Cardiology in the Young

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Electrocardiographic proarrhythmic changes in pregnancy of women with CHD

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Abstract

Objectives: Pregnancy-related physiological adaptations result in increased heart rate as well as electrocardiographic changes such as a mean QTc prolongation of 27 ms. Pregnant women with CHD are at increased risk for cardiovascular complications. The aim of this study was to identify risk factors for abnormally prolonged QTc interval—a risk factor for ventricular arrhythmias—in pregnant women with CHD. *Material and method:* Retrospective longitudinal single-centre study. Pre-pregnancy demographic and electrocardiographic risk factors for abnormal QTc duration during pregnancy of (a) > 460 ms and (b) >27 ms increase were analyzed. *Results:* Eighty-three pregnancies in 63 women were included, of which three had documented arrhythmias. All five Modified World Health Organization Classification of Maternal Cardiovascular Risk (mWHO) classes were represented, with 15 pregnancies (18.1%) in mWHO class I, 26 (31.3%) in mWHO II, 28 (33.7%) in mWHO II-III, 11 (13.3%) in mWHO III, and three pregnancies (3.6%) in mWHO class IV. Heart rate and QTc interval increased, while QRS duration and PR interval shortened during pregnancy. QTc duration of > 460 ms was associated with increased pre-pregnancy QTc interval, QRS duration, and weight, as well as body mass index. QTc increase of > 27 ms was associated with increased heart rate prior to pregnancy. No significant associations of electrocardiographic changes with mWHO class or CHD type were identified. *Conclusion:* Increased QTc in pregnant women with CHD was associated with being overweight or having higher heart rate, QRS, or QTc duration prior to pregnancy. These patients should be monitored closely for arrhythmias during pregnancy.

Advances in medical and surgical treatment of children with CHD have led to increased survival into adulthood over the last decades.[1] As a result, the population of adults with CHD has been growing worldwide.[2] Today, CHD is the most prevalent cause of maternal cardiac disease during pregnancy.[3] CHD is a heterogenous group with a wide variation of complexity and severity.[2,3] Consequently, many forms of CHD allow a pregnancy with small to minimal risk for the mother and child, while women with other forms are at increased risk—sometimes even at prohibitively high risk for the mother and unborn child.[2–5] Cardiac risk prediction models for pregnant women with heart disease in general have been developed.[5–7] The Modified World Health Organization Classification of Maternal Cardiovascular Risk (mWHO) model, which is thought to be the most reliable, diagnoses are classified into five groups with risk predictions of pregnancy ranging from low (2–5%) risk of maternal cardiac events to high (40–100%).[5,8]

Increased susceptibility to arrhythmias during pregnancy is thought to be a consequence of altered ion channel conductance, as well as altered expression of sex hormones during pregnancy.[4,9–13] Although arrhythmias on 24-hour electrocardiographic Holter monitoring are rare and generally benign in pregnant women without previous cardiac disease.[13,14] Studies have reported that cardiac arrhythmias account for about 0.17% of hospital admissions during pregnancy.[13] In spite of this, arrhythmias may be an important complication during pregnancy of women with pre-existing cardiac disease and/or an already increased risk of arrhythmias.[10]

Patients with CHD are generally at increased risk for tachyarrhythmias.[2] This can be caused by factors such as scarring, altered myocardial structure, and ventricular dilation following pressure/volume overload.[10] Some may have additional risk factors for arrhythmias during pregnancy, such as pre-existing heart failure, arrhythmias, transient ischaemic attack or stroke.[5,15–17] Additionally, some medications prolong the QT interval and thus elevate the risk for ventricular arrhythmias.[18] This makes arrhythmias a relevant complication for pregnant women with CHD.[10]

As a result of increased metabolic demands and sympathetic activity during pregnancy, heart rate increases in normal pregnancy by 15–25% starting early and peaking in the third

trimester.[19] Accordingly, the PR- and QT intervals as well as QRS duration decrease, but remain within the normal range during a normal pregnancy.[14,20] As the QT interval decreases with increasing heart rate, the reported QT interval is usually reported as a function of heart rate, the so-called QTc.[18] The QTc is commonly calculated using the Bazett's formula [$QTc=QT/RR^{0,5}$].[18] Prolongation of the QTc is associated with ventricular arrhythmogenesis and can predispose to potentially fatal ventricular tachycardia.[18] The upper limit of normal for women is 460 ms.[21] Interestingly, in women with long QT-syndrome, pregnancy is associated with a decreased risk of cardiac events. However, there is an increased risk for cardiac events during the postpartum period.[22]

