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Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology

Jolien W. Roos-Hesselink[1]*, Titia P.E. Ruys[1], Jörg I. Stein[2], Ulf Thilén[3], Gary D. Webb[4], Koichiro Niwa[5], Harald Kaemmerer[6], Helmut Baumgartner[7], Werner Budts[8], Aldo P. Maggioni[9], Luigi Tavazzi[10], Nasser Taha[11], Mark R. Johnson[12], and Roger Hall[13], on behalf of the ROPAC Investigators

[1]Department of Cardiology, Erasmus Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands; [2]Department of Paediatric Cardiology, Innsbruck Medical University, Innsbruck, Austria; [3]Department of Cardiology, Lund University Hospital, Lund, Sweden; [4]Department of Cardiology, Cincinnati Children's Hospital, Cincinnati, OH, USA; [5]Department of Cardiology, St Luke's International Hospital, Tokyo, Japan; [6]Department of Cardiology, Deutsches Herzcentrum, München, Germany; [7]Adult Congenital and Valvular Heart Center, Department of Cardiology, Münster, Germany; [8]Department of Congenital and Structural Cardiology, University Hospitals, Belgium; [9]ANMCO Research Center, Firenze, Italy; [10]GVM Care&Research—E.S. Health Science Foundation—Maria Cecilia Hospital, Cotignola, Italy; [11]Department of Cardiology, Al-Minya University Hospital, Cairo, Egypt; [12]Academic Department of Obstetrics and Gynaecology, Imperial College School of Medicine, Chelsea and Westminster Hospital, 369 Fulham Road, London SW10 9NH, UK; and [13]Norwich Medical School, University of East Anglia, Norwich, UK

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Aims To describe the outcome of pregnancy in patients with structural or ischaemic heart disease.

Methods and results In 2007, the European Registry on Pregnancy and Heart disease was initiated by the European Society of Cardiology. Consecutive patients with valvular heart disease, congenital heart disease, ischaemic heart disease (IHD), or cardiomyopathy (CMP) presenting with pregnancy were enrolled. Data for the normal population were derived from the literature. Sixty hospitals in 28 countries enrolled 1321 pregnant women between 2007 and 2011. Median maternal age was 30 years (range 16–53). Most patients were in NYHA class I (72%). Congenital heart disease (66%) was most prevalent, followed by valvular heart disease 25%, CMP 7%, and IHD in 2%. Maternal death occurred in 1%, compared with 0.007% in the normal population. Highest maternal mortality was found in patients with CMP. During pregnancy, 338 patients (26%) were hospitalized, 133 for heart failure. Caesarean section was performed in 41%. Foetal mortality occurred in 1.7% and neonatal mortality in 0.6%, both higher than in the normal population. Median duration of pregnancy was 38 weeks (range 24–42) and median birth weight 3010 g (range 300–4850). In centres of developing countries, maternal and foetal mortality was higher than in centres of developed countries (3.9 vs. 0.6%, $P < 0.001$ and 6.5 vs. 0.9% $P < 0.001$)

Conclusion The vast majority of patients can go safely through pregnancy and delivery as long as adequate pre-pregnancy evaluation and specialized high-quality care during pregnancy and delivery are available. Pregnancy outcomes were markedly worse in patients with CMP and in developing countries.

Keywords Pregnancy • Congenital heart disease • Valvular heart disease • Cardiomyopathy • Ischaemic heart disease

Introduction

In women with heart disease, maternal mortality is reported to be much higher than average and the risk appears to be increasing such that in western countries heart disease is the major cause of maternal death.[1–3] However, we do not fully understand what the impact of pregnancy is on the progression of heart disease or how heart disease affects the outcome of pregnancy. The full spectrum of structural heart disease including congenital heart disease (CHD), valvular heart disease (VHD), and

* Corresponding author. Tel: +31 10 70 32 432, Fax: +31 10 70 35 498, Email: j.roos@erasmusmc.nl

cardiomyopathy (CMP), and also ischaemic heart disease (IHD) may be encountered in pregnant women. In developing countries that still struggle with a high prevalence of rheumatic fever, acquired VHD dominates, whereas in developed countries, CHD is the main diagnostic group.[4–8] In addition, over the last few years, the incidence of an acute coronary event during pregnancy has increased, due to older child-bearing age, and changes in lifestyle with more hypertension, smoking, and obesity in women.[9–15] CMP is uncommon during pregnancy, but it is difficult to manage a pregnancy in the context of left ventricular dysfunction or peripartum cardiomyopathy (PPCM) with a high risk of an adverse outcome for both the mother and the baby.[16,17]

In developed countries, optimal care and preconception counselling are available in all centres, although quite often not accessed by the women concerned. In developing countries, only a minority of women with heart disease are assessed and appropriately counselled prior to conception. Not surprisingly, this may have a major adverse influence on pregnancy outcome.

