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Pregnancy outcomes in women with Ebstein's anomaly: data from the Registry of Pregnancy And Cardiac disease (ROPAC)

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ABSTRACT

Objective Ebstein's anomaly is a rare congenital cardiac condition and data regarding pregnancy outcomes in this patient group are scarce. We evaluated the maternal and perinatal risks of pregnancy in 81 women with Ebstein's anomaly.

Methods The Registry of Pregnancy and Cardiac disease is a prospective global registry of pregnancies in women with structural cardiac disease. Pregnancy outcomes in women with Ebstein's anomaly were examined. The primary outcome was the occurrence of a major adverse cardiac event (MACE) defined as maternal mortality, heart failure, arrhythmia, thromboembolic event or endocarditis. Secondary endpoints were obstetric and perinatal outcomes and the influence of pregnancy on tricuspid valve regurgitation as well as right atrial and ventricular dimensions.

Results In the 81 women with Ebstein's anomaly (mean age 29.7±6.1 years, 46.9% nulliparous), MACE occurred in 8 (9.9%) pregnancies, mostly heart failure (n=6). There were no maternal deaths. Prepregnancy signs of heart failure were predictive for MACE. Almost half of the women were delivered by caesarean section (45.7%) and preterm delivery occurred in 24.7%. Neonatal mortality was 2.5% and 4.9% of the infants had congenital heart disease. In the subgroup in which prepregnancy and postpregnancy data were available, there was no difference in tricuspid valve regurgitation grade or right atrial and ventricular dimensions before and after pregnancy.

Conclusions Most women with Ebstein's anomaly tolerate pregnancy well, but women with prepregnancy signs of heart failure are at higher risk for MACE during pregnancy and should be counselled accordingly.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Women with uncomplicated Ebstein's anomaly are categorised in modified WHO (mWHO) risk class II. However, this recommendation is based on typically small and retrospective studies.

WHAT THIS STUDY ADDS

⇒ Women with an uncomplicated Ebstein's anomaly tolerate pregnancy well. However, women with additional risk factors, such as signs of heart failure, have a high risk of maternal morbidity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ It seems reasonable to categorise women with Ebstein's anomaly is mWHO risk class II, and pregnancy and delivery could take place in a secondary centre. However, when additional risk factors are present, such as signs of heart failure, risk class III is more appropriate and pregnancy controls and delivery should take place in an expert centre.

INTRODUCTION

Congenital heart disease (CHD) represents a major health issue with an estimated worldwide prevalence of 9 per 1000 newborns.[1] As an increasing number of women with CHD reach childbearing age, the demand for accurate advice about the possible risks of pregnancy is increasing, particularly in those with residual cardiac defects or diminished cardiac function who are at increased risk of developing heart failure and/or arrhythmias during pregnancy.[2 3] To be able to accurately counsel women with CHD, having an adequate knowledge of the risks of pregnancy for specific congenital diseases is essential. However, prospective data in specific diseases are often limited or not available. Ebstein's anomaly is a rare congenital cardiac condition characterised by displacement of the posterior and septal leaflets of the tricuspid valve towards the apex of the right ventricle.[4 5] It accounts for ~1% of all congenital cardiac defects, with an incidence of 1 per 200 000 live births.[6] The clinical picture of Ebstein's anomaly is very heterogeneous and depends on the age at presentation, the degree of

leaflet displacement and the presence of additional associated cardiac malformations,[7] which makes it challenging to accurately counsel these women. The European Society of Cardiology (ESC) guidelines[8] categorise women with uncomplicated Ebstein's anomaly in modified WHO (mWHO) risk class II, which means a small increased risk of maternal mortality and/or a moderate increased risk of morbidity in pregnancy, while symptomatic patients with cyanosis and/or heart failure are regarded as class IV and the guideline recommends that they should be counselled against pregnancy. However, these recommendations are all based on level C evidence

