



## Review article

# Incidence of atrial fibrillation in pregnancy and clinical significance: A meta-analysis



Ronpichai Chokesuwattanaskul<sup>a,\*</sup>, Charat Thongprayoon<sup>b</sup>, Tarun Bathini<sup>c</sup>, Oisín A. O'Corragain<sup>d</sup>, Konika Sharma<sup>e</sup>, Somchai Prechawat<sup>a</sup>, Patompong Ungprasert<sup>f</sup>, Kanramon Watthanasuntorn<sup>e</sup>, Pavida Pachariyanon<sup>g</sup>, Wisit Cheungpasitporn<sup>h</sup>

<sup>a</sup> Division of Cardiology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

<sup>b</sup> Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA

<sup>c</sup> Department of Internal Medicine, University of Arizona, Tucson, Arizona, USA

<sup>d</sup> Department of Internal Medicine, Temple University, Philadelphia, PA

<sup>e</sup> Department of Internal Medicine, Bassett Medical Center, Cooperstown, NY, USA

<sup>f</sup> Clinical Epidemiology Unit, Department of Research and Development, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

<sup>g</sup> Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas, USA

<sup>h</sup> Department of Medicine, University of Mississippi Medical Center, Mississippi, USA

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## ABSTRACT

**Purpose:** Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia worldwide, and is associated with increased morbidity and mortality. However, the incidence and maternal/fetal outcomes of AF in pregnancy remain unclear. This study's aims were to investigate the pooled incidence of AF in pregnant women and to assess maternal/fetal outcomes of AF in pregnancy.

**Material and methods:** A literature search for studies that reported incidence of AF in pregnancy, was conducted using MEDLINE, EMBASE and Cochrane Database from inception through May 2018. Pooled incidence with 95%CI were calculated using a random-effect model. The protocol for this meta-analysis is registered with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42018095955).

**Results:** We identified 7 cohort studies including 301,638 pregnancies. The pooled estimated incidence of AF in pregnancy among women with no known heart disease, and those with structural heart disease was 0.3% (95%CI: 0.01%–40.6%) and 2.2% (95%CI: 0.96%–5.01%), respectively. Among women with known AF, the pooled estimated incidence of recurrent AF in pregnancy was 39.2% (95%CI: 16.9%–67.2%). The pooled estimated incidence of pre-eclampsia and congestive heart failure among pregnant patients with AF was 4.1% (95%CI: 2.1%–7.8%) and 9.6% (95%CI: 5.7%–15.9%), respectively. The pooled estimated incidence of fetal events including premature birth, small for gestational age, respiratory distress syndrome, intraventricular hemorrhage, death was 26.6% (95%CI: 20.4%–34.0%).

**Conclusion:** The overall estimated incidence of AF and recurrent AF during pregnancy is as high as 2.2% and 39.2%, respectively. AF during pregnancy may result in poor maternal and fetal outcomes.

## 1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide [1]. AF in pregnancy is rare; however, the incidence is increased in those with concurrent underlying heart disease [2]. Rheumatic heart disease is one of the most prevalent AF-related heart diseases among women of childbearing age and younger patients, which

affects 15–20 million people worldwide [3–5]. Of those, previous literature has noted an incidence of AF of up to 40%, for whom anticoagulation treatment may be indicated [4].

Physiologic alterations during pregnancy may facilitate the development of AF with or without underlying heart disease. However, the incidence of AF without structural heart disease, defined as lone AF, has been shown to be substantially lower than in pregnancy with

\* Corresponding author at: Division of Cardiology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Rd, Bangkok, Thailand.

E-mail address: [drronpichai@gmail.com](mailto:drronpichai@gmail.com) (R. Chokesuwattanaskul).

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**Table 1**  
Main characteristic of studies included in meta-analysis of AF and pregnancy.

