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% with structural cardiac defects or diminished cardiac function who are at increased risk of developing heart failure and/or arrhythmias during pregnancy. To be able to accurately counsel women with Ebstein’s anomaly, 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. It accounts for ~1% of all congenital cardiac defects, with an incidence of 1 per 200 000 live births. 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,\textsuperscript{7} which makes it challenging to accurately counsel these women. The European Society of Cardiology (ESC) guidelines\textsuperscript{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>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>Ebstein’s anomaly (n=81)</td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>29.7 (6.1)</td>
</tr>
<tr>
<td>LMIC</td>
<td>17 (21.0)</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>38 (46.9)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1 (1.2)</td>
</tr>
</tbody>
</table>

**Underlying cardiac pathological features**

- **Associated cardiac defects**
  - Atrial septal defect: 12 (14.8) vs 278 (5.1), <0.001
  - Bicuspid aortic valve: 3 (3.7) vs 538 (9.5), 0.076
  - Persistent ductus arteriosus: 2 (2.5) vs 147 (2.6), 0.942
  - Ventricular septal defect: 1 (1.2) vs 715 (12.6), 0.002
- **Prior interventions/surgery**
  - 39 (48.1) vs 3121 (55.2), 0.195
- **Tricuspid valve intervention**
  - 15 (18.5) vs 33 (0.6), <0.001

**Prepregnancy cardiac status**

- **Chronic hypertension**
  - 7 (8.6) vs 373 (6.6), 0.491
- **Diabetes mellitus**
  - 2 (2.5) vs 88 (1.6), 0.521
- **History of heart failure**
  - 5 (6.2) vs 591 (10.4), 0.208
- **Cyanosis**
  - 4 (4.9) vs 59 (1.0), <0.001
- **Atrial fibrillation/flutter**
  - 3 (3.7) vs 103 (1.8), 0.211
- **NYHA class**
  - I: 55 (67.9) vs 4152 (73.4), 0.268
  - II: 21 (25.9) vs 1170 (20.7), 0.248
  - III: 1 (1.2) vs 175 (3.1), 0.335
  - IV: 0 (0) vs 28 (0.5), 0.526
- **Unknown**
  - 4 (4.9) vs 133 (2.4), 0.130

**Prepregnancy cardiac medication**

- **Antiplatelet therapy**
  - 4 (4.9) vs 230 (4.1), 0.693
- **Vitamin K antagonists**
  - 3 (3.7) vs 393 (6.9), 0.253
- **LMWH**
  - 3 (3.7) vs 26 (0.5), <0.001
- **DOAC**
  - 0 (0) vs 3 (0.1), 0.836
- **Beta blockers**
  - 4 (4.9) vs 559 (9.9), 0.138
- **Antiarrhythmic drugs**
  - 2 (2.5) vs 98 (1.7), 0.615
- **Diuretics**
  - 1 (1.2) vs 216 (3.8), 0.226
- **Angiotensin receptor blocker**
  - 1 (1.2) vs 24 (0.4), 0.271
- **ACE inhibitors**
  - 0 (0) vs 157 (2.8), 0.128
- **Aldosterone antagonists**
  - 0 (0) vs 32 (0.6), 0.497
- **Calcium channel blocker**
  - 0 (0) vs 50 (0.9), 0.395
- **Nitrates**
  - 0 (0) vs 9 (0.2), 0.719
- **Statins**
  - 0 (0) vs 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.
January 2018 and were diagnosed with Ebstein’s anomaly included in the ROPAC between January 2007 and 2018. It was embedded in the EURObservational Research Programme of the ESC. Pregnant women who were followed up were 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.

**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. 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.

**Statistical analysis**

Categorical data are presented as frequencies (numbers) and percentages and were compared using χ² 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 Ebstein’s anomaly.
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
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 3 Univariable logistic regression analyses in 81 women with Ebstein’s anomaly

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

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.
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

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Table 4 Obstetric, fetal and neonatal outcomes

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

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.
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. 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%). 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. 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. 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 5.7%–10.5%), 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

### Table 5  Echocardiographic data

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

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

### Figure 1  Serial echocardiographic data pre-pregnancy and post-pregnancy.

(A) Serial echocardiographic data pre-pregnancy and post-pregnancy in 14 cases for tricuspid valve regurgitation grade. (B) Serial echocardiographic data pre-pregnancy and post-pregnancy in 17 cases for right atrial dimension. (C) Serial echocardiographic data pre-pregnancy and post-pregnancy in 17 cases for right ventricular dimensions.
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. In this American study, based on data from the National Inpatient Sample, anomalous atroventricular excitation was independently associated with MACE. Patients with Ebstein’s anomaly are predisposed to arrhythmias, especially Wolff-Parkinson-White syndrome (WPW). 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. 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.

**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. 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 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.

However, a higher-than-expected number of caesarean sections are still being performed for women with heart disease. 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 and higher than observed in the rest of the ROPAC cohort (15.6%). Maternal CHD is associated with prematurity and low birth weight. Despite genetic and epigenetic causes that likely play a role in the pathophysiological mechanism of preterm delivery in women with CHD, 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. The risk of inheriting cardiac defects varies between 3% and 50% depending on the type of parental CHD. Previous data also showed a higher risk (6%) of CHD in the children of mothers with Ebstein’s anomaly compared with the general population. 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 pregnancy were available only in a selection of women. Also, it is likely that the echocardiographs prepregnancy and post-pregnancy 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
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