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CLINICAL RESEARCH
Congenital heart disease

Maternal and neonatal complications in women with congenital heart disease: a nationwide analysis

Astrid Elisabeth Lammers [1,2]*, Gerhard-Paul Diller[1,3], Rieke Lober [1], Mareike Möllers [4], Renate Schmidt[1], Robert M. Radke [1], Fernando De-Torres-Alba[1], Gerrit Kaleschke [1], Ursula Marschall[5], Ulrike M. Bauer[3,6], Joachim Gerß [7], Dominic Enders [7], and Helmut Baumgartner [1,3]

[1]Department of Cardiology III, Adult Congenital and Valvular Heart Disease, University Hospital Muenster, Albert-Schweitzer-Campus 1, 48149 Münster, Germany; [2]Department of Paediatric Cardiology, University Hospital Münster, Albert-Schweitzer-Campus 1, 48149 Münster, Germany; [3]National Register for Congenital Heart Disease, Berlin, Germany; [4]Department of Gynecology and Obstetrics, University Hospital Münster, Albert-Schweitzer-Campus 1, 48149 Münster, Germany; [5]Department of Medicine and Health Services Research, BARMER Health Insurance, Wuppertal, Germany; [6]DZHK (Deutsches Zentrum für Herz-Kreislauf-Forschung), Berlin, Germany; and [7]Department for Biostatistics, University Hospital Muenster, Albert-Schweitzer-Campus 1, 48149 Münster, Germany

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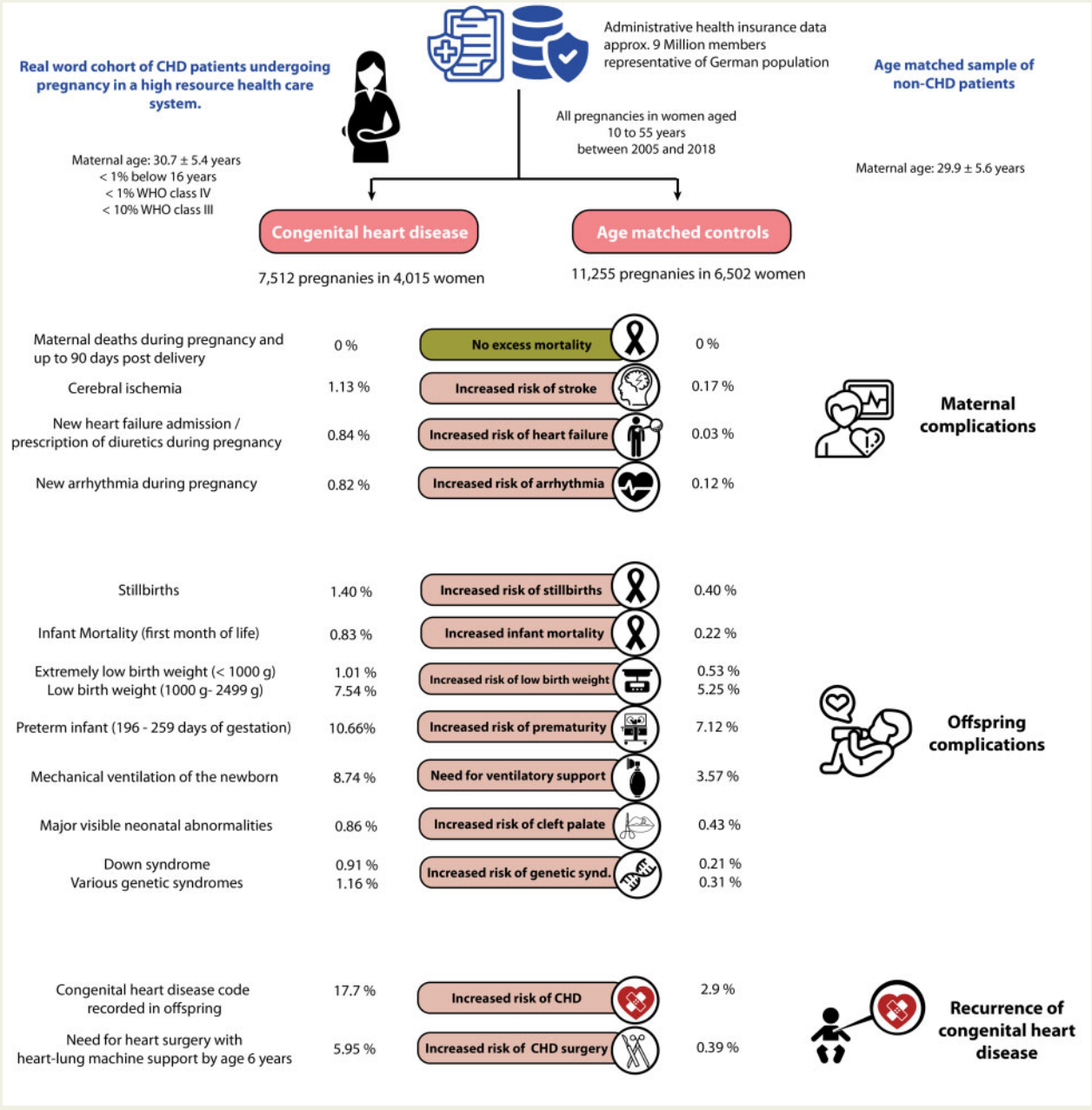
Aims The aim of this study was to provide population-based data on maternal and neonatal complications and outcome in the pregnancies of women with congenital heart disease (CHD).