	Wong et al. [10]	Henry et al. [11]	Sauve et al. [12]	Silversides et al. [13]	Szekely et al. [14]	Salam et al. [22]	Lee et al. [24]
Country	Canada	USA	Canada	USA	UK	Netherlands	USA
Study	cohort study	cohort study	cohort study	cohort study	cohort study	cohort study	cohort study
Year	2017	2016	2017	2006	1961	2015	2016
Number of pregnancies	34,639	143	16	23 (Paroxysmal AF/AFL) 6 (Persistent AF/AFL)	760	1321	264,730
Age	52.9	31.5	33	30 ± 5	30	30 ± 5.6	32.8
Exposure Definition	Number of parity, no arrhythmia at baseline.	Woman with MCD with arrhythmia compare to those without.	AF	Know cardiac arrhythmia transferred for further care (F/U 12 years)	Consecutive pregnancy with rheumatic heart disease between 1942 and 1959	Pregnant Mother with structural heart disease	Pregnant mother
Exposure Measurement	Number of parity of woman in the cohort (34,639 woman) F/u 20.5 years	Medical records	Registry database followed by blinded reviewer	Medical records at Toronto General Hospital and Mount Sinai Hospital from 1990-2002	Patient medical record at Newcastle General Hospital	Medical records	Medical records
Outcome Definition	Incident atrial fibrillation	Mode of delivery Fetal outcome (IUGR)	Morbidity	Recurrence rate of arrhythmia (SVT, AF/AFL, VT) during pregnancy Fetal outcome	Immediate risk and remote effect of pregnancy with RHD and AF	Incidence of AF during pregnancy	Prevalence of AF Maternal and fetal outcome in pregnancy with AF compared to those without AF
Outcome Measurement	Medical review confirmed by cardiologists, EKG.	Medical records	Medical records	EKG, Holter monitor, Telemetry monitoring.	Incident of heart failure. Medical record.	Medical records	Medical records
Prevalence of preexisting AF	Study incident of AF with history of parity to look for association	N/A	Paroxysmal AF 15/16 (94%)	Paroxysmal AF/AFL 18 women with 23 pregnancies Persistent AF/AFL 6 women with 6 pregnancies	31/760	N/A	93 women with 112 pregnancies
Incidence AF/what trimester	1,532 (higher parity has higher incident AF)	3/143	Recurrence Same pregnancy 5/16 (31%) In subsequent pregnancy 4/16 (25%)	Recurrence among paroxysmal AF/AFL 12/23 (52.2%) Among persistent AF/AFL 6/6 (100%)	29/760	17/1321	45 women with 45 pregnancies (during pregnancy or during the 6-month postpartum period)
Maternal events	N/A	Preeclampsia 2/36	N/A	Pulmonary edema 7/29	Acute pulmonary edema 3/60 Maternal death 3/60	Maternal mortality 2/17 Heart failure 2/17 Preeclampsia 0/17	Heart failure/pulmonary edema 2/157 Preeclampsia 6/157 Eclampsia 0/157

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Table 1 (continued)

	Wong et al. [10]	Henry et al. [11]	Sauve et al. [12]	Silversides et al. [13]	Szekely et al. [14]	Salam et al. [22]	Lee et al. [24]
Fetal events	N/A	Intrauterine fetal demise 0/36 IUGR 6/36 Preterm 7/36 SGA 2/36 5 min Apgar < 7 6/36 NICU admission 10/36	Preterm 0/16	Premature birth 11/29 Small for gestational age 2/29 Respiratory distress syndrome 3/29 Intraventricular hemorrhage 1/29 Fetal demise 0/29	Fetal death 12/60	Fetal death 0/17 Neonatal death 0/17 Apgar score < 7 1/17 Premature birth 5/17 Birth weight < 2500 g 8/17	Premature labor 9/157 SGA < 10 percentile 11/157 SGA < 3 percentile 4/157 Fetal death 1/157 Need for NICU admission 17/157
Quality Assessment (Newcastle Ottawa Scale)	S4 C2 O3	S4 C2 O3	S4 C2 O3	S4 C0 O3	S4 C2 O3	S4 C2 O3	S4 C2 O3

Abbreviations: AF - Atrial Fibrillation; AFL - Atrial Flutter; AT - Atrial Tachycardia; EKG - Electrocardiogram; IUGR - Intrauterine Growth Retardation; MCD - Maternal Cardiac Disease; N/A - not available; RHD - Rheumatic Heart Disease; SGA - Small for Gestational Age; S / C / O - selection / comparability / outcome; VT - Ventricular Tachycardia.

underlying heart disease [6,7]. Li et al. [8] reported the incidence of AF in pregnancy-related admissions of about 2/100,000. Shotan et al. [9] confirmed an increased incidence of arrhythmias during normal pregnancy, which appeared to be mostly premature atrial complexes (PAC) rather than AF.

