

## Atrial Fibrillation and Atrial Flutter in Pregnant Women— A Population-Based Study

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**Background**—The goal of this study was to determine the prevalence of atrial fibrillation and atrial flutter (AF) in pregnant women and to examine the impact of AF on maternal and fetal outcomes.

**Methods and Results**—Between January 1, 2003 and December 31, 2013, there were 264 730 qualifying pregnancies (in 210 356 women) in the Kaiser Permanente Southern California hospitals, among whom AF was noted in 157 pregnancies (129 women; 61.3 per 100 000 women, or 59.3 per 100 000 pregnancies). Prevalence of AF (per 100 000 women) in white, black, Asian, and Hispanic women was 111.6, 101.7, 45.0, and 34.3, respectively. Older age was associated with higher odds of having AF. Compared to women <25 years of age, the odds ratio (OR) of AF was 4.1 in women age 30 to 34 years, 4.9 in women age 35 to 39 years, and 5.2 in women age  $\geq$ 40. Odds of AF episodes were higher during the third trimester compared to the first trimester (OR, 3.2; 95% CI: 1.5–7.7). Among AF patients, adverse maternal cardiac events were rare—2 women developed heart failure and there were no strokes or systemic embolic events and no maternal death. There were 156 live births (99.4% of all pregnancies). Compared to women without AF, fetal birth weights were similar, but rate for neonates' admission to the neonatal intensive care unit was higher (10.8% vs 5.1%;  $P=0.003$ ).

**Conclusions**—AF is rare in pregnant women. Certain factors such as increased maternal age and white race increase the odds of having AF. Major maternal and fetal complications are infrequent, albeit a source of concern. (*J Am Heart Assoc.* 2016;5:e003182 doi: 10.1161/JAHA.115.003182)

**Key Words:** atrial fibrillation • atrial flutter • pregnancy • women

There is limited information on the prevalence and prognosis of atrial fibrillation and atrial flutter (AF) in pregnant women. The purpose of this study was to report on the prevalence of AF among pregnant women in a large, demographically diverse, integrated health care system and to determine the clinical characteristics, treatment strategies, maternal cardiac outcomes, obstetric outcomes, and fetal outcomes.

Significant hemodynamic and physiologic changes occur in pregnancy. These changes include an increase in cardiac output, expansion in plasma volume, increase in heart size, a

rise in heart rate, a fall in systemic vascular resistance, and an increase in wall tension.<sup>1–3</sup> All of these changes can predispose the mother to new-onset cardiac arrhythmias and increase the likelihood of arrhythmia recurrence in women with a history of cardiac arrhythmias.<sup>4,5</sup>

AF is one of the most common cardiac arrhythmias. Hemodynamic abnormalities and thromboembolic events related to AF result in significant morbidity and mortality.<sup>6</sup> In the pregnant patient, AF can lead to hemodynamic compromise and result in an increased risk to the mother and fetus. The increased cardiac demand during pregnancy may cause AF to be less well tolerated and increase the risk of heart failure. Women with a history of any type of arrhythmias before pregnancy have an increased risk of cardiac events, including recurrent arrhythmias, stroke, heart failure, and cardiac death during pregnancy.<sup>7</sup> AF is also associated with an increased risk of stroke.<sup>8</sup> Pregnancy is accompanied by an increased concentration of clotting factors and a decrease in anticoagulant factors, resulting in a hypercoagulable state.<sup>9–11</sup> Though it is a concern that this hypercoagulable state can predispose pregnant women with AF to an elevated risk of thromboembolic complications,<sup>12</sup> the extent of this risk is not known.

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The management of AF during pregnancy has important implications for both maternal and fetal outcomes. Organogenesis occurs during the first trimester, and the developing fetus is sensitive to potential teratogenic effects of medications. In the second and third trimesters, medications may have potential effects on fetal growth or lead to fetal arrhythmias.<sup>13</sup> Many commonly used medications in AF, such as warfarin and some beta-blockers, have been shown to increase the risks of adverse fetal outcomes.<sup>14–17</sup> Decisions regarding medication use are often difficult, given that though fetal exposure to a medication may pose risk, failure to treat AF could lead to significant hemodynamic compromise and, in turn, lead to poor fetal outcome.