Previous studies have shown that QTc increases during pregnancy without previous cardiac disease although remain within the normal range.[8,14,19,20] A study comparing QT and QTc intervals between 40 pregnant and 40 non-pregnant women without previous heart disease found a mean difference of 27 ms between QTc in the two cohorts.[8] In this study, the mean QTc in the pregnant group was 430 ms compared to 403 in the non-pregnant group.[8] A study on twin pregnancy compared to single pregnancy reveals that QTc intervals are longer and QTc prolongation is more prevalent in women who are delivering twins.[23]

The aim of the study was to evaluate electrocardiographic changes in pregnant women with CHD longitudinally (i.e. before, during, and after pregnancy) in order to identify risk factors for abnormally prolonged QTc, which is a risk factor for ventricular arrhythmias. Our primary hypothesis was that women with CHD have similar electrocardiographic changes during pregnancy as what has been described for women without CHD. Our secondary hypothesis was that QTc prolongation during pregnancy can be predicted based on pre-pregnancy demographic and electrocardiographic factors.

Materials and methods

For this retrospective longitudinal cohort study, the study group consisted of women with CHD who were pregnant and delivered their babies at the maternity ward at Skånes Universitetssjukhus in Lund between 2009 and 2021. The total cohort consisted of 162 pregnancies of 114 women. Inclusion criteria were an existing pre-pregnancy electrocardiogram from the age of 18 years or older, as well as at least one electrocardiogram during pregnancy. Patients with a ventricular pacemaker were excluded. The final cohort fulfilling the inclusion criteria consisted of 83 pregnancies. There was no control group of patients without CHD. Demographic and clinical data were collected retrospectively from the patients' medical records.

The electrocardiograms analysed for the purpose of this study were: 1. The most recent electrocardiogram prior to pregnancy and after the age of 18 (pre-pregnancy), 2. the last electrocardiogram of each trimester during pregnancy and 3. the first electrocardiogram within 4 weeks of delivery (post-pregnancy). Values for heart rate, PR time, QRS duration, QT-time and QTc using the Bazett's formula were collected from the values obtained from the automated electrocardiogram machine readings and checked manually if abnormal. As electrocardiograms were recorded at variable frequencies and intervals during pregnancy, the parameters chosen for analysis were the maximal recorded heart rate and QTc and the minimal recorded PR interval and QRS duration—as the former are known to increase and the latter are known to decrease during pregnancy.

Statistical analyses were performed using IBM SPSS Statistics, version 27 (IBM Corp, Armonk, New York, USA). Continuous variables are presented as mean (standard deviation) and categorical variables as number (per cent). Groups were compared using the student t-test for independent samples, and changes during pregnancy were analysed using t-test for paired samples. Categorical variables were compared using the Chi square or Fisher exact test as appropriate. If p for potential risk factors was < 0.1, logistic regression was performed for that variable. In addition, Pearson correlation analyses were carried out. $P < 0.05$ was the cut-off value for statistical significance.

This retrospective study was approved by the national Swedish ethics committee (EPN #2021-01636). The need for informed consent was waived.

Results

The study cohort consisted of 83 pregnancies in 63 patients who met the inclusion criteria of having at least one available electrocardiogram prior to pregnancy and one during pregnancy. The baseline characteristics were mean age at delivery was 30.1 ± 5.0 years and the mean body mass index prior to pregnancy was 23.9 ± 4.2kg/m^2. All five mWHO classes were represented, with 15 pregnancies (18.1%) in mWHO class I, 26 (31.3%) in mWHO II, 28 (33.7%) in mWHO II-III, 11 (13.3%) in mWHO III, and three pregnancies (3.6%) in mWHO class IV. The subsequent study cohort included pregnancies with twenty-eight (34.1%) simple shunt lesions, and 23 (28.0%) left-sided defects such as mitral valve defects, aortic valve defects, and aortopathy. The study included sixteen pregnancies (19.5%) with right-sided lesions such as tetralogy of Fallot and pulmonary valve defects and fifteen pregnancies (18.3%) with complex CHD (double outlet right ventricle, transposition after mustard/senning repair, transposition after arterial switch repair, single ventricle, and coronary artery anomaly). Thirteen (15.7%) were treated with medications that have an antiarrhythmic effect during pregnancy, of which five (6.0%) had no antiarrhythmic medication prior to pregnancy. One woman was treated with only beta blockade and this woman had arrhythmias during the pregnancy (see below). Another two women had arrhythmias (see below) during pregnancy and were both prescribed beta blockers, although one of these women also was on Digoxin, Verapamil, or Flecainide at different times throughout the pregnancy. The remaining 10 (12.1%) women were treated with beta blockers for indications other than arrhythmias. During the pregnancy, 17 (20.7%) experienced palpitations as a symptom of possible arrhythmias, three (3.6%) had documented arrhythmias, and two (2.4%) had pre syncope. There were no deaths. Of the 83 study participants, 75 (90.2%) had normal left ventricular function and seven (8.4%) had depressed systolic left ventricular function defined as a systemic ventricular ejection fraction of 50% or less at the first echocardiography during pregnancy. These women had the following diagnoses: repaired Tetralogy of Fallot with pulmonary insufficiency and peripheral pulmonary artery stenosis, double-chambered right ventricle with pulmonary stenosis, transposition of the great arteries following Mustard/Senning procedures (n = 3), and mitral insufficiency due to cleft or prolapse of the mitral valve (n = 2).