Methods and results Based on administrative data from one of the largest German Health Insurance Companies (BARMER GEK, ~9 million members representative for Germany), all pregnancies in women with CHD between 2005 and 2018 were analysed. In addition, an age-matched non-CHD control group was included for comparison and the association between adult CHD (ACHD) and maternal or neonatal outcomes investigated. Overall, 7512 pregnancies occurred in 4015 women with CHD. The matched non-CHD control group included 6502 women with 11 225 pregnancies. Caesarean deliveries were more common in CHD patients (40.5% vs. 31.5% in the control group; $P < 0.001$). There was no excess mortality. Although the maternal complication rate was low in absolute terms, women with CHD had a significantly higher rate of stroke, heart failure and cardiac arrhythmias during pregnancy ($P < 0.001$ for all). Neonatal mortality was low but also significantly higher in the ACHD group (0.83% vs. 0.22%; $P = 0.001$) and neonates to CHD mothers had low/extremely low birth weight or extreme immaturity (<0.001) or required resuscitation and mechanical ventilation more often compared to non-CHD offspring ($P < 0.001$ for both). On multivariate logistic regression maternal defect complexity, arterial hypertension, heart failure, prior fertility treatment, and anticoagulation with vitamin K antagonists emerged as significant predictors of adverse neonatal outcome ($P < 0.05$ for all). Recurrence of CHD was 6.1 times higher in infants to ACHD mothers compared to controls ($P < 0.0001$).

Conclusions This population-based study illustrates a reassuringly low maternal mortality rate in a highly developed healthcare system. Nevertheless, maternal morbidity and neonatal morbidity/mortality were significantly increased in women with ACHD and their offspring compared to non-ACHD controls highlighting the need of specialized care and pre-pregnancy counselling.

* Corresponding author. Tel: +49 251 83 46110, Fax: +49 251 83 46109, Email: astrid.lammers@ukmuenster.de

Graphical Abstract



Overview over the main findings of the study. The results illustrate significantly increased risk of maternal and neonatal complications as well as a significantly increased risk of recurrence of congenital heart disease in the children of congenital heart disease mothers. For details, please see Tables 1–4.

Keywords Pregnancy • Adult congenital heart disease • Congenital heart disease • Recurrence rate • Maternal morbidity • Neonatal outcome

Introduction

During the last decades, we have witnessed an increasing number of adolescents with congenital heart disease (CHD) entering adulthood and now reaching reproductive age.[1–3] Particularly CHD women with defects of moderate and severe complexity, aiming to start a family, are increasingly presenting to CHD centres and seek advice on potential maternal or neonatal risks associated with pregnancy.

This is in part due to the fact that in Western countries CHD has now become one of the leading causes of maternal mortality.[4–7] Commendable international efforts, including large-scale multicentre registries, have provided important information regarding maternal risk and have led to the development of risk scores for quantifying especially maternal complication rates.[8–11] In addition, major tertiary centres have contributed their extensive experience in providing specialized care for pregnant CHD patients to the literature.[6,11,12] However, most of these reports are prone to selection bias and very limited data are still available on a population-based level.[13] In addition, the risks to mother and child cannot be seen in isolation of the healthcare system involved. In resource-rich, contemporary healthcare systems, it is expected that more selected CHD women with lower-risk profiles will proceed to pregnancy and this should alter outcomes across the spectrum of CHD. In largely decentralized health systems as in Germany or the USA, CHD women of reproductive age will be jointly managed by paediatric cardiologists, adult cardiologists, gynaecologists, general practitioners, and regional and supra-regional adult CHD (ACHD) centres. As a consequence, risk profiles described in the literature originating from heterogeneous geographies (including developing countries) or highly centralized health systems (such as the English NHS) will not necessarily reflect the outcomes and risk factors observed across the spectrum of disease in devolved community-based and decentralized settings with established ACHD accreditation and large ACHD programmes.[14–16]

Using administrative data from one of Germany's largest health insurance companies, covering over 9 million members representative for the country's population and a time period of more than a decade, we aimed to provide contemporary population-based data on maternal and neonatal complications and outcome, quantify maternal and neonatal risk, and investigate potential predictors of maternal or neonatal outcome specifically in women linked to the healthcare system.

