Prevalence and clinical significance of arrhythmias during labour in women with structurally normal hearts

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ABSTRACT

Objectives Examine the association between arrhythmias and adverse maternal outcomes in women with structurally normal hearts.

Methods This was a case–control study of women admitted in labour to one of eight hospitals of Northwell Health from January 2015 to June 2021. After excluding women with structurally abnormal hearts, we identified women with an arrhythmic event and randomly subsampled the rest of the cohort to create a control group of 1025 patients. Multivariate analysis was performed to examine the association between arrhythmias and the incidence of caesarean section (CS), preterm labour (PTL), admission to the neonatal intensive care unit and longer length of stay (LOS).

Results Of 141,769 women admitted in labour with a structurally normal heart, 137 had at least one arrhythmic event (0.097%). Supraventricular tachycardia (SVT), atrial fibrillation/flutter (AF) and frequent premature ventricular complexes or non-sustained ventricular tachycardia (VA) were present in 65 (0.046%), 22 (0.016%) and 46 (0.032%) women, respectively. Arrhythmia was previously diagnosed in 58.0% SVT cases but only in 9.7% AF and 8.1% VA cases. After adjusting for age, parity and comorbidities, the presence of any arrhythmia was an independent predictor of CS (OR 1.7 95% CI 1.2 to 2.5), PTL (OR 1.8, CI 1.1 to 3.0) and LOS (mean ratio 1.6, CI 1.4 to 1.8). This association was driven by presence of SVT and AF, whereas VAs were not associated with adverse outcomes.

Conclusions Arrhythmias, specifically SVT and AF, during labour in women with structurally normal heart are independently associated with adverse obstetrical outcomes.

INTRODUCTION

Cardiovascular disease represents a significant cause of morbidity and mortality in pregnancy. While roughly 1–4% of the 4 million pregnancies each year in the USA are affected by cardiovascular disease, studies suggest cardiovascular disease is responsible for 26.5% of pregnancy-related deaths in the USA. In addition, the prevalence of cardiac arrhythmias in pregnant women is rising, likely due to the rise in maternal age and chronic disease.

Previous studies have demonstrated that arrhythmias are prevalent in women with structural heart disease; however, few studies have investigated the prevalence of arrhythmias in the general population and their potential association with adverse maternal outcomes. Physiologic changes during pregnancy can predispose mothers to new-onset cardiac arrhythmias, along with exacerbations of previously diagnosed arrhythmias. On the other hand, a previously well-tolerated arrhythmia can more easily affect haemodynamics when it occurs during pregnancy. Finally, management of arrhythmias during pregnancy and labour is particularly challenging due to restrictions on the use...
of antiarrhythmic agents and inability to resort to ablative therapies. It is unclear how the above might affect maternal outcomes either directly or through changing common obstetrics practice.

Determining the prevalence and association of arrhythmias in women not traditionally thought to be in a high pregnancy risk, in addition to providing awareness, might provide evidence for prophylactic management of arrhythmias in women of reproductive age.

METHODS

Study population

The medical records of women admitted from January 2015 to June 2021 for delivery at any of eight Northwell Health Hospitals were reviewed using the common, systemwide electronic medical record (EMR). The study protocol was approved by the Northwell Health Institutional Review Board. The data that support the findings of this study are available from the corresponding author on reasonable request.

Data collection

Structural heart disease was identified in the study design as a confounder given our objective; therefore, we restricted our cohort to women with no known structural heart disease. Patients with structural heart disease, as identified by International Classification of Diseases (ICD) codes, were excluded from the study during the initial EMR query. As cardiac workup is not performed routinely in the general population, this was the most sensitive method to detect structural abnormalities in the cohort. Furthermore, all charts of those included in the final cohort were manually reviewed for presence of structural heart disease.

For data extraction, a detailed EMR search was performed of all medical notes, diagnoses, medications, orders and ECG and telemetry interpretations. Progress notes, consult notes and ECG reports were scanned for keywords such as ‘atrial fibrillation’, ‘supraventricular tachycardia’, ‘ventricular tachycardia’ and all possible variants (eg, ‘atrial flutter’, ‘paroxysmal atrial fibrillation’, ‘narrow complex tachycardia’, ‘ventricular ectopy’, ‘wide complex tachycardia’, ‘premature ventricular contractions’, ‘atrial tachycardia’) and abbreviations (eg, ‘PAC’, ‘AVNRT’, ‘AF’, ‘afib’, ‘attach’, ‘VT’, ‘PVC’, ‘VPD’).