Eectrocardiographic changes during pregnancy

In 83 pregnancies, we had an available electrocardiogram prior to pregnancy, 28 had an electrocardiogram during the first trimester

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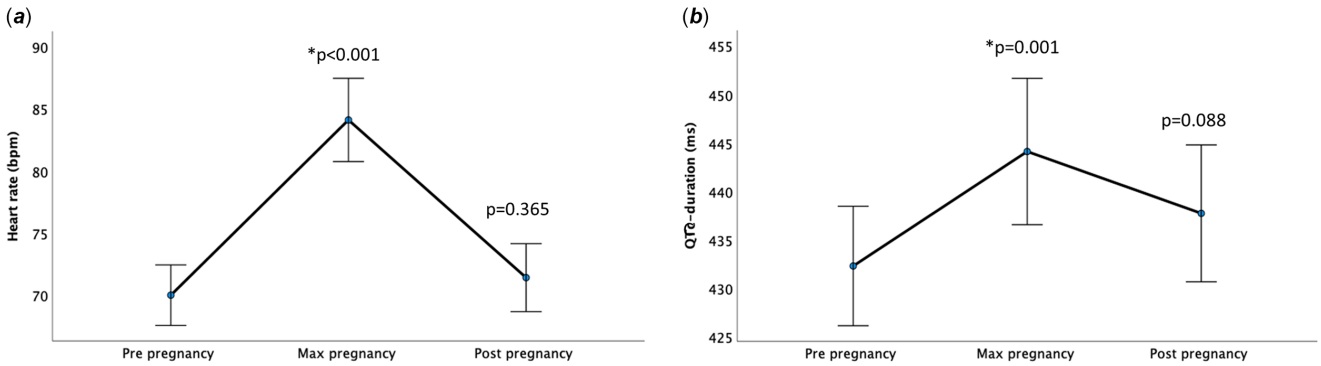
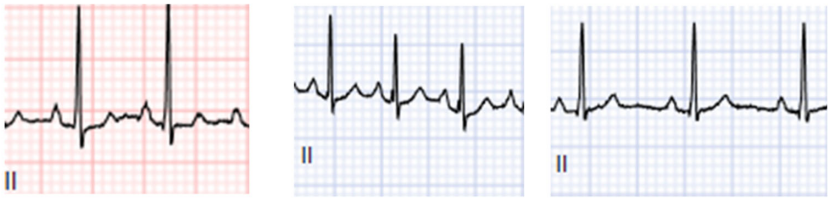


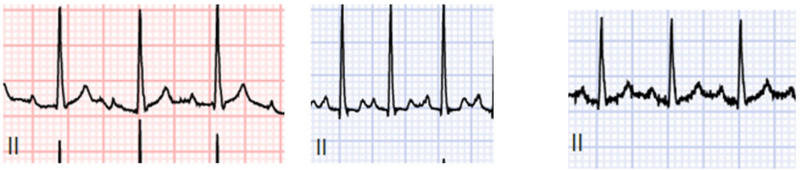
Figure 1. ***A*** and ***B***: heart rate and QTc duration prior to, maximal during and post-pregnancy in women with CHD presented as mean with 95% CI. T-test for paired samples comparing values during pregnancy with pre-pregnancy and post-pregnancy. * p values denoted statistical significance. Bpm = beats per minute.

