1.05)	1.00 (0.99-1.01)	1.00 (1.00-1.01)	0.94 (0.86-1.02)
FBG	1.00 (1.00-1.00)	1.00 (1.00-1.01)	1.00 (1.00-1.00)	0.99 (0.97-1.01)	1.00 (0.93-1.00)	1.00 (1.00-1.00)	0.94 (0.88-0.99)
AST	1.00 (1.00-1.00)	1.00 (1.00-1.01)	1.00 (1.00-1.00)	1.00 (0.97-1.02)	1.00 (0.99-1.01)	1.00 (1.00-1.00)	1.00 (0.98-1.02)
ALT	1.00 (1.00-1.00)	1.00 (1.00-1.01)	1.00 (1.00-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (1.00-1.00)	0.89 (0.75-1.05)
Total cholesterol	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (0.99-1.01)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.01)
Current smoker	1.17 (1.05-1.30)	1.24 (0.55-2.79)	1.35 (0.98-1.86)	0.34 (0.05-2.43)	1.16 (0.79-1.70)	1.14 (0.99-1.30)	-

PIH, pregnancy-induced hypertension; HR, hazard ratio; CI, confidence interval; AV, atrioventricular; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

*Adjusted for age, primipara, cesarean section, and multiple pregnancy, body mass index, systolic and diastolic blood pressures, fasting blood glucose, aspartate aminotransferase levels, alanine aminotransferase levels, total cholesterol levels, and current smoking.

Table S11. Predictors of arrhythmia within 7 years after delivery and subcategorical analysis including only women with significant arrhythmias (Dataset B2).

HR (95% CI)	**Arrhythmia**	**Lethal arrhythmias**	**Atrial flutter or fibrillation**	**AV block**	**Paroxysmal tachycardia**	**Premature beats**	**Right bundle branch block**
Unadjusted							
PIH	1.48 (1.38-1.59)	1.36 (0.78-2.35)	1.86 (1.54-2.26)	1.66 (0.82-3.36)	1.54 (1.21-1.96)	1.48 (1.36-1.62)	4.17 (0.99-17.65)
Adjusted*							
PIH	1.41 (1.32-1.52)	1.33 (0.77-2.32)	1.77 (1.46-2.14)	1.64 (0.80-3.32)	1.47 (1.15-1.87)	1.42 (1.30-1.55)	4.33 (1.01-18.66)
Age	1.15 (1.11-1.19)	1.37 (1.07-1.74)	1.27 (1.14-1.40)	0.94 (0.64-1.37)	1.19 (1.06-1.34)	1.17 (1.12-1.22)	1.21 (0.35-4.18)
Primipara	0.95 (0.93-0.97)	1.09 (0.90-1.30)	0.96 (0.89-1.03)	1.25 (0.96-1.61)	0.92 (0.85-1.01)	1.01 (0.98-1.04)	0.40 (0.16-0.96)
Cesarean section	1.11 (1.08-1.14)	1.09 (0.91-1.32)	1.14 (1.06-1.23)	1.24 (0.96-1.61)	1.08 (0.99-1.18)	1.15 (1.15-1.19)	0.63 (0.26-1.51)
Multiple pregnancy	1.02 (0.92-1.12)	0.79 (0.35-1.78)	1.00 (0.75-1.33)	0.93 (0.34-2.55)	1.14 (0.83-1.56)	0.95 (0.84-1.07)	-

PIH, pregnancy-induced hypertension; AV, atrioventricular; HR, hazard ratio; CI, confidence interval.

*Adjusted for age, primipara, cesarean section, and multiple pregnancy.

Figure S1. Risk of specific arrhythmia during 1 year after delivery in pregnancy-induced hypertension (PIH) and normotensive pregnancy. (A) Atrial flutter or fibrillation (B) paroxysmal tachycardia and (C) premature beats.