A systemic search through the past 50 years found a lack of consensus regarding AF in pregnancy in terms of incidence, morbidity, and mortality. Most of the previous literature comprises of case reports and several observational studies reporting conflicting data [10–14]. Therefore, there is currently limited data regarding the incidence and maternal/fetal outcomes of AF in pregnancy.

We performed a systematic review to investigate the pooled incidence of AF in pregnant women and to assess maternal/fetal outcomes of AF in pregnancy.

## 2. Methods

### 2.1. Literature review and search strategy

The protocol for this meta-analysis is registered with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42018095955). A systematic literature search of MEDLINE (1946 to May 2018), EMBASE (1988 to May 2018), and the Cochrane Database of Systematic Reviews (database inception to May 2018) was conducted to investigate the pooled incidence of AF in pregnant women and to assess maternal/fetal outcomes of AF in pregnancy.

The systematic literature review was undertaken independently by two investigators (R.C. and C.T.) applying the search approach that incorporated the terms of “pregnancy” or “pregnant” AND “atrial fibrillation” which is provided in Supplementary data 1. A manual search for conceivably relevant studies using references of the included articles was also performed. No language limitation was applied. This study was conducted in line with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) [15] and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement [16].

### 2.2. Selection criteria

Eligible studies must be observational studies (cohort, case-control, or cross-sectional studies) that reported incidence of AF in pregnancy or maternal/fetal outcomes of pregnancy with AF. They must provide the data on the incidence with 95% confidence intervals (CI). Inclusion was not limited by study size. Retrieved articles were individually reviewed for their eligibility by the two investigators noted previously. Discrepancies were discussed and resolved by mutual consensus. The Newcastle-Ottawa quality assessment scale was used to appraise the quality of study for case-control studies and outcome of interest for cohort studies [17]. The modified Newcastle-Ottawa scale was used for cross-sectional studies [18], as shown in Table 1.

### 2.3. Data abstraction

A structured data collecting form was utilized to derive the following information from each study: title, year of the study, name of the first author, publication year, country where the study was conducted, demographic and characteristic data of pregnant women, methods used to identify AF, incidence of AF, and maternal and fetal outcomes.

### 2.4. Statistical analysis

Analyses were performed using the Comprehensive Meta-Analysis 3.3 software (version 3; Biostat Inc, Englewood, NJ, USA). Adjusted point estimates from each study were consolidated by the generic inverse variance approach of DerSimonian and Laird, which designated