Methods

This was a retrospective analysis based on administrative data from the BARMER GEK German Health Insurance Company. The BARMER insures ~9 million members (i.e. around 1/9 of the German population of 83 million in 2018). All out- and inpatient procedures and diagnoses occurring between 2005 and 2018 in the insured population are routinely coded in the BARMER database for reimbursement purposes and were available in an anonymized manner for our analysis. The dataset is complete, and its integrity and representativeness for Germany's population have been demonstrated.[17] To compare pregnancy outcomes in ACHD patients with women without CHD, an age-matched cohort of women under observation was also included. Patients with CHD were identified based on the German modification of ICD-10 codes (Q20–26; for detailed codes and additional information on classification of disease complexity, see Supplementary material online, *Appendix Table SA*). We included all ACHD women who were between 10 and 55 years old during the study period. Women with an isolated atrial septal defect were excluded as this defect shares an ICD code with patent foramen ovale in the German ICD-10 system. Pregnancies were identified based on a panel of pregnancy-specific ICD and inpatient procedural codes [German OPS (operational and procedural system)] as well as reimbursement codes used exclusively by office-based physicians. With a similar system of codes (see Supplementary material online, *Appendix* for details), miscarriages, abortions, complications, and the mode of delivery were recorded. Neonates were linked to the mother via a joint identification number and the frequency of neonatal complications, resuscitation, mortality, and recurrence of CHD was evaluated. To validate the recurrence rates of CHD and account for possible forward carrying of a congenital code from the mother to the neonate, the rate of cardiac specific operations/interventions in newborns were also assessed. The study was approved by the relevant Ethics committee as part of the overarching research project using anonymized administrative health insurance data (OptAHF project).

Patient and public involvement

No particular patient involvement was sought for this specific research question. However, this project forms part of a larger group of CHD analyses and patients as well as the broader public are continuously involved in choosing and prioritizing projects relevant to CHD within the framework of the National Register for Congenital Heart Disease.

Statistical analysis

Categorical variables are presented as number and percentages, while continuous variables are shown as mean ± standard deviation or median and interquartile ranges, respectively. Differences between groups are assessed by Man–Whitney *U* test or χ^2 tests depending on data type. The association between maternal baseline characteristics and neonatal adverse outcome was evaluated using uni- and multivariable mixed effect logistic regression analyses and odds rations (OR) are presented. The regression models include a random intercept to account for the clustering of the data, i.e. mothers contributing multiple births to the analysis. Model selection was carried out with backward stepwise regression methods based on the Akaike information criterion. A two-sided *P*-value of <0.05 was considered significant throughout the study.

Results

Overall, 25 585 women with ACHD between the age of 10 and 55—included in the database during the study period—formed the basis of the analysis. Of these, 4015 had at least one pregnancy between 2005 and 2018. In addition, an age-matched cohort of 50 813 women without CHD was identified and served as a control group. In this non-CHD group, 6502 women became pregnant at least once during the observation period. Overall, 7512 pregnancies were observed in the ACHD group and 11 225 pregnancies in the non-CHD group. Of the 7512 pregnancies in the ACHD group, 4663 (62.1%) led to delivery, 2592 (34.5%) to miscarriage/abortion and in 257 cases (3.4%) the outcome could not be determined (e.g. because the health insurance contract was terminated during pregnancy). The majority of non-completed pregnancies were due to miscarriages/spontaneous abortions ($n = 1879$; 72.5%), while 713 (27.5%) were terminated medically. The rate of miscarriage/abortion was slightly but significantly higher in the ACHD cohort compared to the non-CHD cohort (34.5% vs. 31.0%; $P < 0.001$). Age at pregnancy in the congenital cohort was 30.5 ± 6.5 years, with 13 (0.17%) of women being ≤14 years, 53 (0.71%) 15–16 years of age and 146 (1.96%) 17–18 years of age at the onset of pregnancy.

The vast majority of ACHD deliveries occurred in hospital ($n = 4642$; 99.5%), which was similar to the non-CHD control group ($n = 6623$ of total 6686 deliveries, 99.1%).

Table 1 Overview over type of delivery by congenital heart disease complexity compared to age-matched non-congenital heart disease women

Patient group	N	Maternal age	Type of delivery			Stillbirth (%)	Mean pregnancy duration (weeks)
			Caesarean (%)	Assisted vaginal (%)	Vaginal (%)		
Non-CHD patients	6623	29.9 ± 5.6	31.5	1.6	67.0	0.4	38.9
ACHD patients	4642	30.7 ± 5.4	40.5	1.7	57.8	1.4	38.6
Simple complexity	3157	30.5 ± 5.5	39.3	2.0	58.7	0.7	38.7
Medium complexity	956	30.9 ± 5.3	42.1	0.9	57.0	2.2	38.3
High complexity	529	31.3 ± 5.0	44.8	1.7	53.5	4.2	38.0
UVH	269	31.9 ± 4.7	40.5	1.5	58.0	8.2	37.5
Eisenmenger	21	28.3 ± 5.5	42.9	4.8	52.4	0.0	38.4
TGA	196	31.1 ± 5.3	49.5	1.0	49.5	0.0	38.8
Other complex CHD	43	30.0 ± 4.8	51.2	4.7	44.2	0.0	38.4
Heart failure patients	81	30.6 ± 5.7	64.2	3.7	1.2	1.2	37.2
Hypertension patients	510	31.3 ± 5.2	5.16	1.8	46.7	1.0	38.1
Patients with diabetes	35	31.5 ± 6.5	71.4%	5.7	22.9	2.9	37.5

ACHD, adult congenital heart disease; CHD, congenital heart disease; TGA, transposition of the great arteries; UVH, univentricular heart.