Table 1 Baseline characteristics

Characteristic	Ebstein's anomaly (n=81)	Other ROPAC (n=5658)	P value
Age, mean (SD), years	29.7 (6.1)	29.5 (5.6)	0.350
LMIC	17 (21.0)	2264 (40.0)	**<0.001**
Nulliparity	38 (46.9)	2535 (44.8)	0.724
Current smoking	1 (1.2)	227 (4.0)	0.247
Underlying cardiac pathological features			
Associated cardiac defects			
Atrial septal defect	12 (14.8)	278 (5.1)	**<0.001**
Bicuspid aortic valve	3 (3.7)	538 (9.5)	0.076
Persistent ductus arteriosus	2 (2.5)	147 (2.6)	0.942
Ventricular septal defect	1 (1.2)	715 (12.6)	**0.002**
Prior interventions/surgery	39 (48.1)	3121 (55.2)	0.195
Tricuspid valve intervention	15 (18.5)	33 (0.6)	**<0.001**
Prepregnancy cardiac status			
Chronic hypertension	7 (8.6)	373 (6.6)	0.491
Diabetes mellitus	2 (2.5)	88 (1.6)	0.521
History of heart failure	5 (6.2)	591 (10.4)	0.208
Cyanosis	4 (4.9)	59 (1.0)	**<0.001**
Atrial fibrillation/flutter	3 (3.7)	103 (1.8)	0.211
NYHA class			
I	55 (67.9)	4152 (73.4)	0.268
II	21 (25.9)	1170 (20.7)	0.248
III	1 (1.2)	175 (3.1)	0.335
IV	0 (0)	28 (0.5)	0.526
Unknown	4 (4.9)	133 (2.4)	0.130
Prepregnancy cardiac medication			
Antiplatelet therapy	4 (4.9)	230 (4.1)	0.693
Vitamin K antagonists	3 (3.7)	393 (6.9)	0.253
LMWH	3 (3.7)	26 (0.5)	**<0.001**
DOAC	0 (0)	3 (0.1)	0.836
Beta blockers	4 (4.9)	559 (9.9)	0.138
Antiarrhythmic drugs	2 (2.5)	98 (1.7)	0.615
Diuretics	1 (1.2)	216 (3.8)	0.226
Angiotensin receptor blocker	1 (1.2)	24 (0.4)	0.271
ACE inhibitors	0 (0)	157 (2.8)	0.128
Aldosterone antagonists	0 (0)	32 (0.6)	0.497
Calcium channel blocker	0 (0)	50 (0.9)	0.395
Nitrates	0 (0)	9 (0.2)	0.719
Statins	0 (0)	31 (0.5)	0.504

Data in n (%) unless otherwise specified. Bold values denote statistical significance at the p<0.05 level.
DOAC, direct oral anticoagulants; LMIC, low-income and middle-income country; LMWH, low-molecular-weight heparin; NYHA, New York Heart Association functional classification; ROPAC, Registry Of Pregnancy And Cardiac disease.

Table 2 Maternal cardiac outcomes

Outcome	Ebstein's anomaly (n=81)	Other ROPAC (n=5658)	P value
MACE	8 (9.9)	887 (15.7)	0.153
Maternal mortality*	0 (0)	40 (0.7)	0.448
Heart failure	6 (7.4)	605 (10.7)	0.341
Arrhythmia	3 (3.7)	178 (3.1)	0.776
Supraventricular	3 (3.7)	92 (1.6)	0.146
Ventricular	0 (0)	90 (1.6)	0.253
Thromboembolic events	2 (2.5)	85 (1.5)	0.479
Endocarditis	0 (0)	33 (0.6)	0.491
Aortic dissection	0 (0)	5 (0.1)	0.789
Hospital admission for cardiac reason	10 (12.3)	748 (13.2)	0.817

Data in n (%) unless otherwise specified.
*Maternal mortality up to 6 months post partum.
MACE, major adverse cardiac event; ROPAC, Registry of Pregnancy and Cardiac disease.