Our understanding of the consequences of heart disease on pregnancy outcome is limited and prevents us from designing relevant randomized controlled trials. To improve our understanding of this complex subject, a registry has been established with the aim of determining patterns of outcome and correlating these with management strategies to determine the areas of danger for both mother and baby and to identify the best forms of treatment. To have any use, such a registry has to be large to include sufficient patients with a wide range of diagnoses. Consequently, the European Registry on Pregnancy and Structural Heart Disease was initiated by the European Society of Cardiology (ESC).

Methods

Study design

In 2007, the European Registry on Pregnancy and Heart Disease was initiated jointly by the ESC Working Group on Grown-up Congenital Heart Disease and on Valvular Heart Disease and embedded in the Euro Heart Survey Programme of the ESC. All national societies of the ESC were informed and invited to contact centres in their countries dealing with pregnancy and heart disease and all members of the two ESC working groups were invited to participate. In addition, other centres from around the world who were interested in the registry were invited to participate. Consecutive patients with structural heart disease or IHD presenting with pregnancy, regardless of age, any concomitant diseases, and type of heart disease could be enrolled, including patients who already participated in trials or other registries. When warranted, ethical approval or Institutional Review Board approval was obtained (e.g. Germany, USA, Canada, and Belgium); however, in many countries, the procedure to obtain ethical approval was waived because of the anonymized and untraceable nature of the data.

The registry started in January 2008. Pregnant patients from 2007 were included retrospectively at that time, as it was believed that the complete data of these patients were available and reliable. From January 2008, patients were included prospectively. Exclusion criteria were non-structural heart disease, for example, arrhythmias occurring in the context of a normal heart.

Information included in this article refers to the patients enrolled up to June 2011.

Data

Baseline data from before pregnancy were recorded, including cardiac diagnosis, New York Heart Association (NYHA) functional class, prior cardiac events, surgery or interventions, rhythm status, co-morbidities , obstetric history, the use of medication, and smoking. Estimation of maternal risk associated with pregnancy was done by classifying the patients according to the modified World Health Organisation (WHO) categories, which integrates the available knowledge from the literature on known risk factors. WHO I is low risk, II medium, and III represents high risk. Importantly, WHO IV means a contraindication for pregnancy.[18] Countries were divided into developed or developing according to the International Monetary Fund Classification (IMF).[19]

The following data relating directly to the pregnancy were collected: age at conception, cardiac complications, obstetric complications, perinatal complications, medication use, pregnancy duration, and mode of delivery. *Cardiac complications* included hospitalization, heart failure requiring treatment, symptomatic documented arrhythmia, endocarditis, cardiac intervention during pregnancy, thrombo-embolic, and haemorrhagic complications, or acute coronary syndrome (ACS). *Obstetric complications* consisted of intra-uterine growth retardation, pregnancy-induced hypertension [PIH, i.e. new-onset hypertension (>140/90 at two occasions) after >20 weeks of gestation], pre-eclampsia (PIH criteria plus >0.3 g proteinuria in the 24 h urine sample), eclampsia (pre-eclampsia with grand mal seizures), premature rupture of membranes (membrane rupture before onset of uterine contractions), premature labour (spontaneous onset of labour <37 weeks of gestation), post-partum haemorrhage (vaginal delivery >500 mL, caesarean delivery >1000 mL or requiring transfusion), and placental abruption. *Perinatal complications* recorded were foetal death (>22 weeks of gestation or >500 g), perinatal death (<30 days post-partum), and CHD in the baby of a mother with CHD. After birth, gender, birth weight, and Apgar score were recorded.

Six months after pregnancy, information on additional events and complications as well as neonatal outcome was collected.