The pregnancy rate per patient under follow-up was slightly higher in the ACHD cohort compared to the non-CHD cohort (0.29 vs. 0.22 pregnancies per patient, $P < 0.001$). Within the ACHD group, the highest frequency of pregnancies per patient was observed in patients with complex heart disease (0.46 pregnancies per patient), compared to 0.32 and 0.27 in the moderate complexity and simple complexity group ($P < 0.001$). Considering various maternal diagnoses, the lowest pregnancy rate overall was observed in patients with Eisenmenger syndrome (13%). Overall, 21 successful deliveries were recorded for 14 Eisenmenger mothers (maternal age 28.5 ± 5.6 years) at a median of 38.4 weeks of gestation. Characterizing these patients further showed that all but two Eisenmenger patients had an isolated ventricular septal defect as an underlying lesion and none of the patients were treated with specific pulmonary hypertension drugs before pregnancy. In the complex disease group, the rate of complications leading to abortion was lowest in the transposition of the great arteries group (17.8% loss of pregnancy due to complications), compared to 32.8% in women with univentricular heart, 22.9% in Eisenmenger syndrome, and 20.0% in complex uncorrected CHD, respectively. *Table 1* illustrates mode and outcome of delivery by complexity group, showing that ACHD patients had a higher proportion of caesarean deliveries (40.5% vs. 31.5% in the non-congenital group, $P < 0.001$). Caesarean section rate increased with ACHD disease complexity group of the mother (caesarean in simple/moderate and complex heart defect groups: 39.3/42.1/44.8%, respectively; $P = 0.031$).

No maternal death was observed during pregnancy and up to 90 days post-delivery in the ACHD group and one woman died in the non-ACHD group. Maternal complications tended to be higher in ACHD patients compared to the non-CHD control group. Statistical significance for the difference was only reached for cerebral ischaemia (see *Table 2* and *Graphical Abstract*). The stroke rate was 9.8 times higher for patients with moderate defect complexity and 6.6 times higher for those with high complexity compared to non-CHD controls ($P < 0.001$ for both). A co-existent atrial septal defect (ICD-10 code Q21.1), a history of arrhythmias, and anticoagulation with vitamin K antagonists or antithrombotic drug treatment (probably reflecting risk factors and prosthetic valves) were significantly related to the risk of stroke in our population ($P > 0.05$ for all; for details see Supplementary material online, *Table SG*). To further assess maternal morbidity during pregnancy, the incidence of heart failure admissions during pregnancy or new prescription of loop diuretics during pregnancy was assessed (Supplementary material online, *Appendix Table SC*). Patients who experienced similar episodes in the year preceding pregnancy were excluded. Although low in absolute terms, compared to non-ACHD pregnancies, the rate of heart failure admission/new prescription of diuretics was significantly higher in ACHD patients during pregnancy (0.84% vs. 0.03%, $P < 0.001$). Similarly, assessing only hospitalization, ACHD patients had a significantly higher rate of heart failure-related admissions compared to non-ACHD women (0.69% vs. 0.02%, $P < 0.001$). The complication rates during pregnancy increased in line with increasing ACHD complexity (simple/moderate and complex heart defect groups: 0.48%, 0.94% and 2.84%, respectively). Similarly, pregnant ACHD patients had a higher rate of arrhythmia-related complications during pregnancy (0.82% vs. 0.12%, $P < 0.001$). Within the ACHD group, patients with moderate and complex heart defects had higher arrhythmia rates (1.46% and 1.32%, respectively) compared to simple defect patients (0.54%).

Overall, the percentage of stillbirths was significantly higher in ACHD patients compared to the non-congenital cohort (1.4% vs. 0.4%, $P < 0.001$). Patients with simple defects had a stillbirth rate of 0.7%, those with moderate complexity defects of 2.2% and ACHD patients with severe complexity defects of 4.2%. Among those with high complexity, patients with univentricular hearts exhibited a stillbirth rate of 8.2% ($P < 0.001$ vs. non-congenital controls). Among the live births, the percentage of twins was not significantly different in ACHD compared to non-congenital women (1.66% vs. 1.61%, $P = 0.82$).

Table 2 Overview over maternal complications by complexity group as well as overall, compared to non-congenital heart disease patients

Disease complexity	Simple	Medium	Complex	ACHD	Non-CHD group	*P*-value*
n (% total ACHD)	3157 (68.0%)	956 (20.6%)	529 (11.4%)	4642 (100%)	6.623	
Complication						
Death	0.00%	0.00%	0.00%	0.00%	0.02%	1.00
Stroke	0.82%	1.67%	1.13%	1.03%	0.17%	<0.001
Myocardial infarction	0.03%	0.21%	0.00%	0.06%	0.03%	0.41
Pulmonary embolism	0.06%	0.21%	0.00%	0.09%	0.08%	1.00
CPR	0.00%	0.00%	0.19%	0.02%	0.02%	1.00
Sepsis	1.08%	1.26%	1.51%	1.16%	0.97%	0.35
Eclampsia	0.35%	0.31%	0.00%	0.3%	0.3%	1.00
Severe preeclampsia	2.12%	1.88%	1.7%	2.02%	2.01%	0.95
Maternal bleeding	6.53%	7.32%	7.37%	6.79%	6.28%	0.29
Bleeding requiring transfusion	0.57%	0.52%	0.95%	0.6%	0.56%	0.80

ACHD, adult congenital heart disease; CHD, congenital heart disease; CPR, cardiopulmonary resuscitation. *Comparison between ACHD and non-congenital group.