(*a*)



	Pre Conception	Pregnancy	Post Partum
Heart rate [1/min]	80	111	65
QT [ms]	368	324	388
QTc [ms]	424	440	403

(*b*)



	Pre Conception	Pregnancy	Post Partum
Heart rate [1/min]	66	101	76
QT [ms]	422	390	430
QTc [ms]	432	505	458

(*c*)

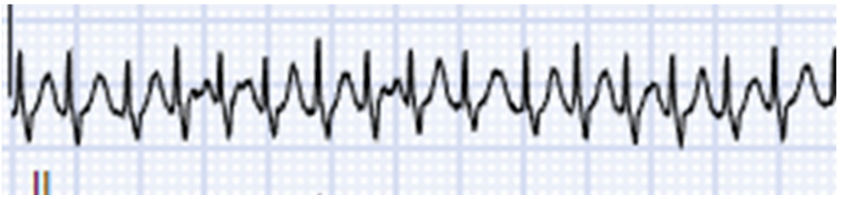


Figure 2. Examples of a patient's electrocardiographic (lead II). ***A*** and ***B***: Electrocardiographic tracings taken pre-conception, during the third trimester of pregnancy, and following pregnancy. Heart rate, as well as QT and QTc are shown below. ***C***: Electrocardiographic tracing from a patient with an irregularly irregular rhythm due to atrial fibrillation at a ventricular rate of 191 beats per minute.

of pregnancy, 66 during the second trimester, 54 during the third trimester, and 75 patients post-pregnancy. Electrocardiogram from all five occasions were available for only 14 pregnancies. Of the 28 who had an electrocardiogram during the first trimester, only seven had no other electrocardiogram during pregnancy.

There was a statistically significant increase in heart rate and QTc as well as a decrease in PR-interval and QRS duration during pregnancy (all $p < 0.001$) (Table 1). Post-partum, heart rate, QRS duration, and QTc returned close to pre-pregnancy values, while PR interval was significantly higher compared to pre-conception (Figs. 1 and 2, Table 1). Similarly, the JTc (defined as the QTc – ORS duration) increased during pregnancy (pre-conception 326.6 ± 27.1ms, pregnancy 340.9 ± 27.3ms, $p < 0.001$) and returned to near baseline post-partum (330.8 ± 25.2ms, $p = 0.152$).

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Table 1. Electrocardiographic changes during pregnancy in women with congenital disease. T-test for paired samples comparing pre-pregnancy electrocardiographic parameters to those obtained during pregnancy and to those obtained following delivery. If multiple electrocardiograms were available during pregnancy, the maximal values for heart rate and QTc and the minimum values for PR and QRS were used

	Pre-pregnancy Mean ± SD	Pregnant Mean ± SD	P	Post-partum	P
HR (bpm)	69.7 ± 10.4	83.5 ± 14.2	<0.001	71.4 ± 11.9	0.365
PR interval (ms)	150.3 ± 28.9	141.2 ± 22.5	<0.001	155.4 ± 31.2	0.016
QRS duration (ms)	105.4 ± 23.2	101.2 ± 22.5	<0.001	107.0 ± 23.8	0.224
QTc (ms)	432 ± 27.1	442.1 ± 33.0	0.001	437.8 ± 30.7	0.088

Bpm = beats per minute.

Table 2. Risk factors for QTc prolongation over 460 ms prior to pregnancy in women with congenital disease evaluated with logistic regression

	QTc pre-pregnancy>460 ms	
	OR (95% CI)	P
Age at delivery (years)	0.96 (0.85–1.08)	0.477
Weight (kg)	1.08 (1.02–1.14)	0.007
BMI (kg/m^2)	1.19 (1.05–1.36)	0.009
HR pre (bpm)	1.03 (0.97–1.10)	0.27
PR interval pre (ms)	1.00 (0.98–1.02)	0.690
QRS duration pre (ms)	1.06 (1.03–1.09)	<0.001
Bundle branch block (QRS>120ms)	8.14 (2.14–30.94)	0.002

Weight = weight at enrolment in maternal health care in the beginning of the pregnancy; BMI = body mass index; Pre = prior to pregnancy, Bpm = beats per minute.