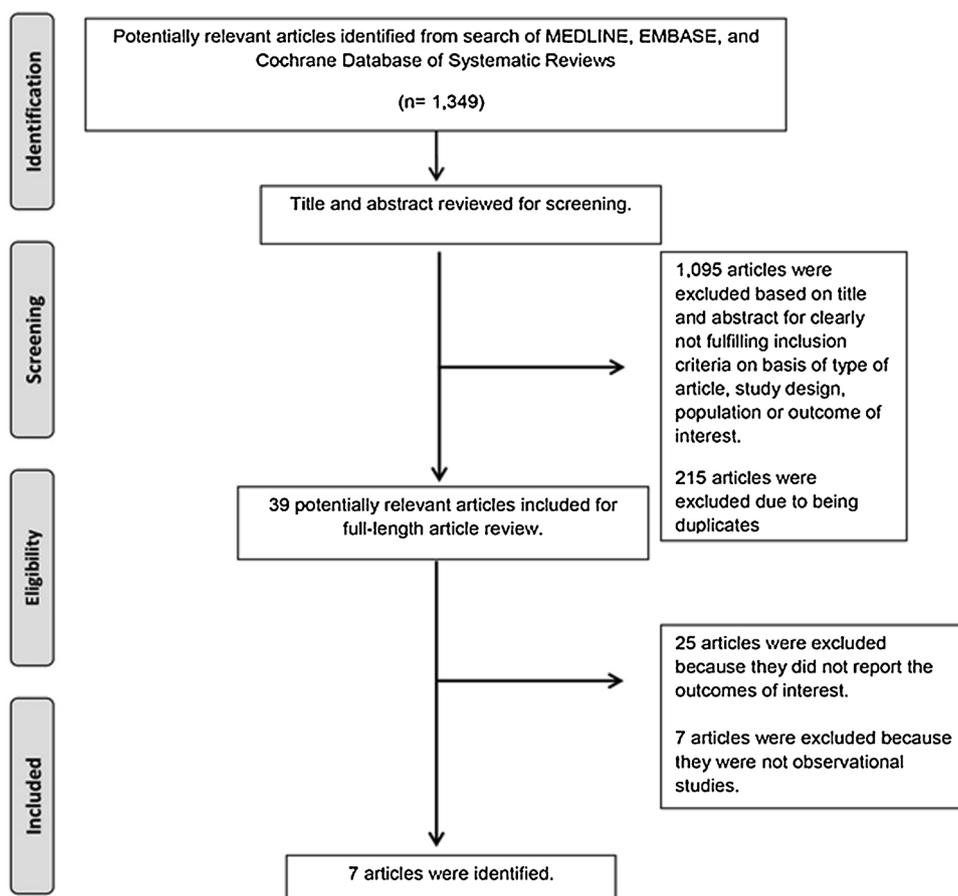


Fig. 1. PRISMA flowchart of study selection. Adapted from Moher et al. [16].

the weight of each study based on its variance [19]. Given the likelihood of between-study variance, we used a random-effect model rather than a fixed-effect model. Cochran’s Q test and  $I^2$  statistic were applied to determine the between-study heterogeneity. A value of  $I^2$  of 0–25% indicates insignificant heterogeneity, 26–50% low heterogeneity, 51–75% moderate heterogeneity and 76–100% high heterogeneity [20]. The presence of publication bias was evaluated via the Egger test [21].

### 3. Results

A total of 1349 potentially eligible articles were identified using our search strategy. After the exclusion of 215 duplicate articles and 1095 articles because they were case reports, correspondences, review articles, *in vitro* studies, pediatric patient population, or animal studies, 39

articles remained for full-length review. We excluded 25 articles from the full-length review as they did not report the outcome of interest, and 7 articles because they were not observational studies.

Thus, in the final analysis, we considered 7 articles [10–14,22,23], including 301,638 pregnancies. The literature retrieval, review, and selection process are demonstrated in Fig. 1. The characteristics and quality assessment of the included studies are presented in Table 1 [10–14,22,24].

#### 3.1. Incidence of atrial fibrillation in pregnancy

The pooled estimated incidence of AF in pregnancy among women with no known heart disease, and those with structural heart disease was 0.3% (95%CI: 0.01%–40.6%,  $I^2 = 99%$ ; 2 studies [10]) and 2.2% (95%CI: 0.96%–5.01%,  $I^2 = 85%$ ; 3 studies [11,14,22]; Fig. 2),

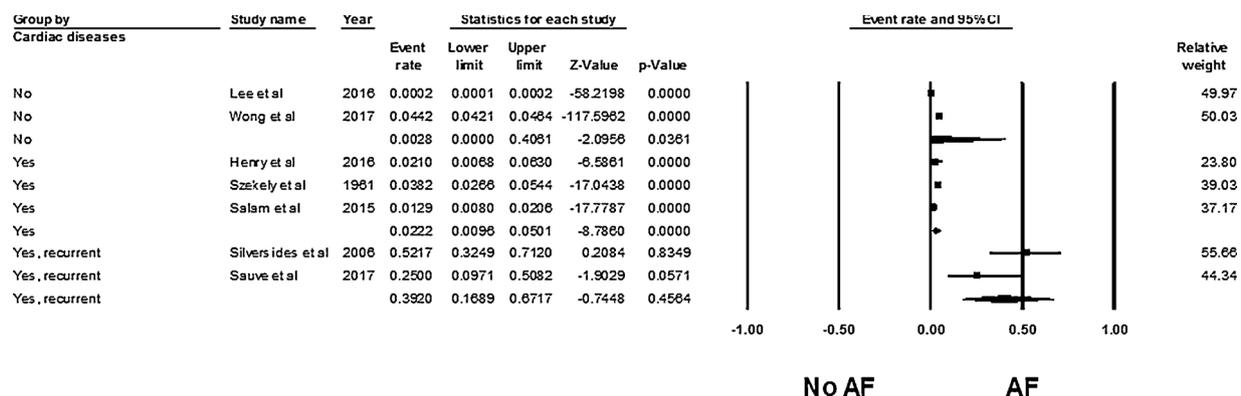


Fig. 2. Forest plots of the included studies assessing incidence of atrial fibrillation in pregnancy.