Large population-based studies are important to estimate the prevalence of AF in pregnancy, identify risk factors, and report outcomes. We investigated the health records of patients in the Southern California Kaiser Permanente health care system to study the prevalence and prognosis of pregnancy-related AF. Information from this study would potentially be useful for prepregnancy counseling and decision making regarding treatment strategies.

## Methods

This is a retrospective, population-based study that included all births in the Kaiser Permanente Southern California (KPSC) Health System between January 1, 2003 and December 31, 2013. Patients who were not health plan enrollees or did not have continuous 1-year enrollment (9 months preceding estimated date of delivery [EDD] and 3 months post-EDD) were excluded from the study to allow adequate follow-up data. The research protocol used in this study was reviewed and approved by the Kaiser Permanente Institutional Review Board. Informed consent was waived for this retrospective observational study.

KPSC is a large group-model health maintenance organization that had enrolled more than 3 million members in each of the study years. It includes 14 medical centers and over 200 medical office buildings. Health plan members have a demographic, racial/ethnic, and socioeconomic profile similar to the overall southern California population.<sup>18</sup> Over 20 000 deliveries occur within KPSC hospitals every year. Given that comprehensive electronic medical records are maintained for all patients for various types of medical services and patients typically have long enrollment histories, we had the unique opportunity to study details regarding patients' medical history, treatment strategies, medications used, and clinical outcomes.

Patients with atrial fibrillation or atrial flutter (grouped together as AF in this study) were identified by searching the KPSC Research Data Warehouse (which contains diagnoses

from all ambulatory visits, emergency room visits, and inpatient admissions) using International Classification of Disease, Ninth Revision, Clinical Modification codes 427.3, 427.31, and 427.32. Women with a diagnosis of AF before their deliveries, or within 6 months after their deliveries, were identified. The medical records of these women were manually reviewed to confirm the diagnosis of AF, and data relating to the pregnancy were extracted. Information collected included maternal date of birth, maternal race/ethnicity, maternal cardiac history, concomitant diseases, obstetric history, laboratory values, electrocardiograms, radiographic studies, echocardiographic parameters, pregnancy duration, mode of delivery, infant gender, birth weight, Apgar score, and fetal complications. Information on medication exposure during pregnancy was obtained by both reviewing each patient's medical records and by extracting the pharmacy dispensing records from the KPSC Research Data Warehouse. Data relating to hospitalizations for AF were reviewed and information on cardiac interventions, medication given, outcomes, and any complications were recorded. The self-reported racial/ethnic data was obtained from California birth certificates.

Maternal cardiac events during pregnancy included cardiac arrhythmias requiring treatment, heart failure, stroke, systemic thromboembolic events, transient ischemic attacks, myocardial infarction, or cardiac death. Verification of cardiac end points was performed by a cardiologist by manual review of electronic medical records. Obstetric complications included pregnancy-induced hypertension (new-onset hypertension >140/90 on at least 2 occasions after >20 weeks of gestation), pre-eclampsia, hemolysis elevated liver enzymes low platelets (HELLP) syndrome, premature rupture of membranes (membrane rupture before onset of uterine contractions), premature labor (spontaneous onset of labor <37 weeks of gestation), postpartum hemorrhage, and placental abruption. Fetal complications included premature delivery (<37 weeks gestation), small-for-gestational-age birth weight (<10th percentile or <3rd percentile), fetal demise ( $\geq$ 20 weeks gestation), neonatal death (within 28 days after birth), and need for neonatal intensive care unit admission.

Descriptive statistics for categorical data were reported in absolute numbers and percentages. Continuous variables were analyzed by calculating mean values and SDs. Differences in categorical data between patient groups were compared by Fisher's exact tests. Differences in continuous data between patient groups were compared by Student *t* tests. *P* values <0.05 (2-sided test) were considered statistically significant. Logistic regression analyses were used to estimate odds ratios (ORs) with 95% CIs. To avoid bias, for patients with multiple pregnancies, only one randomly selected pregnancy for each patient was included in the

analyses. Statistical analysis was performed using STATA software (version 12; StataCorp LP, College Station, TX).