Risk factors for arrhythmias during pregnancy

The three women who experienced documented arrhythmias during pregnancy had asymptomatic supraventricular tachycardia, and atrial fibrillation or flutter, respectively (Fig. 2b). The underlying diagnoses were a history of a shunting lesion (n = 2) and double outlet right ventricle (n = 1). Logistic regression of demographic and electrocardiogram parameters from the three patients with confirmed arrhythmic events during pregnancy revealed that increasing age (OR 1.76, CI:1.03–3.00, p = 0.037) as well as maximal heart rate (OR:1.09, CI:1.00–1.18, p = 0.047) and maximal QTc duration (OR:1.03, CI:1.00–1.05, p = 0.036) during pregnancy were associated with documented arrhythmias. There was no statistically significant association between documented arrhythmias and weight, body mass index, or other electrocardiogram parameters. Given the low number of documented arrhythmias in our cohort, these results need to be viewed with caution.

Risk factors for QTc prolongation prior to pregnancy

On the last electrocardiogram prior to pregnancy, 12 (14%) had a QTc > 460 ms and 71 (86%) did not. Logistic regression analyses revealed that QTc prolongation > 460 ms prior to pregnancy was associated with higher weight, body mass index, and QRS duration (Table 2). Other demographic (including diagnosis and mWHO-group, NYHA stage > 1 and reduced EF) and electrocardiographic parameters were not associated with QTc prolongation over 460 ms at a statistically significant level (all p > 0.1, data not shown). Of note, NYHA classification of 22 pregnancies was missing or indeterminate due to comorbidities.

Risk factors for QTc prolongation > 460 ms during pregnancy

Next, pre-pregnancy predictors of QTc prolongation > 460 ms during pregnancy were investigated (Table 3). The 17 (20%) who had QTc > 460 ms during pregnancy had significantly longer QRS duration as well as QTc prior to pregnancy. Amongst the patients with QTc prolongation over 460 ms during pregnancy, 41.2% had QTc prolongation over 460 ms before pregnancy as well. There was no statistically significant association of QTc > 460 ms during pregnancy with CHD type, mWHO class, or maternal symptoms during pregnancy (p > 0.1, data not shown). Women who had a documented QTc during pregnancy had the following diagnoses: Tetralogy of Fallot (n = 6), septal defect (n = 4), transposition of the great arteries following arterial switch operation (n = 2), double outlet right ventricle (n = 2), aortic valve disease (n = 2), and atrioventricular septal defect (n = 1).

Logistic regression analyses confirmed that weight, body mass index, pre-pregnancy QRS duration, and QTc were positively associated with QTc of > 460 ms during pregnancy (Table 4). Lastly, correlation analyses revealed strong positive correlations of maximal pregnancy QTc with pre-pregnancy QRS and QTc durations and moderate correlations with pre-pregnancy weight and body mass index (Table 5).

Risk factors for more than average QTc prolongation during pregnancy

Next, differences between the 49 (59%) women who experienced a more than average QTc increase (defined as 27 ms) during pregnancy and the 34 (41%) who did not were evaluated. Only pre-pregnancy heart rate was higher in women who had a QTc increase of > 27 ms compared to pre-pregnancy QTc. In addition, there was a trend towards higher weight. Again, there was no statistically significant association with CHD type, mWHO class, or maternal symptoms during pregnancy (p > 0.1).

Logistic regression analyses confirmed that heart rate pre-pregnancy was positively associated with QTc increase > 27 ms during pregnancy and that there was a trend towards an effect of pre-pregnancy weight (Table 5). Lastly, correlation analyses revealed a strong correlation between absolute QTc increase during pregnancy and pre-pregnancy heart rate, and a trend

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Table 3. Risk factors for QTc prolongation over 460 ms respectively QTc increase during pregnancy compared to prior to pregnancy over 27 ms in women with CHD

	QTc > 460ms Mean ± SD or n(%) (n = 17)	QTc ≤ 460ms Mean ± SD or n(%) (n = 66)	P	QTc increase > 27ms Mean ± SD or n(%) (n = 49)	QTc increase ≤ 27ms Mean ± SD or n(%) (n = 34)	P
Age at delivery (years)	28.4 ± 5.8	30.5 ± 4.8	0.122	30.4 ± 5.0	29.7 ± 5.1	0.514
BMI (kg/m^2)	26.2 ± 5.9	23.4 ± 3.6	0.096	24.5 ± 5.0	23.3 ± 2.9	0.164
HR pre (bpm)	73.9 ± 10.0	68.6 ± 10.3	0.061	75.0 ± 9,0	62.0 ± 8.0	<0.001*
PR pre (ms)	156.5 ± 41.8	148.7 ± 24.6	0.324	149.5 ± 31.8	151.4 ± 24.5	0.767
QRS pre (ms)	126.4 ± 28.0	100.0 ± 18.5	0.002*	107.2 ± 24.8	102.8 ± 20.7	0.403
QTc pre (ms)	460.9 ± 30.1	424.5 ± 20.8	<0.001*	434.8 ± 29.3	427.9 ± 23.5	0.260
QTc pre>460ms	7 (41.2%)	5 (7.6%)	0.002*	7 (14.3%)	5 (14.7%)	1

BMI = body mass index; Pre = prior to pregnancy; Bpm = beats per minute.
*p values denote statistical significance.