('consensus of opinion of the experts and/or small studies, retrospective studies, registries'), because data regarding pregnancy outcomes in women with Ebstein's anomaly are scarce and typically derived from small retrospective studies.[9–15] Therefore, this study aims to evaluate the maternal and perinatal outcomes of pregnancy in women with Ebstein's anomaly, based on the prospective, observational Registry of Pregnancy and Cardiac disease (ROPAC) of the EURObservational Research Programme of the ESC. Prepregnancy risk factors for poor maternal cardiac outcome were assessed and finally a possible effect of pregnancy on tricuspid valve function and right atrial and ventricular dimensions was investigated.

METHODS

Study design

The ROPAC is an international, prospective, observational registry of pregnant patients with structural heart disease. The ESC working groups on CHD and valvular heart disease initiated ROPAC in 2007 and subsequently it was embedded in the EURObservational Research Programme of the ESC. Pregnant women who were included in the ROPAC between January 2007 and January 2018 and were diagnosed with Ebstein's anomaly were included in this study.[16]

Definitions and outcomes

The reported prepregnancy characteristics were age, parity, living in a low-income or middle-income country (LMIC) (based on The International Monetary Classification), underlying cardiac pathological features including prior interventions, current smoking, chronic hypertension, diabetes mellitus, signs of heart failure (in the past or pre-existent), cyanosis, atrial fibrillation or flutter, New York Heart Association (NYHA) functional class and use of cardiac medication. The provision of echocardiographic data was facultative. The primary combined outcome was the occurrence of a major adverse cardiac event (MACE), defined as the occurrence of any of the following: maternal mortality, heart failure, arrhythmia, thromboembolic event, endocarditis or aortic dissection during pregnancy and up to 6 months post partum. Heart failure was defined according to the American College of Cardiology/American Heart Association guidelines, and heart failure episodes were only included when they required hospital admission, new treatment or change in the existing treatment regime.[17] Secondary outcomes were obstetric and perinatal outcomes. Preterm birth was defined as birth before 37 weeks of gestation, small for gestational age as birth weight less than the 10th percentile, and low Apgar score as <7 at 5 min after birth. Neonatal mortality was defined as the death of a live-born baby within the first month of life. Finally, in the subgroup of patients with echocardiographic data prepregnancy and postpregnancy, the tricuspid valve regurgitation and right atrial and ventricular dimensions were investigated.[18 19]

Statistical analysis

Categorical data are presented as frequencies (numbers) and percentages and were compared using χ^2 tests. One sample Kolmogorov-Smirnov tests and histograms were used to assess the distribution of continuous data. These are presented as mean values with SD when normally distributed, or as median with IQR if skewed. The Mann-Whitney U test was used to compare differences between continuous data which were not normally distributed. Univariable logistic regression analyses were performed to identify baseline patient characteristics and echocardiographic data associated with MACE, presented as OR with 95% CIs and p value. The following baseline variables were assessed: age, body mass index, living in an LMIC, nulliparity, twin pregnancy, current smoking, chronic hypertension, cardiac medication use, diabetes mellitus, atrial fibrillation or flutter, signs of heart failure, NYHA class>I, severe tricuspid valve regurgitation and prior tricuspid valve intervention. In case of missing data, this was mentioned in the relevant table or figure legends. For the univariable logistic regression, multiple imputation was used to handle missing values. A two-sided p<0.05 was considered significant for all analyses. All statistical tests and analyses were performed using IBM SPSS Statistics V.28.0.