## Results

### Patient Population

Between January 1, 2003 and December 31, 2013, there were 342 751 pregnancies identified in the KPSC hospitals, among which 78 021 cases were excluded either because they were not health plan members or did not have continuous 1-year coverage. The study cohort thus comprised of 264 730 pregnancies (in 210 356 women). In this population, there were 157 pregnancies in 129 women with a confirmed diagnosis of AF, corresponding to a prevalence of AF of 59.3 per 100 000 pregnancies, and 61.3 per 100 000 women.

Among the group identified, 112 pregnancies in 93 women (42.3 per 100 000 pregnancies; 44.2 per 100 000 women) had a pre-existing diagnosis of AF documented before pregnancy. For 45 pregnancies in 45 women (17.0 per 100 000 pregnancies; 21.4 per 100 000 women), AF was first diagnosed during pregnancy or during the 6-month postpartum period.

Table 1 lists the baseline characteristics of the study population. The mean age of pregnant women with AF was  $32.8 \pm 5.2$  years. The mean BMI was  $28.9 \pm 7.8$  kg/m<sup>2</sup>. A subset of AF patients had pre-existing comorbidities, including hypertension (7.0%), hyperlipidemia (12.4%), and diabetes (7.0%). The majority of women had structurally normal hearts, with the mean left ventricular ejection fraction being  $62.0 \pm 5.8\%$ . Only 7 patients (5.4%) had structural heart disease, with rheumatic heart disease, congenital heart disease, and a history of cardiomyopathy each accounting for  $\approx 2\%$  of the group. Compared to pregnant women without AF, pregnant women with AF were older and had higher BMI. A higher proportion of those with AF had hyperlipidemia and diabetes.

Prevalence of AF differed by race/ethnicity (Table 2). Prevalence of AF (per 100 000 women) was 111.6 in white women, 101.7 in black women, 45.0 in Asian women, and 34.3 in Hispanic women. Compared to white women, the OR of having AF was OR 0.3 (95% CI: 0.2–0.5) in Hispanic women and OR 0.4 (95% CI: 0.2–0.8) in Asian women.

Prevalence of AF also differed by age. There was no significant difference in the rate of AF in mothers who were <25 years and 25–29 years of age ( $P=0.8$ ; Table 2). The rate of AF significantly increased after age 30 years, with a rate of 87.1 per 100 000 pregnancies in mothers age 30 to 34 ( $P<0.001$ ) and further increased to 104.7 per 100 000 pregnancies in mothers age 35 to 39 ( $P<0.001$ ) and 109.7 per 100 000 pregnancies in mothers age  $\geq 40$  ( $P<0.001$ ). Compared to women <25 years of age, the OR of having AF

**Table 1.** Baseline Characteristics

Characteristics	Pregnant Women With AF	Pregnant Women Without AF	P Value
No. of pregnancies	157	264 573	
No. of women	129	210 227	
Age at delivery, y	$32.8 \pm 5.2$	$29.8 \pm 5.9$	<0.0001
Maternal preconception BMI, kg/m <sup>2</sup>	$28.9 \pm 7.8$	$26.3 \pm 6.1$	<0.0001
Medical history (%)			
HTN (pre-existing)	9 (7.0)	7682 (2.9)	0.05
HLD	16 (12.4)	5596 (2.1)	<0.001
DM (pre-existing)	9 (7.0)	5865 (2.2)	0.009
Maternal cardiovascular history (%)*			
Cardiomyopathy	2 (1.6)		
Rheumatic heart disease	2 (1.6)		
Congenital heart disease	3 (2.3)		
CVA	1 (0.8)		
CHA2DS2-VASc Score	$1.2 \pm 0.5$		
Left ventricular ejection fraction (%)	$62.0 \pm 5.8$		
Obstetric history (%)			
Gravida			
1	36 (22.9)	76 197 (28.8)	0.11
2	47 (30.0)	76 726 (29.0)	0.79
3	31 (19.7)	52 915 (20.0)	1.0
$\geq 4$	43 (27.4)	58 735 (22.2)	0.12

Values are mean $\pm$ SD or n (%). AF indicates atrial fibrillation or atrial flutter; BMI, body mass index; CVA, cerebrovascular accident; DM, diabetes; HLD, hyperlipidemia; HTN, hypertension.