Table 4. Odds ratio for risk factors for QTc > 460 ms or QTc increase > 27 ms during pregnancy in women with CHD evaluated with logistic regression

	QTc preg max > 460ms		QTc increase > 27ms	
	OR (95% CI)	P	OR (95% CI)	P
Weight (kg)	1.06 (1.01-1.11)	0.026	1.04 (0.99-1.09)	0.087
BMI (kg/m^2)	1.14 (1.01-1.29)	0.032	1.09 (0.96-1.23)	0.171
HR pre (bpm)	1.05 (1.00-1.11)	0.066	1.21 (1.11-1.33)	<0.001*
QRS duration pre (ms)	1.05 (1.02-1.08)	<0.001*	1.01 (0.99-1.03)	0.399
QTc pre (ms)	1.07 (1.03-1.11)	<0.001*	1.01 (0.99-1.03)	0.260

Weight = weight at enrolment in maternal health care in the beginning of the pregnancy; BMI = body mass index; Pre = prior to pregnancy; bpm = beats per minute.
*p values denote statistical significance.

Table 5. Correlation analysis of the significant risk factors for QTc prolongation from Table 3

	QTc max during pregnancy		QTc Increase	
	R	P	R	P
Weight (kg)	0.328	0.003*	0.198	0.081
BMI (kg/m^2)	0.313	0.005*	0.195	0.087
HR pre (bpm)	0.166	0.133	0.667	<0.001*
QRS duration pre (ms)	0.602	<0.001	0.173*	0.118
QTc pre (ms)	0.589	<0.001*	0.111	0.319

R = Pearson correlation coefficient; Weight = weight at enrolment in maternal health care in the beginning of the pregnancy; BMI = body mass index; Pre = prior to pregnancy; bpm = beats per minute.
*p values denote statistical significance.

towards a weak-moderate correlation with weight and body mass index (Table 5).

Subgroup analyses

Of the 83 pregnancies reported herein, 13 women had multiple documented pregnancies. When including only the first documented pregnancy, the results were unchanged (data not shown). We then proceeded with a subgroup analysis of the 13 women with more than one documented pregnancy, comparing the first and most recent documented pregnancy with available electrocardiograms. None of the electrocardiographic variables prior to, during and post-pregnancy showed significant changes between pregnancies. As the number of patients included is very small, the chance of a type 2 error is high.

Discussion

Pregnant women with CHD have similar electrocardiographic changes during pregnancy as previously reported for healthy women. However, they may be more prone to develop abnormally prolonged QTc during pregnancy, which constitutes a potential risk for serious arrhythmias. The risk factors of having an increased QTc during pregnancy in our cohort were increased body mass index prior to pregnancy as well as having a higher QRS duration or abnormal QTc on pre-conception electrocardiogram. In addition, women with higher baseline heart rates appear to have a higher QTc increase during pregnancy.

Importantly, the present study shows that increased body mass index is a risk factor for QTc prolongation over 460 ms prior to as well as during pregnancy. Previous studies comparing QTc prolongation between obese versus non-obese women found significantly longer QTc duration in obese women supporting the present study's finding of increased QTc duration in women with higher pre-conception body mass index.[24,25] As a consequence, overweight women with CHD who are pregnant may be at increased risk for arrhythmias. This adds to the overall increased

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risk for adverse pregnancy-related outcome of overweight and obese women including miscarriage, intrapartum obstetrical complications, prolonged labour, caesarean postpartum thromboembolism, and future cardiometabolic diseases resulting from weight retention after pregnancy among other things.[26] Thus, we propose that overweight or obese pregnant women with CHD should be monitored carefully for perhaps asymptomatic but potentially life-threatening arrhythmias.