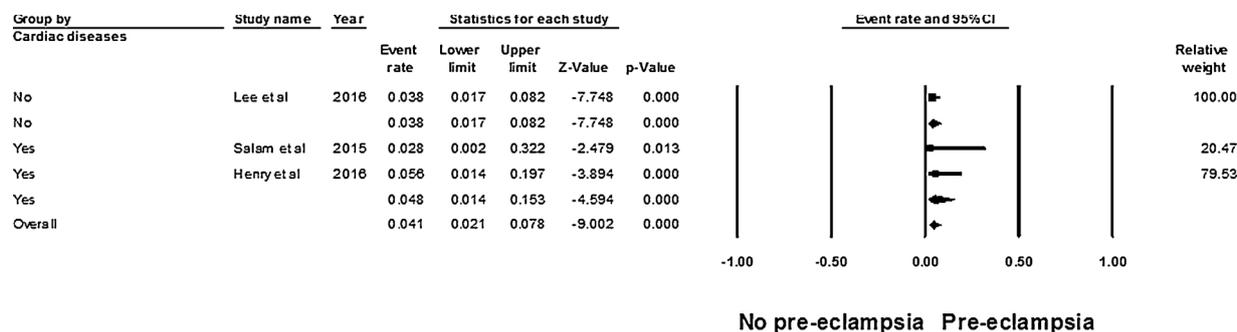


Fig. 3. Forest plots of the included studies assessing incidence of pre-eclampsia in pregnancy with atrial fibrillation.

respectively. Among women with known AF, the pooled estimated incidence of recurrent AF in pregnancy was 39.2% (95%CI: 16.9%–67.2%,  $I^2 = 64$ ; 2 studies [12,13]; Fig. 2). Lee et al. [24] demonstrated that among newly-developed AF during pregnancy, patients in the third trimester had a 3-fold increased risk of AF compared to those in the first trimester. In addition, a study by Salam et al. [22] conducted in pregnancy with structural heart disease also showed that the second trimester was the most common period (61.5% of women developed AF/AFL during pregnancy) for patients to develop AF.

### 3.2. Maternal and fetal outcomes of AF in pregnancy

The pooled estimated incidence of pre-eclampsia and congestive heart failure (CHF) during pregnancy with AF was 4.1% (95%CI: 2.1%–7.8%,  $I^2 = 0\%$ ; 3 studies [11,22,24]; Fig. 3) and 9.6% (95%CI: 5.7%–15.9%,  $I^2 = 0\%$ ; 4 studies [13,14,22,24]; Fig. 4), respectively. The pooled estimated incidence of fetal events including premature birth, small for gestational age, respiratory distress syndrome, intraventricular hemorrhage and death was 26.6% (95%CI: 20.4%–34.0%,  $I^2 = 97\%$ ; 6 studies [11–14,22,24]; Supplementary Fig. 1). When the analysis included only 5 studies [11–13,22,24] excluding Szekely et al. [14], which was published in 1961, the pooled estimated incidence of fetal events was 22.0% (95%CI: 3.1%–71.4%,  $I^2 = 98\%$ ).

While fetal death was reported at 20% in pregnancy with AF in 1961 [14], more recent studies demonstrated no fetal death [22], or only up to 0.65% [24]. The pooled estimated incidence of maternal and fetal outcomes of AF in pregnancy is summarized in Tables 2 and 3.

We separately analyzed the data of AF in pregnant patients with and without underlying structural heart disease (Table 2). As we expected, higher incidence of CHF and poor maternal outcomes were observed in those with AF with underlying structural heart disease [11,14,22], while those without structural heart disease showed lower incidence of heart failure and preeclampsia [24].

### 3.3. Evaluation for publication bias

Funnel plots (Supplementary Figs. 2–5) and Egger’s regression asymmetry tests were performed to evaluate for publication bias in analyses evaluating the incidence of AF, maternal outcomes (pre-eclampsia and CHF), and fetal outcomes, respectively. There was no significant statistically publication bias,  $p = 0.53, 0.98, 0.25,$  and  $0.80,$  respectively.

## 4. Discussion

Our study demonstrated that AF in pregnancy is rare and mainly found in women with underlying structural heart disease. Regardless of the presence of structural heart disease, AF increased the risk of poor maternal and fetal outcomes. Poor maternal outcomes mainly included CHF and preeclampsia while the fetal events included being small for gestational age, intraventricular hemorrhage, respiratory distress, premature birth, NICU admission, and most seriously, fetal death.