Comparison groups and outcome measures

The medical records identified by the data query were reviewed manually and adjudicated for the presence of a newly diagnosed arrhythmic event during hospitalisation. Newly diagnosed arrhythmic events were identified as follows: supraventricular tachycardia (SVT) or atrial fibrillation (AF) with presence of recurrent symptoms (palpitations, shortness of breath or dizziness) with at least one sustained episode documented on telemetry or ECG lasting longer than 30s. Ventricular arrhythmias (VA), defined as non-sustained VT (>3 beats) of frequent premature ventricular complexes (PVCs) in quadrigeminy or more. Patients with VAs were included irrespective of symptoms. All patients included in the arrhythmia cohort were noted to have had a cardiology consult called during their admission. As this was a real-world retrospective case–control study, electrocardiography that was available was reviewed. There are no systematic protocols for monitoring that were discernable from our review. Sinus tachycardia was included in the arrhythmia cohort for data collection. We chose not to focus on women with sinus tachycardia in this analysis and these patients were not included in the analysis group.

We also identified women with history of arrhythmias, irrespective of whether an arrhythmic event occurred during the index admission. History of arrhythmia was defined as recurrence of a known arrhythmia diagnosed prior to the current pregnancy. Regardless of prior history of arrhythmia, the arrhythmia group included only patients with an arrhythmic event during the periparturient period who also had a structurally normal heart. Specifically, we excluded patients with known cardiac conditions, including peripartum cardiomyopathy, depressed left ventricular ejection fraction, congenital heart disease, coronary artery disease, pulmonary hypertension, rheumatic heart disease and severe valvular heart disease. To elucidate the association of arrhythmias on the clinical outcomes, in addition to excluding those with structural heart disease, comorbidities were collected to demonstrate the low incidence rates in the cohort.

Mothers who had more than one delivery at a Northwell Hospital were included only during their first Northwell encounter. Multiple gestational pregnancies were included. We excluded patients with arrhythmias encountered during cardiopulmonary resuscitation. A random set of control patients, with no history of arrhythmia or arrhythmia during the peripartum period and structurally normal hearts, were selected by subsampling the available set of patients without arrhythmias. A 1:4 ratio between arrhythmias and control patients was selected to maximise the efficiency of any statistical tests performed.

Clinical outcomes

Outcomes evaluated between the arrhythmia and control groups included caesarean section (CS), preterm labour (PTL) at <37 weeks of gestation, length of stay (LOS) longer than median and infant requiring care in the neonatal intensive care unit (NICU). No mortality was noted in the cohort.

Instances in which CS was performed were reviewed to assess whether the decision to proceed with CS was arrhythmia mediated due to haemodynamic compromise or fetal distress. Haemodynamic compromise was defined as presence of symptomatic hypotension at baseline or postadministration of atrioventricular nodal agents (systolic blood pressure (SBP) <100 mm Hg).
Statistical analysis
The proportion of patients with an arrhythmic event in the absence of structural heart disease out of the total number of patients screened was calculated. Normally distributed data are presented as mean±SD and non-normal data as median (IQR). Categorical data are presented as frequency (percentage of the total). The association between history of an arrhythmia and arrhythmia in the perilabour period was compared using $\chi^2$ tests. Fisher’s exact tests were used when greater than 20% of the cells had expected frequencies less than 5.

Association between arrhythmias in the perilabour period and delivery outcomes (C-section and preterm birth modelled separately) were tested using multiple logistic regression. Association between arrhythmias in the perilabour period and hospital LOS was tested using negative binomial regression. Association between arrhythmias in the perilabour period and NICU admission was tested using Fisher’s exact tests.

Models for arrhythmia, AF and VA were adjusted for age, parity, history of hypertension and history of diabetes. The model for SVT was adjusted for age and parity only. Models were adjusted for confounders deemed clinically relevant to the specific arrhythmia.

Statistical significance was determined for each test at the significance level $\alpha=0.05$. Data analysis was generated using SAS software (2021 SAS Institute, Cary, North Carolina).

RESULTS
Patient characteristics
There were 1194 (0.084%) patients excluded from the initial data query due to the presence of structural heart disease as determined by ICD codes resulting in 141 769 patients. Arrhythmia and control groups were derived from a cohort of 141 769 unique patients admitted in labour. Keyword search for patients with arrhythmic events in the EMR yielded 1867 patients. During manual adjudication, one control and two arrhythmia patients were removed due to presence of structural heart disease.

These records were manually reviewed and resulted in a total of 256 (0.181%) patients with an arrhythmic event during hospitalisation that met the inclusion criteria. Patients with sinus tachycardia were excluded, and the final arrhythmia cohort was comprised of 137 patients (0.098%). The control group contained 1025 patients.