Table 3 Neonatal immaturity and low birthweight by complexity compared to the non-congenital heart disease control cohort

Disease complexity	ICD/OPS code	Simple	Medium	Complex	ACHD	Non-congenital group	*P*-value*
n (% total ACHD)		2715 (68.4%)	806 (20.3%)	447 (11.3%)	3968 (100%)	5.831	
Extremely low birth weight (<1000 g)	P07.0	0.99%	0.99%	1.12%	1.01%	0.53%	0.007
Low birthweight (1000–2499 g)	P07.1	6.70%	9.18%	9.62%	7.54%	5.25%	<0.001
Extreme prematurity (<196 days gestation)	P07.2	0.99%	0.99%	1.34%	1.03%	0.72%	0.12
Preterm infant (196–259 days gestation)	P07.3	9.80%	13.90%	10.07%	10.66%	7.12%	<0.001
Convulsions of newborn	P90	0.26%	1.12%	0.22%	0.43%	0.15%	0.015
Mechanical ventilation of the neonate	OPS 8-711	6.15%	10.05%	22.15%	8.74%	3.57%	<0.001
Resuscitation	OPS 8-77	0.74%	0.74%	3.58%	1.06%	0.34%	<0.001
ECS	OPS 8-851/852	0.41%	1.24%	12.98%	1.99%	0.05%	<0.001
ECS without concomitant cardiac surgery		0.00%	0.12%	0.22%	0.05%	0.00%	0.09
Intensive care therapy	OPS 8-98	0.11%	0.62%	1.34%	0.35%	0.09%	0.004
Thoracic drain	OPS 8-144	0.22%	0.99%	4.03%	0.81%	0.14%	<0.001
Blood transfusion (erythrocytes)	OPS 8-800.c	1.10%	3.60%	13.20%	2.97%	0.46%	<0.001

ACHD, adult congenital heart disease; ECS, extracorporeal circulatory support. *Comparison between ACHD and non-congenital group.

Overall, in 85.7% of deliveries (3906 ACHD and 5745 non-ACHD deliveries), the neonate could be linked to the mother using the unique identification number provided. In neonates born to ACHD mothers, infant mortality was significantly higher compared to controls. Infant mortality in the first week (first month) of life was 0.5% (0.83%) in neonates to ACHD mothers, compared to 0.19% (0.22%) in neonates from non-ACHD women ($P = 0.004$ and $P < 0.001$, respectively). *Table 3* illustrates that neonates of ACHD mothers had significantly more prematurity, low birth weight, and extremely low birth weight compared to neonates of non-ACHD mothers. Furthermore, these neonates had higher morbidity rates and required more intensive care treatment including mechanical ventilation and mechanical circulatory support.

Comparisons between major visible abnormalities in neonates to ACHD and non-ACHD mothers are presented in *Table 4*. This illustrates that children to ACHD mothers had a two-fold increase in the rate of lip/palate cleft and an approximately four-fold increase in the risk of genetic syndromes compared to newborns of non-ACHD mothers.

Predictors of neonatal outcome, chromosomal anomalies, and visible abnormalities

To assess risk factors for neonatal outcome, logistic regression analyses were performed correlating various demographic and pre-pregnancy parameters to neonatal outcome. A primary composite endpoint of death, neonatal seizures, need for thoracic drainage, mechanical ventilation, resuscitation, transfusion, intensive care therapy, or mechanical circulatory support (detailed ICD/OPS codes