The finding of a statistically significant increase in heart rate in pregnant women with CHD is consistent with previous studies showing elevated heart rate in healthy pregnancies as well as pregnancies with maternal CHD in order to compensate for increased oxygen demand.[4,14] Previous studies have described that heart rate elevation in pregnancy is due to sympathetic activation as well as altered activity of ion channels controlling cardiac pacemaker cells.[14] With increased heart rate, the absolute QT decreases in general as well as during normal pregnancies.[13] Our findings are consistent with this. In spite of this, an increase in QTc during pregnancy even for women without cardiac disease has been reported by studies that found a mean QTc difference of 27 ms in pregnant women compared to non-pregnant women.[8] Nonetheless, QTc remains within the normal range in healthy pregnant women.[8] By contrast, the present study found QTc prolongation above 460 ms during pregnancy in 17 (20.5%) patients, which demonstrates that pregnant women with CHD may be at increased risk for QTc prolongation above 460 ms. This could predispose them to arrhythmic events.

The mean QTc prior to pregnancy was 432 ms in the present study, compared to 403 ms in a study of healthy women.[8] Therefore, a possible explanation for the higher maximal QTc in pregnancy of women with CHD compared to healthy women might be increased baseline QTc. A substantial number ($n = 19$, 22.9%) of women in our CHD cohort had a bundle branch block pattern with a widened QRS complex (>120 ms) at baseline, which contributed to an increased QTc ($R = 0.60$, $p < 0.001$) during pregnancy, as expected based on the fact that the QRS complex is part of the QT interval. However, QRS duration did not correlate with absolute QTc increase during pregnancy ($R = 0.17$, $p = 0.118$), arguing against a significant role of QRS duration as an effect-modulating factor for additional QTc prolongation during pregnancy. By contrast, the finding of a positive correlation between heart rate prior to pregnancy and absolute QTc increase ($R = 0.67$, $p < 0.001$) during pregnancy suggests that heart rate prior to pregnancy might have an effect-modulating influence on QTc increase during pregnancy.

Previous studies found reduced PR interval in pregnant women without cardiac disease.[27,28] This may be a consequence of accelerated AV-node conduction due to factors such as increased sympathetic tone and increased heart rate during pregnancy Our findings were consistent with that.

Furthermore, previous studies have found an association between mWHO classification and diagnosis group and cardiac complications in general, including arrhythmias.[5–7] The present study was not able to replicate this, however, the previous studies did not study QTc duration and were not specific for patients with CHD or risk for arrhythmias.[5–7] The low number of patients within a specific diagnosis group or mWHO class (only three patients in mWHO IV) in the present study may have resulted in a type II error that could be a plausible explanation for the insignificant results.

Only three women experienced clinically documented arrhythmias in the present study. However, as shown in Table 2, 13 women were treated with antiarrhythmic medication during pregnancy, whereas five of these women had no antiarrhythmic treatment prior to pregnancy. The medications used were Digoxin and beta blockers, which both may have been added for reasons other than arrhythmias. Nonetheless, the fact that antiarrhythmic medications were added in a few patients during pregnancy may have reduced the observed risk of arrhythmic events in the study cohort.

Limitations

This is a retrospective study that is based on medical record data. Holter monitoring was done only in selected cases to confirm suspected arrhythmias, which may have led to a falsely low rate of arrhythmias. The low number of patients in mWHO class III and IV might contribute to selection bias resulting from under-representation of patients with high risk for maternal cardiac events. To overcome these limitations, larger prospective studies are needed.

Conclusion

In conclusion, this study found that electrocardiographic changes in pregnant women with CHD differ from those previously reported during pregnancies in healthy women. Our results suggest that CHD patients with long QRS duration or long QTc interval, high weight, and/or body mass index, or high heart rate prior to pregnancy may harbour electrocardiographic changes that may put them at increased risk for ventricular arrhythmias during pregnancy. Thus, patients at risk should be monitored more closely for arrhythmias during pregnancy, regardless of mWHO classification and diagnosis group. Recognising risk for arrhythmias early could help prevent potentially life-threatening cardiac arrhythmias in pregnant patients with CHD.

Availability of data and materials. Data may be available on request.

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Author contribution. CGW, FW, and JH contributed to the design or conception of this study. Acquisition, analysis or interpretation was made by CGW and TL. CGW drafted the manuscript with TL and JH, and FW and EW revised the manuscript critically. All authors gave final approval of the manuscript and agreed to be accountable for integrity and accuracy in all aspects of the work.

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Competing interests. None.

Ethical standard. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by The Swedish Ethical Review Authority.