Non-specific clinical complaints such as palpitations, dyspnea and dizziness, which are common in normal pregnancy could be a clue for underlying arrhythmias [25]. Both, normal pregnancy and arrhythmias, share many common features, which may make it difficult to distinguish between these two clinical syndromes. Furthermore, symptoms of AF may vary from asymptomatic to debilitating symptoms based on individual perception [26]. Therefore, a thorough clinical examination accompanied by a high index of suspicion is required to detect AF in the pregnant patient.

Pregnancy and labor are risk factors for maternal cardiac arrhythmias by multiple mechanisms, principally via alterations in normal physiology, emotions, autonomic nervous system regulation and hormonal equilibrium [27]. Physiologic changes during pregnancy ensure an appropriate environment for the developing fetus by increasing blood volume and augmentation of cardiac output. This physiologic change leads to an increase in left ventricular diameter and left ventricular hypertrophy [28,29] causing left atrial stretch and increased left atrial pressure which results in alteration of atrial

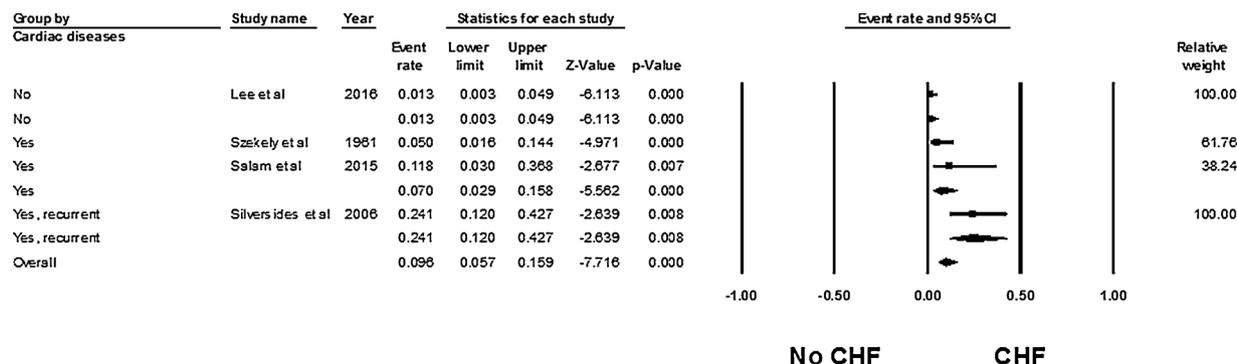


Fig. 4. Forest plots of the included studies assessing incidence of congestive heart failure in pregnancy with atrial fibrillation.

**Table 2**  
Incidence of maternal outcomes of AF in pregnancy.

Population	Reference	Outcome (Maternal)
No known structural heart disease	Lee et al. [24]	Preeclampsia 3.8% (95% CI: 1.8%–8.2%)
	Lee et al. [24]	CHF 1.3% (95% CI: 3%–4.9%)
With structural heart disease	Salam et al. [22]	Preeclampsia 2.8% (95% CI: 0.2%–32.2%)
	Henry et al. [11]	Preeclampsia 5.6% (95% CI: 1.4%–19.7%)
	Szekely et al. [14]	CHF 5% (95% CI: 1.6%–14.4%)
	Salam et al. [22]	CHF 11.8% (95% CI: 3%–36.8%)
Recurrence AF	Silversides et al. [13]	CHF 2.41% (95% CI: 1.2%–4.27%)

electromechanical coupling. Furthermore, increased blood volume leads to an increase in resting heart rate, typically 10–15 beats above their baseline, which also predisposes to the development of arrhythmias in pregnancy [30–32]. This fact is supported by electrophysiologic evidence. Increased P-wave dispersion and atrial electromechanical coupling in pregnant patients compared to non-pregnant women of comparable age are known predictors of AF and may facilitate the occurrence of AF during pregnancy [33]. Tension, anxiety and fatigue, most prominent during labor, may explain the higher incidence of PACs in labor but not generalized pregnancy, as reported by some authors [34]. This surging of physical and emotional strain is the major cause of tachycardia [31,35]. Marked changes in autonomic regulation, increased cardiac output and high cardiac contractility have been proposed as major contributors to maternal cardiac arrhythmias [36,37]. Hormonal changes also play a role in susceptibility to AF via increased adrenergic hypersensitivity induced by estrogen [2]. Therefore, complex combinations of metabolic, hormonal, autonomic and physiologic changes during pregnancy synergistically play a role in the development of AF in pregnancy. The magnitude of physiological alteration in pregnancy is continually changing, and the first trimester appears to be the lowest risk period for the development of AF due to the minimal change in the pregnancy physiology compare to the pregnancies in the second and third trimester [22,24].