Table 4 Major visible neonatal abnormalities

Disease complexity	ICD codes	Simple	Medium	Complex	ACHD	Non-congenital group	*P*-value*
***n* (% total ACHD)**		**2715 (68.4%)**	**806 (20.3%)**	**447 (11.3%)**	**3968 (100%)**	**5.831**	
Major visible neonatal abnormalities							
Anencephaly	Q00.0	0.00%	0.00%	0.00%	0.00%	0.00%	1.00
Lip/palate cleft	Q35, Q36, Q37	0.81%	0.99%	0.89%	0.86%	0.43%	**0.011**
Diaphragmal hernia	Q79.0, Q79.1	0.07%	0.25%	0.22%	0.13%	0.03%	0.13
Encephalocele	Q01	0.00%	0.00%	0.00%	0.00%	0.00%	1.00
Gastroschisis	Q79.3	0.04%	0.00%	0.00%	0.03%	0.05%	0.65
Hypospadia penis	Q54 except Q54.4	0.85%	1.36%	1.12%	0.98%	0.63%	0.10
Exomphalos	Q79.2	0.04%	0.37%	0.22%	0.13%	0.03%	0.13
Spina bifida	Q05	0.04%	0.25%	0.00%	0.08%	0.09%	1.00
Reduction defects upper limb	Q71	0.07%	0.25%	0.00%	0.10%	0.09%	1.00
Reduction defects lower limb	Q72	0.18%	0.25%	0.00%	0.18%	0.15%	0.80
Reduction defect unspecified location	Q73	0.04%	0.00%	0.00%	0.03%	0.05%	0.65
Down syndrome	Q90	0.52%	2.48%	0.45%	0.91%	0.21%	**<0.001**
Various genetic syndromes	Q91–93, Q95–99	0.88%	2.36%	0.67%	1.16%	0.31%	**<0.001**
Any of the above		3.06%	6.07%	2.91%	3.78%	1.85%	**<0.001**

ACHD, adult congenital heart disease. *Comparison between ACHD and non-congenital group.

presented in the online supplement) was employed to this end. On multivariate analysis including various potential risk factors, heart defect complexity, arterial hypertension, treatment with vitamin K antagonists in the year before pregnancy, as well as fertility treatment preceding pregnancy emerged as significant adverse predictors of outcome (*Figure 1*). Further multivariate analyses revealed an association between pre-pregnancy diagnosis of heart failure (OR 2.0, $P = 0.02$), maternal arterial hypertension (OR 1.4, $P = 0.02$), previous vitamin K antagonist treatment (within 1 year before pregnancy, OR 3.2, $P = 0.004$), and prior fertility treatment (within 1 year before pregnancy, OR 1.5, $P = 0.004$) with neonatal immaturity or low birth weight (Supplementary material online, *Table SD*). In addition, maternal age (OR 2.1/10 years, $P < 0.001$) and moderate complexity maternal heart defect (OR 2.26 vs. simple defects, $P < 0.001$) emerged as significant predictors of neonatal chromosomal anomalies or visible abnormalities on multivariate logistic regression analysis (Supplementary material online, *Table SE*).

Neonatal recurrence rate of congenital heart disease

To assess recurrence rates in neonates of mothers with CHD compared to the control population, the percentage of newborn/children with a documented CHD code was quantified. Overall, 17.7% of children to ACHD mothers and 2.9% of children from the non-congenital control group had a congenital heart defect code recorded ($P < 0.001$). To further exclude liberal coding including suspicion of CHD only, we also evaluated the percentage of children requiring cardiac surgery with heart–lung machine (HLM) support. As some cardiac defects are not detected immediately at birth and there may be time delay in coding, we assessed the prevalence of congenital codes within the first month of life, the first year of life, as well as ≤6 years of age. At 1 month of age, 3.18% of children to congenital mothers compared to 0.21% of newborn in the control group had a documented CHD code and required cardiac surgery with HLM ($P < 0.001$). Within the first year (≤6 years) of age, 5.47% (5.95%) of children to ACHD mothers vs. 0.36% (0.39%) of children in the control group required surgery for ACHD ($P < 0.001$ for both). Within the group of liveborn children to congenital mothers, the percentage of children with heart defects requiring cardiac surgery with HLM increased from 1.77% (2.03%) to 9.06% (9.93%) and 21.48% (22.60%) at ≤1 (≤6 years) of age ($P < 0.001$ for both) with increasing cardiac defect complexity of the mother (simple vs. moderate vs. complex defect). As a group the recurrence risk for CHD requiring surgery with HLM was highest in mothers with univentricular hearts (26.5% ≤6 years of age).

Information on the temporal changes in neonatal and maternal morbidity is provided in the Supplementary material online, *Appendix Figures SH–SJ*.

Discussion

Based on a large administrative dataset of women with CHD and pregnancy, the current study supports the notion that maternal death is uncommon in contemporary high-resource healthcare systems providing appropriate management and counselling for women with CHD. In this study including over 7000 ACHD pregnancies, no affected woman died as a result of pregnancy. Although maternal morbidity was in absolute terms also reassuringly low, it was nevertheless increased compared to non-CHD controls and especially neonatal complications including mortality were more frequent. In addition, a relevant proportion of neonates had visible or chromosomal abnormalities, or presented with CHD themselves, thus requiring cardiac surgery within the first years of life. Therefore, the