Clinical and demographic characteristics of the patient population are listed in table 1 for both the arrhythmia and control cohorts. Arrhythmia and control groups had similar age, parity and comorbidities except hypertension that was more prevalent in the arrhythmia group (11.3% vs 4.0%). There was no statistically significant difference in baseline demographics and comorbidities.

History and present arrhythmias
Out of the 137 patients with arrhythmia, 65 (47.5%) had SVT, 22 (16.1%) had AF and 46 (33.0%) had VA. There were four patients noted to have multiple arrhythmia diagnoses. Specifically, three patients with SVT also had AF, and one patient with AF also was noted to have frequent PVCs. In 62 of 137 patients (45.3%), the arrhythmia was a recurrence of a previously diagnosed arrhythmia, whereas the arrhythmia was newly diagnosed during the perilabour period in the remaining 75 patients (54.7%). Specifically, a prior diagnosis was present in 36 (58.0%) patients with SVT, 6 (9.7%) patients with AF and 5 (8.1%) patients with VA.

Of the 36 patients with prior SVT diagnosis, 13 also had SVT during labour, 5 were on medical therapy during their pregnancy (three beta blockers, one digoxin, one sotalol) and 11 had an attempted ablation prior to pregnancy that was unsuccessful. There were also 23 patients with a prior diagnosis of SVT but no recurrence during labour. Of those, medical therapy was present in 13 (10 on beta blockers, 1 on digoxin, 2 on sotalol) and 4 had a successful ablation prior to the current pregnancy. The presence of known diagnosis of SVT conferred a 9.7 times higher risk of developing SVT during labour (95% CI 4.6 to 20). Acute management for SVT included administration of adenosine, initiation or uptitration of beta blockers, and initiation of antiarrhythmics and cardioversion in 34, 52, 11 and 3 patients, respectively. In 14 patients, no intervention was performed. After careful review of the EMR, it was determined that the decision to proceed with induction of labour or emergency CS primarily in response to SVT was made in 12 out of 65
patients (18.5%). We found that the decision to proceed with C-section or induction was due to acute haemodynamic compromise in seven cases and fetal distress in five cases.

The majority of AF cases during labour was diagnosed denovo (72.7%). Of the six (27.3%) patients with AF with known diagnosis of AF, two were on medical therapy and two had undergone prior ablation before current pregnancy. There were also four patients with known diagnosis of AF but no recurrence during labour. Of these four patients, there were two on medical therapy, and neither had undergone a previous ablation. In our series, the presence of known AF diagnosis could not be tested to determine whether it conferred a higher risk of developing AF during labour due to a zero cell in the contingency table. Acute management for AF included initiation or up-titration of beta blockers/calcium channel blockers, initiation of antiarrhythmics and anticoagulation and cardioversion in 11, 7, 15 and 2 patients, respectively. In eight patients, no intervention was performed. The decision to proceed with induction of labour or emergency CS primarily in response to AF was made in two patients in which fetal distress was noted.

Similarly to AF, VAs were diagnosed denovo in most cases. Of the five patients with prior PVC diagnosis, three were on medical therapy with beta blockers, whereas four patients had an attempted ablation prior to pregnancy. Acute management of VA included initiation of beta blockers in 27 (58.7%) patients. None of the patients underwent induction of labour or emergency CS in response to VA. Figure 1 describes the rate and management of caesarean section by arrhythmia.

Clinical events and outcomes

The incidence of C-section in the overall arrhythmia group and stratified by specific arrhythmia diagnosis are shown in figure 2. Table 2 also presents the ORs adjusted for age, parity, history of hypertension and diabetes for the arrhythmia group and specific diagnoses compared with control. Figure 3 shows the adjusted ORs and 95% CI for clinical outcomes and arrhythmias.

C-section

There were 71 patients (51.8%) who underwent CS in the arrhythmia cohort and 364 patients (35.5%) in the control group (figure 1). Patients who experienced arrhythmias during labour were 1.7 times more likely to undergo CS (95% CI 1.20 to 2.51, p=0.0037) when adjusted for age, parity, history of hypertension and history of diabetes. This independent risk was mostly driven by patients in AF (OR 2.5, CI 1.0 to 6.0, p=0.040). There was no association between SVT and CS. The presence of VA was not associated with increased incidence of CS.

Length of Stay

Patients with arrhythmias during labour, as well as those in the control group, had a median LOS of 3 days. Arrhythmia during labour was associated with longer LOS when adjusted for age, parity, history of hypertension and history of diabetes (p<0.0001). Overall, those with arrhythmia had hospital stays 1.6 times the length than patients without (CI: 1.4 to 1.8).