\*Information on maternal cardiovascular history, CHA2DS2-VASc score, and left ventricular ejection fraction was not readily and reliably available for women without AF. P value: 2-sided P value calculated using Fisher's exact test for categorical variables and Student t test for continuous variables.  $P<0.05$  was considered statistically significant.

was 4.1, 4.9, and 5.2 in women 30 to 34, 35 to 39, and  $\geq 40$  years of age, respectively.

### Timing and Management of AF Episodes

Not all patients with a diagnosis of AF experienced clinically significant AF events that required hospitalization or medical interventions. Among the 157 pregnancies (in 129 women) with a diagnosis of AF, there were 60 pregnancies (in 56 women) for which clinically significant AF episodes occurred during pregnancy or during the postpartum period and required hospitalization and/or intervention.

Table 3 lists the time of first-detected clinically significant AF episode by trimester of onset. When compared to the

**Table 2.** Pregnancy-Related AF by Race/Ethnicity and by Age

Demographic Variable	No. of Women (n=129)	Rate Per 100 000 (95% CI)	OR (95% CI)	P Value
<b>Race/ethnicity</b>				
White	59	111.6 (83.2–140.0)	1	—
Hispanic	38	34.3 (23.4–45.2)	0.3 (0.2–0.5)	<0.001
Black	19	101.7 (56.0–147.4)	0.9 (0.5–1.6)	0.79
Asian	12	45.0 (19.6–70.5)	0.4 (0.2–0.8)	0.002
Multiple/other	1	—	—	—
<b>Age, y</b>				
<25	9	21.2 (7.4–35.1)	1	—
25 to 29	14	24.8 (11.8–37.9)	1.2 (0.5–3.1)	0.8
30 to 34	56	87.1 (64.3–110.0)	4.1 (2.0–9.4)	<0.001
35 to 39	39	104.7 (71.9–137.6)	4.9 (2.4–11.6)	<0.001
≥40	11	109.7 (44.9–174.6)	5.2 (2.0–14.1)	<0.001

White was used as the reference group for race/ethnicity. The age <25 group was used as the reference group. Rates per 100 000 were unadjusted rates. P value: 2-sided P value calculated using Fisher's exact test. P<0.05 was considered statistically significant. AF indicates atrial fibrillation or atrial flutter; OR, odds ratio.

first trimester, the odds of having clinically significant AF episodes were numerically higher during the second trimester, but this did not reach statistical significance. The odds significantly increased during the third trimester (OR, 3.2; 95% CI: 1.5–7.7) compared to the first trimester. Of note, 12 of the 29 cases detected during the third trimester occurred within 24 hours of delivery. Postpartum, the risk of clinically significant AF episodes declined back to baseline levels.

Among these 60 pregnancies (in 56 women) with clinically significant AF events, 15 (in 11 women) had pre-existing diagnosis of AF made before their pregnancies. The remaining

45 (in 45 women) did not have a diagnosis of AF before their pregnancy.

Review of electronic medical records showed that the majority of AF episodes were self-limited. Forty-five cases converted to normal sinus rhythm (NSR) after treatment with medications alone, and 7 cases spontaneously converted to NSR without medications. Beta-blockers, digoxin, and diltiazem were the most common medications given (Table 4). Among the 60 cases, 2 cases were treated with direct-current

**Table 4.** Management and Outcome of Pregnancy-Related AF Episodes

Management	No. of Cases (n=60)
Direct current cardioversion (DCCV) with conversion to NSR (%)	2 (3.3)
Spontaneous conversion to NSR without medications (%)	7 (11.7)
Recurrent AF/permanent AF, rate-controlled (%)	6 (10)
Converted to NSR after medications (%)	45 (75)
<b>Medications given*</b>	
Beta-blockers <sup>†</sup>	17
Digoxin	11
Diltiazem	21
Verapamil	4
Ibutilide	1
Procainamide	1

Values are n (%). AF indicates atrial fibrillation or atrial flutter; NSR, normal sinus rhythm.

\*Some patients were treated with more than 1 medication.

<sup>†</sup>Beta-blockers used included metoprolol in 11 cases, atenolol in 1 case, propranolol in 1 case, labetalol in 3 cases, and esmolol in 1 case.