Patients and public involvement

Patients were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Baseline characteristics

Of 5739 pregnancies enrolled in the ROPAC registry between 2007 and 2018, 81 (1.4%) were in women with

Table 3 Univariable logistic regression analyses in 81 women with Ebstein's anomaly

	MACE (n=8)	No MACE (n=73)	Univariable logistic regression			
			OR	95% CI lower limit	95% CI upper limit	P value
Characteristic						
Age, mean (SD), years	30.2 (8.4)	29.6 (5.9)	1.01	0.88	1.16	0.871
BMI, mean (SD)	27.0 (6.6)	24.1 (3.8)	1.09	0.91	1.32	0.346
LMIC	3 (37.5)	14 (19.2)	2.53	0.54	11.86	0.239
Nulliparity	5 (62.5)	33 (40.7)	2.02	0.45	9.09	0.359
Twin pregnancy*	0 (0)	2 (2.7)	NM	NM	NM	NM
Current smoking*	0 (0)	1 (1.4)	NM	NM	NM	NM
Chronic hypertension	1 (12.5)	6 (8.2)	1.60	0.17	15.22	0.685
Cardiac medication use before pregnancy	2 (25.0)	5 (6.8)	4.53	0.72	28.55	0.107
Diabetes mellitus	1 (12.5)	1 (1.4)	8.93	0.49	161.37	0.138
Atrial fibrillation/flutter	1 (12.5)	2 (2.7)	5.07	0.41	63.21	0.207
History of heart failure	3 (37.5)	2 (2.7)	21.30	2.87	158.32	**0.003**
Cyanosis	1 (12.5)	3 (4.1)	3.33	0.31	36.48	0.324
NYHA class>I	3 (37.5)	19 (26.0)	1.71	0.37	7.83	0.492
Severe tricuspid valve regurgitation	2 (25.0)	10 (13.7)	2.10	0.37	11.89	0.402
Tricuspid valve repair*	0 (0)	7 (9.6)	NM	NM	NM	NM
Tricuspid valve replacement	1 (12.5)	7 (9.6)	0.74	0.08	6.94	0.794

Data in n (%) unless otherwise specified. Bold script denotes p<0.05. After multiple imputation for age (9.9%), BMI (40.1%), current smoking (22.2%), prior diabetes mellitus (1.2%) and signs of heart failure (1.2%).
*OR could not be computed because of complete separation.
BMI, body mass index; LMIC, low-income and middle-income country; MACE, major adverse cardiac event; NM, not measurable; NYHA, New York Heart Association .

Ebstein's anomaly. Baseline characteristics are presented in table 1. The mean age was 29.7±6.1 years and 38 (46.9%) of the women were nulliparous. Seventeen (21%) women lived in an emerging country as opposed to 40% in the rest of the ROPAC cohort (p<0.001). Most of the women were asymptomatic and in NYHA class I (n=55, 67.9%) while 21 (25.9%) women were classified in NYHA class II and one woman in NYHA class III. Five (6.2%) women had signs of heart failure and compared with the other women of the ROPAC cohort, prepregnancy cyanosis was more common in the women with Ebstein (4.9% vs 1.0%, p<0.001). None of the women with Ebstein has undergone a Glenn procedure. Tricuspid valve intervention had been performed in 15 cases: 7 (8.6%) had a repair and 8 (9.9%) had a tricuspid valve replacement (6 with a bioprosthesis, 2 with a mechanical valve), of which 2 after an initial tricuspid valve repair. There was no difference in the presence of severe tricuspid valve regurgitation in women with and without tricuspid valve repair (28.6% vs 13.5%, p=0.276) or in those with and without tricuspid valve replacement (12.5% vs 15.1%, p=0.846). Before pregnancy, women with Ebstein's anomaly used low molecular weight heparin (LMWH) more often compared with the rest of the ROPAC cohort (3.7% vs 0.5%; p<0.001). The indications for the use of LMWH were not reported.

Maternal cardiac outcomes

Maternal cardiac outcomes are presented in table 2. There were no maternal deaths either in pregnancy or up to 6 months after delivery. At least one MACE occurred in 8 (9.9%) pregnancies, whereas MACE occurred in 15.7% of the other ROPAC pregnancies (p=0.153). Six women (7.4%) developed heart failure and 3 women (3.7%) supraventricular arrhythmia. Two women who had supraventricular arrhythmia during pregnancy also had heart failure. Two women had a thromboembolic event, of which one woman suffered from pulmonary embolism and in the other woman, the nature of the thromboembolic event was not specified. No ventricular arrhythmia, aortic dissections or episodes of endocarditis were reported. Ten (12.3%) women were admitted to the hospital during pregnancy for cardiac reasons: six women with MACE, one with chest pain, one with a severe stenosis of the tricuspid valve prosthesis and in two women the cardiac reason of admission was not reported.