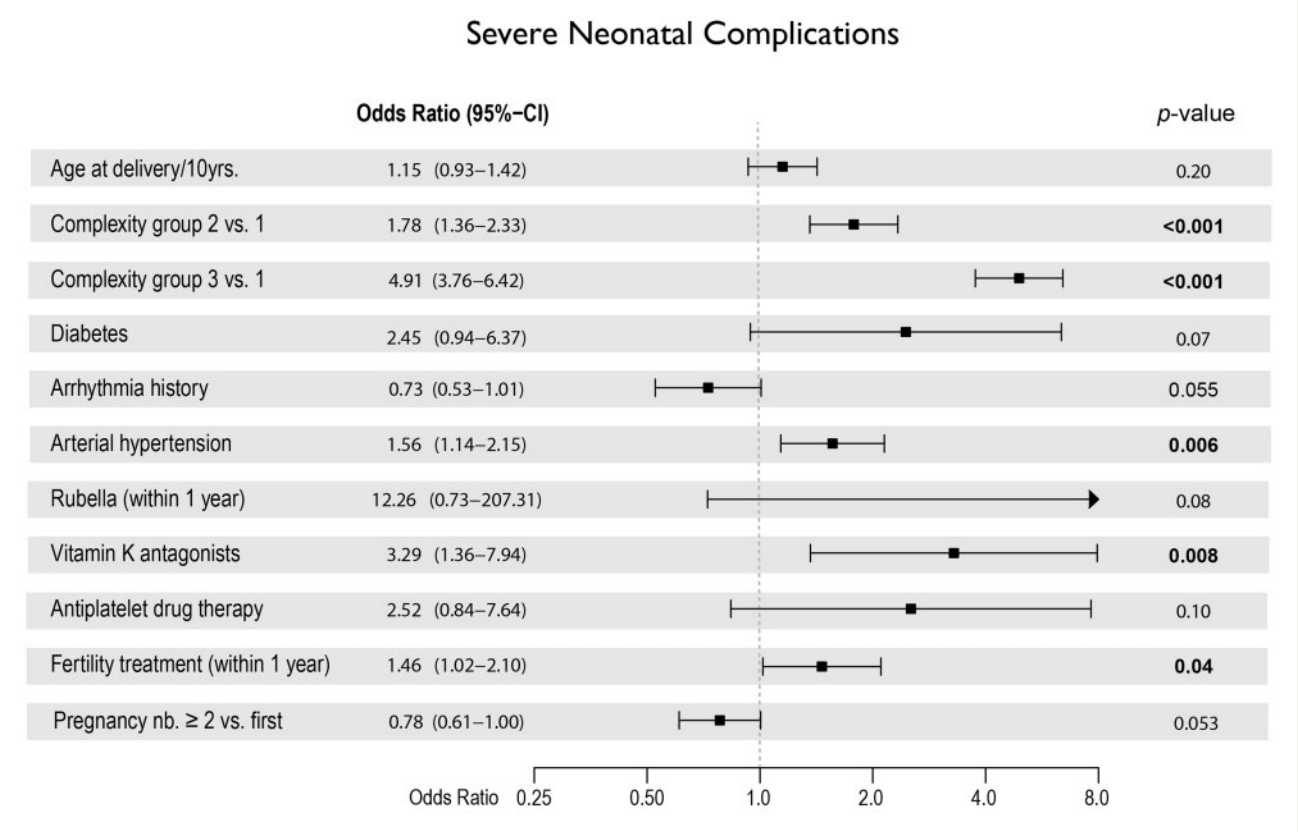


Figure 1 Predictors of severe neonatal complications on multivariate logistic regression analysis. CI, confidence interval.

data suggest that beyond continuing efforts to advise against high-risk pregnancies, the focus of counselling in women with CHD associated with acceptable pregnancy risk should shift to neonatal health issues and complications. The proportion of newborns with congenital heart defects increased in line with disease complexity. The most important multivariable predictors of adverse neonatal outcome were maternal age, complexity of underlying heart defect, need for anticoagulation before pregnancy, and prior fertility treatment.

Large national and international efforts have provided important insights into maternal and neonatal risk factors in CHD. These data include the European Registry on Pregnancy and Heart Disease (ROPAC) reporting a maternal mortality rate of ~1%, mostly due to fatal events in developing countries and associated with valvular lesions.[10] Consistent with our data, CHD patients had relatively low mortality rates and outcome was superior to other forms of structural heart disease in the ROPAC registry. The authors suggested that this may be due to a high proportion of CHD patients who underwent corrective surgery and benefitted from appropriate preconception management.[10] However, considerable maternal morbidity and a high rate of neonatal complications were observed. Specifically investigating pregnancy in women with CHD, Drenthen *et al.*[8] (ZAHARA) and Silversides *et al.*[11] (CARPREG II) developed risk scores of adverse maternal and neonatal outcome. Including 1302 and 1938 pregnancies these studies draw particular attention to important physiological parameters associated with increased risk in this setting. These risk factors include functional class, cyanosis, systolic ventricular dysfunction, aortic dimensions, valvular regurgitation, the presence of mechanical heart valves, as well as pulmonary hypertension. Due to the design of our study, many of these functional parameters were not available for analysis. However, consistent with previous reports, anticoagulation treatment and fertility treatment emerged as risk factor for adverse events in our analysis. Predicting risk to offspring is particularly challenging in the setting of CHD and the external validity of available tools is unfortunately still suboptimal.[18,19] Due to the nature of our study and the lack of more granular data, such as symptoms and imaging parameters of heart size and function, we abstained from developing a risk model for neonatal or maternal outcome. However, on multivariate analysis heart defect complexity, diagnosis of heart failure, arterial hypertension, treatment with vitamin K antagonists before pregnancy, as well as fertility treatment preceding pregnancy emerged as significant adverse predictors of outcome. In addition, higher maternal age and moderate complexity maternal heart defect emerged as significant predictors of neonatal chromosomal anomalies or visible abnormalities. These factors are in line with previous studies and should be considered when gauging risk for the neonate.