**Table 3.** Time of Clinically Significant AF Episode (Requiring Hospitalization or Medical Treatment) by Trimester of Onset

	No. of Cases (n=60)	Rate Per 100 000 Pregnancies (95% CI)	OR (95% CI)	P Value
First trimester	9	3.4 (1.2–5.6)	1	
Second trimester	18	6.8 (3.7–9.9)	2.0 (0.9–5.1)	0.12
Third trimester	29	11.0 (7.0–15.0)	3.2 (1.5–7.7)	0.002
Postpartum (6 months)	4	1.5 (0.03–3.0)	0.4 (0.1–1.6)	0.26

P value: 2-sided P value calculated using Fisher's exact test. P<0.05 was considered statistically significant. Rates per 100 000 were unadjusted rates. AF indicates atrial fibrillation or atrial flutter; OR, odds ratio.

cardioversion (DCCV; Table 4). Six cases had persistent AF or recurrent paroxysmal AF and a rate control strategy was adopted.

### Risk of Clinically Significant AF Requiring Medical Intervention During Pregnancy in Patients With a Prepregnancy Diagnosis of AF

In our cohort, 112 pregnancies (in 93 women) had a diagnosis of AF made before their index pregnancy. In this group, 15 pregnancies (in 11 women) had clinically significant AF episodes that required hospitalization or medical intervention. The remaining 97 pregnancies (in 82 women) completed pregnancy without experiencing any clinically significant AF events.

Table 5 summarizes the univariate analyses for factors associated with clinically significant AF episodes in women with a prepregnancy diagnosis of AF. There was no significant difference in age between patients with or without clinically significant AF. Clinically significant recurrent AF during pregnancy was associated with obesity (OR, 3.8; 95% CI: 1.0–14.1) and obstetric complications (OR, 4.4; 95% CI: 1.1–18.2).

### Medications Prescribed for the Treatment of AF During Pregnancy

Table 6 lists the outpatient medications prescribed for treatment of AF during pregnancy. The majority of patients were not maintained on outpatient regimen for AF. Based on documentation in their medical records, many patients

themselves opted to not be on a maintenance medication. Among the pregnancies in which the patients were treated with medications, 21 (13.4%) were on a beta-blocker, 16 (10.2%) were on a calcium-channel blocker, and 9 (5.7%) were on digoxin. Two (1.3%) patients were on sotalol. No other antiarrhythmic medications were used. The rate of antiplatelet therapy and anticoagulation therapy were low, with aspirin use noted in 4 pregnancies (2.5%) and heparin/low-molecular-weight heparin (LMWH) used in 5 cases (3.3%). Among the 5 cases given heparin/LMWH, 4 cases were in women with additional indications for anticoagulation (including a history of hypercoagulable state, pulmonary embolism, deep vein thrombosis, or stroke). No pregnant patient with AF was prescribed Coumadin.

### Maternal Cardiac Events, Obstetric Outcomes, and Fetal Outcomes

Adverse maternal cardiac events other than arrhythmias were rare. Two women developed heart failure/pulmonary edema (Table 7). One was a woman with hypertrophic cardiomyopathy and pulmonary hypertension. The other was a woman with peripartum cardiomyopathy with a left ventricular ejection fraction of 25%. There were no strokes or systemic embolic events. There was no maternal mortality.

Sixty-four pregnancies (40.8%) were delivered by caesarean section. Obstetric complications were observed in 34 (21.7%) of pregnancies, with the majority being pregnancy-induced hypertension and pre-eclampsia. Other obstetric complications, including premature rupture of membranes,

**Table 5.** Factors Associated With Clinically Significant AF Episodes Requiring Hospitalization/Medical Intervention During Pregnancy Among Patients With a Pre-Pregnancy Diagnosis of AF (n=93)

Parameter	Univariable*			
	AF (n=11)	No Recurrent AF (n=82)	Odds Ratio (95% CI)	P Value
Maternal age, y	31.6±6.0	32.8±5.3	1.0 (0.9–1.1)	0.49
White race	8	35	3.6 (0.9–14.5)	0.07
Maternal preconception weight, lbs	204.7±54.6	165.7±44.1	1.02 (1.00–1.03)	0.02
Hypertension (pre-existing)	1	5	1.5 (0.2–14.6)	0.71
Hyperlipidemia	2	9	1.8 (0.3–9.7)	0.49
Obesity (BMI >30)	7	26	3.8 (1.0–14.1)	0.048
Diabetes (pre-existing)	2	4	4.3 (0.7–27.0)	0.15
Multigravida (gravida ≥2)	8	64	0.8 (0.2–3.1)	0.69
Obstetric complications	4	9	4.4 (1.1–18.2)	0.04