Risk factors for mace

With univariable logistic regression analyses, signs of heart failure were found to be the only risk factor for MACE (OR 21, 95% CI 2.87 to 158.32, p=0.003; table 3). Three out of the five women with signs of heart failure also developed heart failure during pregnancy. Additionally,

Table 4 Obstetric, fetal and neonatal outcomes

Outcome	Ebstein's anomaly (n=81)	Other ROPAC (n=5658)	P value
Obstetric and fetal outcomes			
Miscarriage	1 (1.2)	213 (3.8)	0.233
Therapeutic abortion	2 (2.5)	66 (1.2)	0.282
Twin pregnancy	2 (2.5)	94 (1.7)	0.574
Hypertensive disorders	2 (2.5)	270 (4.8)	0.317
Pregnancy induced hypertension	2 (2.5)	148 (2.7)	0.913
(Pre)eclampsia or HELLP syndrome	0 (0)	159 (2.9)	0.123
Gestational diabetes mellitus	1 (1.2)	159 (2.8)	0.385
Fetal death (>24 weeks)	0 (0)	72 (1.3)	0.307
Delivery			
Gestational age at delivery, median (IQR), weeks	38.0 (36.1–39.1)	38.6 (37.3–39.7)	**0.032**
Caesarean section	37 (45.7)	2644 (46.7)	0.853
Emergency Caesarean section for obstetric reasons	9 (11.8)	757 (14.2)	0.551
Emergency Caesarean section for cardiac reasons	1 (1.2)	131 (2.5)	0.519
Postpartum haemorrhage	0 (0)	170 (3.0)	0.113
Neonatal outcomes			
Preterm birth	20 (24.7)	885 (15.6)	**0.025**
Birth weight, mean (SD), g	3024 (724.0)	2970 (637.8)	0.415
Low birth weight (<2500 g)	7 (8.6)	666 (11.8)	0.385
Small for gestational age	12 (14.8)	572 (10.1)	0.164
Low Apgar score	7 (8.6)	390 (6.9)	0.538
Neonatal congenital heart disease	4 (4.9)	152 (2.7)	0.216
Neonatal death	2 (2.5)	31 (0.5)	**0.023**

Data in n (%) unless otherwise specified. Bold values denote statistical significance at the p<0.05 level.
HELLP, haemolysis, elevated liver enzymes, low platelets; ROPAC, Registry of Pregnancy and Cardiac disease.

one of these three women also had a supraventricular arrhythmia during pregnancy. This resulted in an MACE rate of 60% in the women with signs of heart failure compared with 6.6% in those without. Similar results were found when excluding women with a mechanical valve (n=2) from the analyses.

Obstetric and perinatal outcomes

An overview of obstetric and perinatal outcomes is presented in table 4. Almost half of the women underwent a caesarean section (n=37, 45.7%), of which 10 (27%) were defined as an emergency due to obstetric (n=9) or cardiac (n=1) indications, and 96 (25.1%) of the caesarean sections were planned due to cardiac reasons. The median gestational age at delivery was lower at 38.0 (IQR 36.1–39.1) weeks compared with 38.6 (IQR 37.3–39.7) in the rest of the ROPAC pregnancies (p=0.032). Preterm birth occurred in 24.7%, of which more than half were spontaneous (55%) and the remainder induced (45%). Five (6.2%) babies were small for gestational age. Four (4.9%) of the infants had CHD: there was one infant with Ebstein's anomaly, one with a double inlet left ventricle, one with a perimembranous ventricular septal defect and one with hypertrophic cardiomyopathy. There were 2 (2.5%) neonatal deaths compared with 31 (0.5%) neonatal deaths in the rest of the ROPAC cohort (p=0.023). One baby was born at a gestational age of 26 weeks after placental abruption and died on the day of birth due to prematurity. The other baby died 2 weeks after delivery due to severe hypertrophic cardiomyopathy.