It was reassuring to note that real-world risk stratification and management of women with CHD appear to work in the German

healthcare system. Overall, <1% of CHD women undergoing pregnancy in the current study were in the modified WHO Class IV (i.e. group of patients with prohibitively high pregnancy risk).[9,20] Unfortunately, some criteria required to classify patients into the appropriate WHO class were not available from our administrative dataset (e.g. severe ventricular dysfunction, aortic dimensions, or severity of valve disease), however, based on diagnosis we estimate that <10% are in WHO class III. As a consequence, the lack of observed maternal mortality is probably, both, the result of avoidance of very high-risk pregnancies and appropriate pregnancy management in the current sample. Based on the fact that no case of maternal death was also observed in 7512 CHD pregnancies we calculated an upper 95% confidence interval for CHD maternal rate of 6.4 deaths/10 000 pregnancies in this population. The observed maternal mortality of the control group (1/11 225 pregnancies) is also in line with national statistics suggesting a maternal death rate of 0.3–0.5/10 000 pregnancies. Reassuringly, the percentage of teen pregnancies ≤16 years of age was below 1% in our congenital cohort. While maternal morbidity related to heart failure and cardiac arrhythmias was increased in the current study compared to non-CHD women, the overall rates were relatively low with <0.7% of ACHD women requiring hospitalization for heart failure or arrhythmias during pregnancy overall. Even in patients with complex defects the rate of hospitalization for heart failure or cardiac arrhythmias was 2.7% and 1.0%, respectively. Higher morbidity rates in registry reports may be due to selection bias and the weakness of defining heart failure by the shortness of breath during pregnancy not requiring treatment. Such data may overestimate the complication rate and risk of pregnancy.

Surprisingly, the rate of recurrence of CHD in our cohort was found to be higher than previously suspected especially for mothers with complex underlying congenital defects.[21] Especially the recurrence rates of CHD in mothers affected themselves were twice to three times higher compared to the literature. To exclude that this phenomenon was due to liberal coding, we also evaluated the percentage of offspring requiring well documented cardiac procedures. This revealed that ∼6% of children to ACHD mothers had cardiac surgery by the age of 6 years, therefore suggesting that the overall burden of disease is higher. Especially children to CHD mothers with moderate and high complexity lesions had high recurrence rates of 9.9% and 22.6%, respectively. These aspects require further investigation, are, however, consistent with the notion that incidence rates of CHD may increase with improving diagnostic technology[22,23] and should be considered when providing preconception counselling to women and in the planning of pre-natal screening procedures in this high-risk population.

Strength of the current report

To the best of our knowledge, this is the largest cohort of pregnancies in ACHD reported in the literature providing population-based real-world data for maternal and neonatal complications. The current report highlights the low maternal mortality achievable in high-resource health systems and draws attention to the persistent excess morbidity and mortality rate of offspring to ACHD mothers. Using a robust, complete, and representative administrative database we also highlight the significant recurrence rate of CHD in women with ACHD.

Limitations

The underlying database was not designed for research purposes but represents an administrative database. While this offers the advantage of a complete and validated dataset of diagnostic codes and procedures, it lacks granularity in terms of symptoms, imaging, or laboratory results. While maternal anticoagulation was identified as a significant risk factor for severe neonatal complications we cannot comment on the link between mechanical valves mandating anticoagulation and neonatal complications. Further studies such as the ongoing European ROPAC registry are required to clarify this important issue. Therefore, we cannot assess the impact of these important aspects on maternal of neonatal outcome. In addition, as maternal outcome was generally good in the current study, we lack events to establish a robust risk model for maternal adverse outcome based on the BARMER dataset. Furthermore, the favourable maternal outcome should not be misinterpreted to conclude that all ACHD patients have a low pregnancy risk but rather that in a highly developed healthcare system with assumingly appropriate counselling and pregnancy care such good outcomes can be achieved. This requires that patients who have a high or prohibitively high maternal risk are discouraged from pregnancy. The current sample is biased towards those women who, by interaction with the healthcare system, were not advised against pregnancy or decided to pursue pregnancy.

Conclusions

This population-based study of pregnancy in adults with CHD illustrates a reassuringly low maternal rate of mortality and serious complications in a highly developed healthcare system. These results should not be misinterpreted as a carte blanche for pregnancy in all CHD women but a testimony that the appropriate interaction of patients with the healthcare system can lead to low maternal risk and reasonable maternal complication rates. Maternal morbidity and in particular neonatal morbidity and mortality were nevertheless significantly increased in women with ACHD and their offspring compared to non-ACHD controls highlighting the need of specialized care and pre-pregnancy counselling.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Conflict of interest: none declared.

Data availability

Data onfile in the BARMER data warehouse is not publically available due to confidentiality issues.

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