Values are mean±SD or n (%). Obstetric complications: including pregnancy-induced hypertension, pre-eclampsia, eclampsia (pre-eclampsia with grand mal seizures), hemolysis elevated liver enzymes low platelets (HELLP) syndrome, premature rupture of membranes, premature labor, postpartum hemorrhage, or placental abruption. Multivariable model included maternal age, obesity, and obstetric complications. AF indicates atrial fibrillation or atrial flutter; BMI, body mass index; lbs, pounds.

\*To avoid bias, for patients with multiple pregnancies, only 1 randomly selected pregnancy per patient was included in the logistic regression analysis.



**Table 6.** Outpatient Medication Prescribed to Pregnant Patients With AF

Medications Prescribed	No. of Cases (% Total) (n=157)
Beta-blockers	21 (13.4)
Calcium-channel blockers	16 (10.2)
Digoxin	9 (5.7)
Sotalol	2 (1.3)
Aspirin	4 (2.5)
Coumadin	0
Heparin/low-molecular-weight heparin	5 (3.2)

AF indicates atrial fibrillation or atrial flutter.

premature labor, postpartum hemorrhage, and placental abruption, were observed in a minority of patients (Table 7).

Fetal outcomes are reported in Table 8. There were 156 live births (99.4% of all pregnancies). The 1 case of fetal demise was in a woman who presented at 20 weeks with perforated acute appendicitis and sepsis. She underwent appendectomy and suffered a miscarriage during the immediate postoperative period. Fetal birth weights were not

**Table 7.** Maternal Cardiac Events and Obstetric Outcomes

	No. of Cases (% Total) (n=157)
Maternal cardiac events (other than arrhythmia)	
Heart failure/pulmonary edema	2 (1.2)
Stroke/systemic emboli	0
Cardiac death	0
Mode of delivery	
Cesarean	64 (40.8)
Vaginal-spontaneous	86 (54.8)
Vaginal-assisted	7 (4.5)
Obstetric complications	
Any	34 (21.7)
PHTN	17 (10.8)
Preeclampsia	6 (3.8)
Eclampsia	0
PROM	5 (3.2)
Premature labor	9 (5.7)
PP hemorrhage	5 (3.2)
Placental abruption	1 (0.6)

AF indicates atrial fibrillation or atrial flutter; PHTN, pregnancy-induced hypertension, premature labor (spontaneous onset of labor <37 weeks of gestation); PP hemorrhage, postpartum hemorrhage; PROM, premature rupture of membranes (membrane rupture before onset of uterine contractions).

**Table 8.** Fetal Outcomes

Neonatal outcomes	Pregnant Women With AF (n=157)	Pregnant Women Without AF (n=264 573)	P Value
Live births (%)	156 (99.4)	262 463 (99.2)	1.0
Birth weight, g	3248±738	3335±570	0.06
SGA <10th percentile (%)	11 (7.0)		
SGA <3rd percentile (%)	4 (2.5)		
Need for NICU admission (%)	17 (10.8)	13 309 (5.1)	0.003

Values are mean±SD or n (%). Student *t* test used for continuous variables. *P* value: 2-sided *P* value calculated using Fisher's exact test. *P*<0.05 was considered statistically significant. AF indicates atrial fibrillation or atrial flutter; NICU, neonatal intensive care unit; SGA, small for gestational age at birth.

significantly different between pregnant women with AF and those without. The number of neonates who were small for gestational age was not higher than what would be expected—7.0% were less than 10th percentile in weight and 2.5% were less than 3rd percentile in weight. However, the rate of neonates who required admission to the neonatal intensive care unit were higher in the group with AF (10.8% vs 5.1%; *P*=0.003).

## Discussion

In this large, community-based population in Southern California, the prevalence of AF among pregnant women was low (59.3 per 100 000 pregnancies). Compared to pregnant women without AF, pregnant women with AF were older and had a higher BMI. Epidemiological analyses have identified multiple clinical risk factors that are associated with AF.<sup>6</sup> Some of these risk factors, such as hypertension, hyperlipidemia, and diabetes, were also found to be in higher proportion among pregnant women with AF compared to those without.