Echocardiographic data

Echocardiographic data were available in 41 women prepregnancy and in 31 women postpregnancy (table 5). The postpartum echocardiogram was performed at a median of 7.0 (IQR 5.5–11.5) months after delivery. Right atrial enlargement (61.0% prepregnancy and 67.7% postpregnancy), dilation of the right ventricle (36.6% and 48.4%) and tricuspid valve regurgitation (87.8% and 84.2%) were common. In 14 women, serial data on tricuspid valve regurgitation were available before and after pregnancy and all these women had at least mild tricuspid valve regurgitation. No difference was seen in the severity of the regurgitation prepregnancy and postpregnancy assessment (p=1.000; figure 1A). In 17 women, serial data on right atrial and ventricular dimensions were available before and after pregnancy. There was no significant difference between right atrial (p=0.564) and

Table 5 Echocardiographic data

	Prepregnancy (n=41)	Postpregnancy (n=31)
Right atrial enlargement	25 (61.0)	21 (67.7)
Dilated right ventricle	15 (36.6)	15 (48.4)
Tricuspid valve regurgitation	36 (87.8)	16 (84.2)*
Mild	9 (22.0)	3 (15.8)
Moderate	15 (36.6)	9 (47.4)
Severe	12 (29.3)	4 (21.1)
Tricuspid valve stenosis	4 (9.8)	2 (6.5)

Data in n (%) unless otherwise specified.
*Missing data n=12.

ventricular dimensions (p=0.705) before and after pregnancy (figure 1B,C).

DISCUSSION

This is, to the best of our knowledge, the first prospective study on pregnancy outcomes in women with Ebstein's anomaly. Most women with Ebstein's anomaly tolerated pregnancy well and there were no maternal deaths. However, in 10% an MACE occurred, most frequently heart failure. Signs of heart failure were found to be a risk factor for MACE.

No maternal mortality occurred in our cohort, which is reassuring and important information to use while counselling these women. In the previously published retrospective series on pregnancy outcomes in women with Ebstein's anomaly, no maternal mortality was described either.[9–15] The incidence of heart failure or thromboembolic events that we found is comparable with the rates reported in a study on pregnancy outcomes in women with CHD (7.4% vs 6.6% and 2.5% vs 1.2%), but arrhythmia seems to be more common in women with Ebstein's anomaly (3.7% vs 1.2%).[20] The retrospective study of Connolly *et al*, which included 111 pregnancies in 44 women with Ebstein's anomaly, reported no deaths and no serious maternal complications during pregnancy or post partum, including heart failure, life-threatening arrhythmias, endocarditis or thromboembolic events.[10] This contrasts to our data where we observed an MACE rate of 9.9%, despite similar prepregnancy characteristics. The difference could be due to how data were collected in the study of Connolly *et al* (directly from the women without contacting the obstetricians and cardiologists) as well as its retrospective nature.[10] Therefore, we should be aware of the possibility of these serious complications. The heterogeneity of Ebstein's anomaly can make it difficult to classify everyone with this cardiac disease into the same mWHO risk class, and therefore, an individual assessment seems appropriate. Currently, women with Ebstein's anomaly are categorised in mWHO class II (corresponding with an expected event rate of