References

1. Perloff JK. Congenital heart disease in adults. A new cardiovascular subspecialty. Circulation 1991; 84: 1881–1890.
2. Wu MH, Lu CW, Chen HC, Kao FY, Huang SK. Adult congenital heart disease in a nationwide population 2000-2014: epidemiological trends, arrhythmia, and standardized mortality ratio. J Am Heart Assoc 2018; 7: e007907.

https://doi.org/10.1017/S1047951124000374 Published online by Cambridge University Press

3. Ramage K, Grabowska K, Silversides C, Quan H, Metcalfe A. Association of adult congenital heart disease with pregnancy, maternal, and neonatal outcomes. JAMA Netw Open 2019; 2: e193667.
4. Warnes CA. Pregnancy and delivery in women with congenital heart disease. Circ J 2015; 79: 1416–1421.
5. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018; 39: 3165–3241.
6. Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. J Am Coll Cardiol 2018; 71: 2419–2430.
7. Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J 2010; 31: 2124–2132.
8. Zamani M, Esmailian M, Yoosefian Z. QT interval in pregnant and non-pregnant women. Emergency (Tehran, Iran) 2014; 2: 22–25.
9. MacIntyre C, Iwuala C, Parkash R. Cardiac arrhythmias and pregnancy. Curr Treat Options Cardiovasc Med 2018; 20: 63.
10. Fürniss HE, Stiller B. Arrhythmic risk during pregnancy in patients with congenital heart disease. Herzschrittmacherther Elektrophysiol 2021; 32: 174–179.
11. Rosano GMC, Leonardo F, Luca FD, Sarrel PM, Beale CM, Collins P. Cyclical variation in paroxysmal supraventricular tachycardia in women. Lancet 1996; 347: 786–788.
12. Sedlak T, Shufelt C, Iribarren C, Merz CN. Sex hormones and the QT interval: a review. J Womens Health (Larchmt) 2012; 21: 933–941.
13. Cordina R, McGuire MA. Maternal cardiac arrhythmias during pregnancy and lactation. Obstet Med 2010; 3: 8–16.
14. Fu Q. Hemodynamic and electrocardiographic aspects of uncomplicated singleton pregnancy. Adv Exp Med Biol 2018; 1065: 413–431.
15. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001; 104: 515–521.
16. Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy-related complications in women with heart disease. Circulation 1997; 96: 2789–2794.
17. Tateno S, Niwa K, Nakazawa M, Akagi T, Shinohara T, Yasuda T. Arrhythmia and conduction disturbances in patients with congenital heart disease during pregnancy: multicenter study. Circ J 2003; 67: 992–997.
18. Kallergis EM, Goudis CA, Simantirakis EN, Kochiadakis GE, Vardas PE. Mechanisms, risk factors, and management of acquired long QT syndrome: a comprehensive review. ScientificWorldJournal 2012; 2012: 212178–8.
19. Omidi N, Khorgami MR, Khatami F, Mahalleh M. Electrocardiographic indices and pregnancy: a focus on changes between first and third trimesters. Rev Port Cardiol 2021; 41 1: 43–47.
20. Tanindi A, Akgun N, Pabuccu EG, et al. T peak to end interval and tp-e/QT ratio in pregnancy with respect to trimesters. Ann Noninvasive Electrocardiol 2016; 21: 169–174.
21. Lankaputhra M, Voskoboinik A. Congenital long QT syndrome: a clinician's guide. Int Med J 2021; 51: 1999–2011.
22. Rashba EJ, Zareba W, Moss AJ, et al. Influence of pregnancy on the risk for cardiac events in patients with hereditary long QT syndrome. Circulation 1998; 97: 451–456.
23. Luo C, Duan Z, Jiang Y, Liu P, Yan Y, Han D. Prevalence and risk factors of QTc prolongation during pregnancy. Front Cardiovasc Med 2021; 8: 819901.
24. Park JJ, Swan PD. Effect of obesity and regional adiposity on the QTc interval in women. Int J Obes Relat Metab Disord 1997; 21: 1104–1110.
25. Omran J, Bostick BP, Chan AK, Alpert MA. Obesity and ventricular repolarization: a comprehensive review. Prog Cardiovasc Dis 2018; 61: 124–135.
26. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. BMJ 2017; 356: j1.
27. Goncalves MAA, Pedro JM, Silva C, Magalhaes P, Brito M. Electrocardiographic findings in pregnant women in Angola. Ann Noninvasive Electrocardiol 2022; 27: e12980.
28. Soliman EZ, Rautaharju PM. Heart rate adjustment of PR interval in middle-aged and older adults. J Electrocardiol 2012; 45: 66–69.

https://doi.org/10.1017/S1047951124000374 Published online by Cambridge University Press