Well established risk factors for the development of AF in pregnancy are hyperthyroidism, rheumatic heart disease, congenital heart disease and the administration of terbutaline [38]. AF caused by tocolytics, usually diagnosed by the clear temporal association between the time of drug administration and occurrence of AF, typically spontaneously converts back to sinus rhythm with medication cessation [39]. New-onset lone AF, defined as AF without structural heart disease and the absence of reversible causes such as pulmonary emboli, hyperthyroidism, alcohol abuse, electrolyte imbalances or medications (such as terbutaline) in pregnancy is rare and usually presented as case reports [37,38,40–42].

Risk factors for AF may not only contribute to short-term, but also long-term development of AF. Scantlebury et al. [43] conducted long-term follow-up in thousands of women who had live or stillbirths in their medical center. After adjusting for confounding factors, those with history of hypertension during pregnancy had 2-fold increased risk of AF compared to those without hypertension, and occurred on average 20 years after delivery [42]. This would imply that pregnancy represents a transient risk factor that puts patients at risk to develop AF in the future. Hence, long-term monitoring may be indicated for this

population.

AF can cause a hemodynamic instability in pregnancy, mainly by a rapid ventricular response and in part due to a loss of atrial contraction, which typically contributes to 15–20% of left ventricular filling volume. A shortened diastolic filling time due to a rapid ventricular response results in a reduction in cardiac output, which may lead to maternal systemic hypoperfusion affecting the fetal circulation. This basic pathophysiology illustrates the importance of the prompt detection and early management of AF that could potentially prevent fetal and maternal complications [37]. Most patients with stable AF spontaneously convert to sinus rhythm without requiring medical therapy; however, either pharmacological or electrical cardioversion can be safely employed to restore sinus rhythm in pregnancy, depending on the urgency of the clinical scenario. If pharmacological therapy is needed, Sotalol is the only antiarrhythmic medication classified as category B in pregnancy (generally safe to use as long as renal function is not impaired) [7]. Flecainide has been widely used to treat fetal supraventricular arrhythmias and it also offers an acceptable safety profile in pregnancy [44]. The safety of these approaches is supported by previous literature (albeit mostly in case reports) [6,7,41].

Pharmacologic agents used to control ventricular rate in rapid conducted atrial fibrillation include beta blockers, digoxin and non-dihydropyridine calcium channel blocker [40]. The beta blocker and calcium channel blocker must be used with caution when applied in the presence of acute heart failure and preexcitation [45]. In the presence of preexcitation, the atrial fibrillatory activity will preferentially conduct over bypass tract with the use of atrioventricular nodal blocking agents resulting in even faster ventricular rate to the decompensation state [46]. Cardio-selective beta blockers, metoprolol and atenolol have a better safety profile based on pharmacological effect as beta-2 receptor-mediated uterine relaxation and peripheral vasodilatation causing detrimental effect during pregnancy [45]. Digoxin has long been proved to be safely used without teratogenic effect to the fetus. However, serum digoxin level may be falsely elevated during late trimester due to the presence of a digoxin-like substance in maternal circulation [47,48]. On the contrary, non-dihydropyridine calcium channel blocker, diltiazem and verapamil, should be reserved as a last resort for the ventricular rate control agent based on the data, despite weak evidence as case series, reported fetal malformation associated with the use of calcium channel blockers [49].