The rate of AF in our population is lower than what was reported from ROPAC (Registry on Pregnancy and Cardiac Disease).<sup>19</sup> In the ROPAC registry, 17 of 1321 pregnant women (1.3%) developed AF during pregnancy. Because structural heart disease is one of the most powerful predictors for AF,<sup>20</sup> it is perhaps not surprising that prevalence of AF is higher in the ROPAC population, where all women have structural heart disease, whereas the majority of women in our population have structurally normal hearts.

There is substantial variability in prevalence of AF among different racial/ethnic groups, with the prevalence highest in white women. This finding mirrors the racial/ethnic differences observed with AF in the general population<sup>21</sup> and may

reflect an inherent genetic predisposition of certain racial/ethnic groups to AF.

Age is a powerful risk factor for AF. In women, prevalence of AF increases from 0.1% among those younger than 55 years to 9.1% among those 85 years or older.<sup>22,23</sup> We found that even within this group of pregnant women at a relatively young age (all less than 55 years), age remained an important risk factor, with prevalence of AF significantly increasing after age 30 years.

We found that risk of AF was highest during the third trimester. This may be related to the expansion of plasma volume and increase in red cell mass that peaks at 28 to 34 weeks of gestation, as well as the associated increase in cardiac load.<sup>1,2</sup> The hemodynamic changes related to labor and delivery appeared to be particularly significant, given that 12 of the 29 cases that occurred during the third trimester occurred within 24 hours of delivery.

Obstetric complications were observed in 21.7% of cases of AF. Though the exact mechanism explaining the association of obstetric complications and AF is not known, it is conceivable that obstetric complications, such as preeclampsia, can lead to a heightened adrenergic state and increased inflammatory response, along with stimulation of the renin-angiotensin-aldosterone system, that could induce electrophysiological effects in the atrium and increase arrhythmia susceptibility.<sup>24–26</sup>

The current guidelines for AF recommend the use of digoxin, nondihydropyridine calcium-channel antagonists, or beta-blockers for AF.<sup>6,13</sup> Perhaps because of concern for fetal toxicity, many patients were not maintained on any medications during their pregnancies. Among those on medications, beta-blockers, calcium-channel blockers, and digoxin were the drugs most commonly prescribed. Of note, only 5 patients were treated with anticoagulation, and aspirin use was noted in only 4 patients. Despite the low rate of medication use, the risk of maternal cardiac complications was low. There were no cases of cardiac death or stroke, and the risk of heart failure and pulmonary edema was only observed in 2 cases. The majority of patients in this population had a low CHA2DS2-VASc score of 1 (female sex). The hypercoagulable state associated with pregnancy did not appear to significantly increase the rate of stroke or thromboembolic events beyond what would be expected based on their CHA2DS2-VASc score.

We did find that the rate of need for neonatal intensive care unit admission was higher than the population average. Whether this finding was caused by maternal arrhythmias, related to the fetal effect of cardiovascular drug use, or attributed to some other confounding factors cannot be determined.

There are several limitations to our study. Because patients were initially identified by an electronic data

warehouse, it is possible that we missed some patients with AF. Some patients with AF are asymptomatic and the only way to detect arrhythmia would be through repeated electrocardiogram or continuous ambulatory electrocardiographic monitoring,<sup>27</sup> which was not feasible given our retrospective study design. We excluded patients who did not have continuous 1-year health plan coverage in order to allow adequate follow-up data. However, this exclusion could have introduced a source of bias. Whereas it is difficult to determine how a change or loss of insurance coverage affects health status, one could imagine this being associated with a more unstable socioeconomic background. This was a retrospective observational study and therefore includes all inherent limitations associated with such analyses. For example, treatment differences between groups were not randomized, and it would be difficult to determine whether some of the outcomes were attributed to maternal arrhythmias or an effect of medications used or treatment of arrhythmias. Medication exposure was determined by pharmacy dispensing records, and it was not possible to determine whether each patient was compliant with medication usage. Also, because the majority of patients in this population had structurally normal hearts, our findings may not be generalizable to the group of patients treated at tertiary referral centers with complex congenital heart disease, rheumatic valvular disease, or cardiomyopathies.

## Disclosures

None.

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