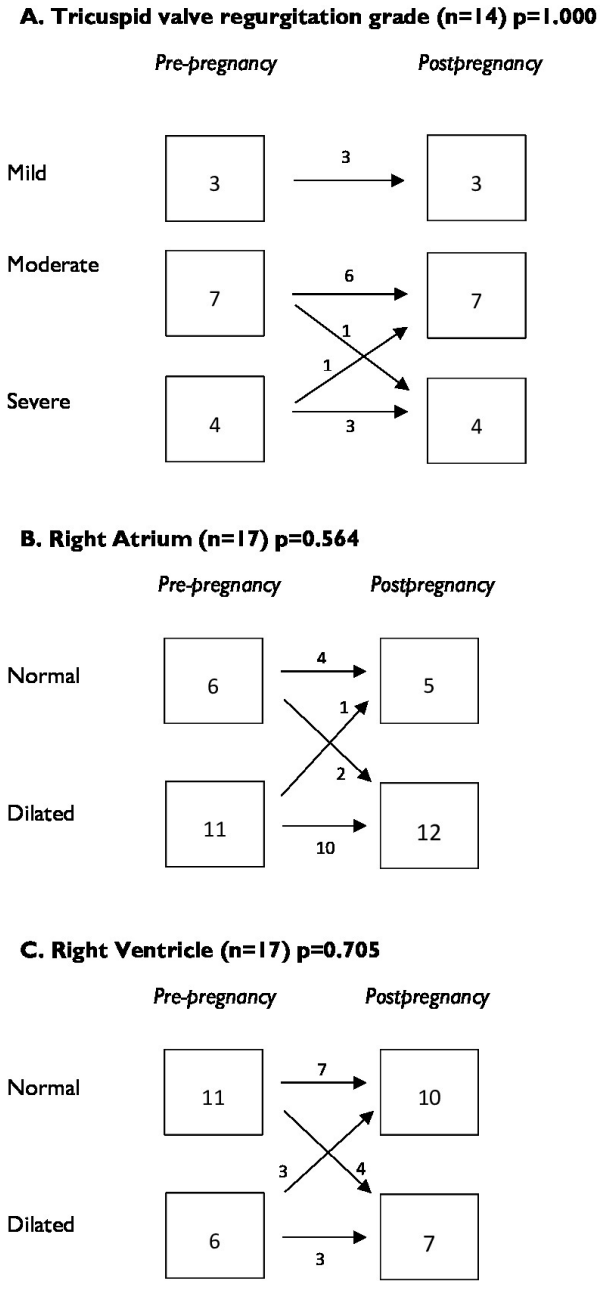

Figure 1 Serial echocardiographic data prepregnancy and postpregnancy. (A) Serial echocardiographic data prepregnancy and postpregnancy in 14 cases for tricuspid valve regurgitation grade. (B) Serial echocardiographic data prepregnancy and postpregnancy in 17 cases for right atrial dimension. (C) Serial echocardiographic data prepregnancy and postpregnancy in 17 cases for right ventricular dimensions.

5.7%–10.5%),[8] and antenatal visits in a secondary centre are recommended. Our study shows that problems are pronounced in those who had previous evidence of heart failure. Therefore, mWHO class II is indeed appropriate for Ebstein's anomaly, however, special care should be taken for women with signs of heart failure, who should be treated as mWHO III. In those cases, antenatal visits as well as the delivery should take place in a tertiary centre. Women who have mechanical tricuspid prosthetic valves

are another special subgroup of whom a high degree of caution is required, mainly because of the problems inherent in anticoagulant control.

Risk factors for MACE

Signs of heart failure were identified as the only risk factor for MACE during pregnancy. One other study determined individual predictors of poor pregnancy outcomes in women with Ebstein's anomaly.[13] In this American study, based on data from the National Inpatient Sample, anomalous atrioventricular excitation was independently associated with MACE. Patients with Ebstein's anomaly are predisposed to arrhythmias, especially Wolff-Parkinson-White syndrome (WPW).[6 21] In our study, two out of three cases of arrhythmia (one with atrial tachycardia in WPW, one with recurrent supraventricular tachycardia) during pregnancy were in women with heart failure during pregnancy, which suggests an association between the two. No atrial fibrillation or atrial flutter was observed.