In respect to arrhythmia diagnosis, LOS was statistically significant for both SVT and AF OR 1.2 (CI 1.03 to 1.38, p=0.0172) and 1.3 (CI 1.04 to 1.66, p=0.0215),
respectively, whereas patients with VA did not have a longer LOS.

Preterm birth
Preterm birth occurred in 21 (15.3%) deliveries in the arrhythmia cohort and 84 (8.2%) deliveries in the control cohort. Patients with arrhythmias had an estimated 1.8 times the risk of delivering preterm birth as those without (CI 1.05 to 3.04, p=0.0314). The adjusted risk for patients with SVT was 2.1 (CI 1.01 to 4.20, p=0.0478). Patients with AF and VA did not have statistically significant associations with pre-term birth.

NICU admission
Arrhythmias were also associated with higher incidence of NICU admission for the neonate with 10 (7.3%) versus 1 (0.10%) admissions (p<0.001). Patients with arrhythmia during labour had 80 times higher risk of NICU admission (CI 10.23 to 635.01).

OR for NICU admission for SVT and AF was 50, (CI 5.08 to 483.27, p=0.0008) and 49 (CI 2.95 to 806.11, p=0.0416), respectively. Finally, patients with VA had an estimated 125 times the odds of having a newborn admitted to the NICU as patients without (CI 14.26 to 1093.29, p<0.0001).

DISCUSSION
With this study, we report that on average 1:1000 women with structurally normal hearts admitted in labour will experience an arrhythmic syndrome—namely SVT, AF or VA—with SVT being the most common (1 in 2000 admissions). More than half of patients with SVT had events prior to admission with only a minority of them being on medical therapy or offered an ablation procedure (28%). History of untreated SVT carried a 10-fold increased risk in developing SVT while in labour. The majority of AF and VA cases were diagnosed denovo during hospitalisation for delivery. Presence of an arrhythmic syndrome was associated with lengthier hospital stay and almost doubled the risk for C-section and PTL. The associated risks were mostly driven by presence of SVT and AF.
while VAs were not associated with increased obstetrical adverse outcomes. The three outcomes examined in our study are interrelated, as the increased incidence of CS would predispose women to increased lengths of stay.

The prevalence of maternal SVT, AF and VA in our patient population was higher compared with prior studies. A study by Li et al reviewed a similar number of pregnancy admissions via a retrospective analysis of discharge ICD-9 codes from the period between 1992 and 2000. Their study found the rate of SVT, AF and VA to be 0.03%. Similarly, Vaidya et al’s review of discharge diagnoses from 2000 to 2012 found the rate of SVT, AF and VA to be 0.071%. There are several potential explanations for this discrepancy. First, there has been a general increase in maternal age and chronic disease in the general population in the time since the publication of those earlier trials, which likely has contributed to an increased burden of maternal arrhythmia. Also, these previous studies relied on a review of discharge diagnoses to identify the frequency of arrhythmias in pregnancy-related hospitalisations. Unlike in our study, additional sources such as the medical notes, ECGs and telemetry tracings of patients were not reviewed. The robust methodology used in our study increased our ability to identify cases of arrhythmia that otherwise may have been missed if solely relying on an administrative database. Therefore, the thorough review of our common EMR using this rigorous method likely improved the sensitivity in identifying arrhythmic events, even among patients with a structurally normal heart.

Arrhythmias in pregnancy have previously been described as a risk factor for adverse maternal and fetal outcomes, including increased mortality. However, it is unclear whether this association is due to underlying heart disease that typically accompanies serious arrhythmia syndromes. In our study, we examined the clinical significance of arrhythmias that are considered ‘benign’ when encountered in the general population with a demographic and clinical profile similar to that of our cohort’s. The independent association of these arrhythmic syndromes with adverse obstetric outcomes suggests that even ‘benign’ dysrhythmias carry different prognoses when occurring during pregnancy, and particularly labour. The aetiology of higher morbidity is multifield and includes pronounced haemodynamic consequences of arrhythmias during pregnancy, limited therapeutic options for pregnant women, lack of experience and clear guidelines in management and also the need for a multidisciplinary approach in the management of these patients. It was determined that all patients in the arrhythmia cohort had a cardiology consult during their admission.