In order to prevent systemic thromboembolism, primary prevention in pregnant patients with AF was set on guidelines which are based on the studies that exclude pregnant patients [46]. Trials of novel

**Table 3**  
Incidence of Fetal outcomes of AF in pregnancy.

Population	Reference	Fetal events
No known structural heart disease	Lee et al. [24]	26.8% (95% CI: 20.4%–34.2%)
With structural heart disease	Szekely et al. [14]	20% (95% CI: 11.7%–32%)
	Salam et al. [22]	1.1% (95% CI: 0.7%–1.9%)
	Henry et al. [11]	86.1% (95% CI: 70.7%–94.1%)
Recurrence AF	Silversides et al. [13]	58.6% (95% CI: 40.4%–74.8%)
	Sauve et al. [12]	2.9% (95% CI: 2%–33.6%)

anticoagulation agents also do not include pregnant patients at the time of enrollment [46]. The most commonly used agent with strong safety profiles in pregnancy is a heparin product. With the long-term requirement, the patient that met the criteria by stroke risk score would be placed with low molecular weight heparin as providing less side effects compared to heparin [50]. Warfarin is iatrogenic substance especially for the first trimester of pregnancy but allowed to be used outside the first trimester and perinatal period [51].

#### 4.1. Limitations of the study

Several limitations of our study are noteworthy. Firstly, the method of detecting arrhythmias among different studies varies considerably, which limits direct comparison. Some examples include intermittent vs continuous cardiac monitoring and differing devices used with differing reliability. Secondly, underlying structural heart disease prior to pregnancy was not consistently available. Thirdly, most of the studies included are observational studies, which have their own inherent limitations. Lastly, the presence of clinical heterogeneity reflected by the wide range of data demonstrated the incidence of AF in pregnancy, could be confounded by several factors, for instance, duration of cardiac monitoring to make the diagnosis of AF. Also, the duration and interval of follow up over time are important determinants of AF incidence in individual study. Despite these limitations, our study presented the information that raises the awareness of importance of AF, not being considered as a benign coincidence of pregnancy-related hemodynamic alteration but rather may confer the long-term risk to both mother and fetal outcome as mentioned above. Additionally, our study results encourage the clinician to seek a life-threatening - if left untreated, but reversible medical conditions commonly found in this age group; thyroid disorder, mitral valve disease or cardiomyopathy. Based on the above limitations, future research studies or large population-based registries of pregnant women are required to offer more informative evidence regarding maternal and fetal outcomes of pregnant patients with AF.

#### 5. Conclusions

Pregnancy increases susceptibility to developing AF via physiologic, hormonal and autonomic changes. In addition, underlying cardiac disease and systemic disease that is commonly found in women of childbearing age may predispose to the development of AF in pregnancy. As AF may cause adverse hemodynamic effects to both maternal and fetal well-being, timely recognition and appropriate treatment should be a cornerstone for the management of AF in pregnancy. Comprehensive evaluation for the presence of underlying structural heart disease should be pursued in all cases of AF during pregnancy. Reversible potential etiologies of AF in pregnancy that may be overlooked include hyperthyroidism, pulmonary emboli, electrolyte imbalances and concurrent obstetric medications that alter autonomic regulation as mentioned above, and should never be missed by the care provider. AF in pregnancy, while uncommon, is associated with poor maternal/fetal outcomes and most of the episodes tend to occur after the first trimester of pregnancy. Our study supports the use of comprehensive approach to treating patients with AF especially in the structural heart disease group, which should not be limited only to peripartum period, but also extend into the postpartum care in the woman with a history of AF during the pregnancy. Pregnant patients without obvious structural heart diseases have better outcomes and, most of the time, AF spontaneously, or with minimal intervention, converted back to sinus rhythm compared to those with underlying structural heart diseases.

#### Declaration of Competing Interest

The authors declare no conflict of interest.

#### Financial disclosure

The authors have no funding to disclose.

#### The author contribution

Study design: Ronpichai Chokesuwattanaskul, Charat Thongprayoon, Wisit Cheungpasitporn.

Data collection: Ronpichai Chokesuwattanaskul, Charat Thongprayoon.

Statistical analysis: Charat Thongprayoon, Wisit Cheungpasitporn.

Data interpretation: Ronpichai Chokesuwattanaskul, Charat Thongprayoon, Wisit Cheungpasitporn.

Manuscript preparation: Ronpichai Chokesuwattanaskul, Charat Thongprayoon, Tarun Bathini, Oisín A. O'Corragain, Konika Sharma, Somchai Prechawat, Patompong Ungprasert, Kanramon Watthanasuntorn, Pavida Pachariyanon, Wisit Cheungpasitporn.

Literature search: Ronpichai Chokesuwattanaskul, Charat Thongprayoon, Wisit Cheungpasitporn.

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#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi: <https://doi.org/10.1016/j.advms.2019.07.003>.

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