Influence of pregnancy on cardiac function

Cardiac deterioration due to pregnancy is a main concern in women with CHD. For example, a previous study in women with transposition of the great arteries with Mustard repair described a deterioration in cardiac function and aortic valve-regurgitation in a subset of patients.[22] Therefore, reliable data on the impact of pregnancy on cardiac function is important for women with Ebstein's anomaly. In our study, no differences in right atrial and right ventricular dimensions were found. Additionally, no deterioration in tricuspid regurgitation was observed. One other study investigated prepregnancy and postpregnancy data in 21 women with Ebstein's anomaly and also found no clear change in tricuspid valve regurgitation.[12]

Mode of delivery

In almost half of the women a caesarean section was performed. In our previous report, we found that caesarean delivery was associated with a higher risk of maternal death, postpartum heart failure and an adverse fetal outcome.[23] It is also associated with complications in a next pregnancy. Cardiac indications for caesarean section are onset of labour while taking oral anticoagulation, severe heart failure, severe pulmonary hypertension or aggressive aortic pathology[8] and in women without these indications or an obstetric indication, a vaginal delivery should be advised and attempted. The ESC guidelines and many supporting studies advise vaginal delivery for women with heart disease.[8 23] However, a higher-than-expected number of caesarean sections are still being performed for women with heart disease.[23] This suggests that the advice for a vaginal delivery is not being followed in real-life practice and the reasons for this need to be investigated.

Perinatal outcomes

The preterm delivery rate was 25%, which is higher than the global average[23] and higher than observed in the rest of the ROPAC cohort (15.6%). Maternal CHD is associated with prematurity and low birth weight.[24–26] Despite genetic and epigenetic causes that likely play a role in the pathophysiological mechanism of preterm delivery in women with CHD,[27] almost half of all the premature births in our registry were medically indicated. Unfortunately, we cannot distinguish between cardiac or obstetric indications for induction based on the ROPAC data, but perhaps caution of the physician for both mother and child could have contributed to the high rate of medically indicated premature deliveries.

We found that CHD occurred in nearly 5% of pregnancies, including one infant with hypertrophic cardiomyopathy who died 2 weeks after birth. The total CHD birth prevalence reached a stable estimate of 0.8% in the last 15 years.[28] The risk of inheriting cardiac defects varies between 3% and 50% depending on the type of parental CHD.[29] Previous data also showed a higher risk (6%) of CHD in the children of mothers with Ebstein's anomaly compared with the general population.[30] This emphasises the need for prepregnancy counselling and the advice for fetal echocardiography in all women with Ebstein's anomaly.

Study limitations

The ROPAC registry reflects a variety of countries and the results are therefore highly generalisable. However, the heterogeneity of Ebstein's anomaly must be taken into account when interpreting the results of our study. Selection bias is not unthinkable, as we cannot guarantee that all consecutive patients from centres were included, although this was clearly stated as goal before and during the study. The study is registry based, meaning that some disease-specific data are limited or not available. Entering echocardiographic data were optional for ROPAC, therefore, serial echocardiographic data prepregnancy and postpregnancy were available only in a selection of women. Also, it is likely that the echocardiographs prepregnancy and postpregnancy of every woman are performed by different sonographers and thereby variation in sonographer performance should be keep in mind. Unfortunately, detailed data on the type of supraventricular arrhythmias (other than atrial fibrillation or atrial flutter) before pregnancy are not available, such as WPW.

CONCLUSIONS

Although mortality was zero, in 10% of the pregnant women with Ebstein's anomaly an MACE occurred, most frequently heart failure or arrhythmia. Importantly, signs of heart failure were a strong predictor for MACE. Therefore, it seems reasonable to categorise women with Ebstein's anomaly as mWHO risk class II, however, when additional risk factors such as signs of heart failure are present, a categorisation of mWHO risk class III is more appropriate. Preconception counselling is

crucial, so that women can be reassured about the risk of maternal mortality. However, they must be made aware of the risks of maternal morbidity, preterm delivery, recurrence of CHD and of the need for careful monitoring during pregnancy and of delivery.

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