The presence of SVT influenced the decision to perform CS on an urgent basis in 7 women due to haemodynamic compromise and five due to fetal distress. Presence of AF determined the decision to proceed with CS

Figure 3  Forest plots of model estimates with confidence intervals. (A) Caesarean section (C-section), (B) length of stay, (C) neonatal intensive care unit (NICU) and (D) pre-term birth.
in two cases due to fetal distress. We acknowledge that the presence of recurrent arrhythmias likely increased the practice of placing women on frequent or continuous heart monitoring, potentially increasing the yield of diagnosing fetal decelerations. The remaining CS performed in the arrhythmia cohort were performed in a semi-elective manner after collaborative decision between the obstetric, anaesthesia and cardiology consultants with the intention to minimise perilabour maternal and fetal complication risk.

Our study also outlines the importance of early diagnosis and management of arrhythmic syndromes in women planning to become pregnant. While most AF and VAs were newly diagnosed, more than half of patients with SVT carried this diagnosis in their medical history. In addition, more than two thirds of patients with a prior SVT diagnosis were not offered preventive treatment at all and were exposed to a 10-fold higher risk of developing acute SVT during labour. According to ACC/AHA, catheter ablation is considered a class I indication for patients in the general population with symptomatic SVT.6 However, observation is also a recommended option for the same population of patients, which may lead to an underutilisation of ablation. A more aggressive approach might be appropriate for women planning to become pregnant,3 as advocated by the European Society of Cardiology.67 In addition, for the acute management of SVT, prior concerns over radiation exposure to the fetus due to fluoroscopy during catheter ablation have been addressed by the rise of non-fluoroscopic tools such as electroanatomic mapping systems and intracardiac echocardiography.8 It is now an effective, mature therapeutic modality for the treatment of SVTs, even in pregnancy.69 Given the likelihood of arrhythmia recurrence during pregnancy with its resulting adverse outcomes, patients with a history of arrhythmias should involve their cardiologists or electrophysiologists when planning their pregnancy to address this treatable condition.

In contrast to SVT cases, the majority of AF cases were newly diagnosed in our cohort. This could be explained by the fact that SVT is typically diagnosed in women of childbearing age, while AF is diagnosed later in life.5 The higher incidence of newly diagnosed AF during labour might support the notion that neurohormonal and haemodynamic changes during pregnancy have an atrial proarrhythmic effect.68 Further studies are needed to examine the long-term prognosis of these women and determine whether this relationship between labour and AF is temporary or long lasting, similar to conditions such as gestational hypertension and gestational diabetes.

Finally, we report that the occurrence of VAs with benign characteristics triggered the most response in acute medical management with the majority being initiated on beta blockers. However, these VAs were not associated with adverse obstetrical management. This finding belies the general perception that ventricular ectopy is associated with worse cardiovascular prognosis. Rather, our study supports that both in the general population and during pregnancy, the occurrence of ventricular ectopy is often triggered by neurohormonal changes that carry a benign prognosis in patients with structurally normal heart.

Study limitation
This study is subjected to the inherent limitations of a case–control study and relies heavily on the accuracy of written documentation. However, the common EMR of our health system allowed for an effective review of a large volume of medical records from multiple hospitals. We were not able to adjust for prior diagnosis of arrhythmias or other major comorbidities in any of the models, as the number was too low to include as effects in the models. Nevertheless, patients with structurally abnormal hearts were excluded from the analysis. Structural heart disease was excluded first through ICD codes and further through manual review of the final cohort. Due to the retrospective nature of this study, we reviewed all available documentation and diagnostic testing to rule out the presence of structural heart disease. However, given the clinical profile of the cohort, not all women had an echocardiogram performed on admission. We cannot rule out the presence of undiagnosed structural heart disease. Structural heart disease was identified as a confounder in our study design and the cohort was restricted to those without structural heart disease. Given the small sample size we employed this methodology rather than adjusting the models in our analysis.

Prior diagnosis of SVT was identified after manual adjudication in the arrhythmia cohort but only by absence of specific diagnoses and key phrases in the control group. It is likely that the previous medical history of arrhythmias was under-reported in the control group, especially for women with infrequent symptomatic episodes and for those who underwent a curative catheter ablation years prior to becoming pregnant. The precise burden of arrhythmia in each patient could not be determined due to the retrospective nature of the analysis. In addition, it is plausible that there was a degree of under-documented history of benign arrhythmias by the obstetric services. The above might have underestimated the importance of medical history on arrhythmia recurrence during labour as well as the importance of early arrhythmia management prior to pregnancy. With the available clinical documentation, we could not ascertain the primary reason for extended LOS in those who underwent caesarean section; however, the main findings of our paper are the increased rate of caesarean section among this population.

CONCLUSION
Episodes of SVT and AF during labour independently lead to increased obstetrical adverse outcomes in women with structurally normal heart. History of arrhythmias, and particularly SVT, should be sought and addressed when consulting patients planning to become pregnant.
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