Data for the normal population were obtained from current publications on maternal health and pregnancy.[6,20–22] Mean birth weight for the normal population was calculated as the mean of the reported birth weight from the countries that included patients in the registry. This figure was obtained in the countries that included most patients (together 55%: Egypt, the Netherlands, Germany, the UK, Italy, and Spain).[6,23–27]

Data analysis

Categorical data are presented as frequencies (numbers) and percentages. One-sample Kolmogorov–Smirnov tests and histograms were used to check the normality of continuous data. Normally distributed continuous data are presented as mean values ± 1 SD, whereas non-normal data are presented as medians with the inter-quartile range. Differences in categorical data between independent patient groups were compared by binomial tests or χ^2 tests. If any expected cell count was <5, Fisher's exact tests or, in case of more than two groups, a Monte Carlo method of approximation was used. Mantel–Haenszel linear-by-linear χ^2 tests were used to compare clinical outcomes in the WHO categories, since linear associations were expected. Differences in continuous data between independent patient groups were compared by Student's *t*-tests, or one-way analyses of variance, as appropriate. All statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Unless specified otherwise, *P*-values <0.05 (2-sided test) were considered statistically significant.

Results

The registry enrolled 1321 women with structural heart disease from 60 hospitals in 28 countries (*Figure 1*).

Baseline characteristics

Median maternal age at pregnancy was 30 years (range 16–53). Fifty-six per cent of the women had one or more previous pregnancies. In *Table 1*, baseline characteristics are given, comparing patients included in the registry vs. the normal population and presenting the data for the different subgroups. Most patients were in NYHA class I (70%), while only 0.3% of the patients were in NYHA class IV. Medication was used during pregnancy by 28% of the patients (*Table 1*).

Diagnoses

The diagnoses are shown in more detail in *Figure 2*. Most patients had CHD (872 patients, 66%) and only a minority had IHD (25 patients, 2%). Of the patients with CHD, 579 (66%) had at least one intervention before pregnancy. Valvular interventions were reported in 291 cases, of which 139 were surgical repairs, 69 percutaneous interventions, and 83 surgical valve replacements (55 mechanical valves were implanted in 52 patients). At baseline, patients with IHD were older, used medication, more often suffered from hypertension and diabetes, and were current smokers. More patients with CMP were in NYHA class III (*Table 1*).

Outcome

Maternal mortality

Maternal death occurred in 13 patients (1%), of which seven were due to cardiac reasons, three thrombo-embolic events, and three suffered from sepsis (*Table 2*).

Maternal morbidity

Outcomes are described for the total population included in the registry, compared with the normal population and for the different subgroups in *Table 3*.

During pregnancy, 338 patients (26% of all pregnancies) were hospitalized, most of these patients only once (257 patients). In 203 cases, this was for cardiac reasons, of which 133 (10% of all pregnancies) were for heart failure. There were six patients with ACS during pregnancy; only one of these patients had a history of previous ACS. In six patients, thrombo-embolic events were reported, consisting of one thrombo-embolic occlusion of the anterior tibial artery, one deep venous thrombosis, one ischaemic cerebrovascular accident, and three mechanical valve thromboses. So three of the 52 patients (6%) with at least one mechanical valve suffered from valve thrombosis. Three patients had endocarditis, two of the mitral valve (both patients had a history of endocarditis).

Obstetric events during pregnancy

Hospital admission for obstetric reasons was necessary in 105 patients. PIH occurred most often (*Table 3*). Other reasons for obstetric admission reported were vaginal bleeding (30 patients), pregnancy-induced diabetes (18 patients), and abortion/missed abortion (27 patients).

Delivery

Forty-one per cent of the patients ($n = 533$) underwent caesarean section (CS), compared with 23% in the general population. This was planned in 393 patients (of which 53 ended up with an emergency CS) and was an emergency in 141 patients who had planned vaginal delivery. Assisted vaginal delivery (forceps, vacuum) was performed in 32% of the vaginal deliveries.

The post-partum period

In the first week after pregnancy, 64 patients suffered a complication, consisting of heart failure in 31 and post-partum haemorrhage in 32. In the 6 months after pregnancy, 38 additional complications occurred (25 patients had heart failure). Of the total study population, 162 patients (12%) had at least one period of heart failure during or after pregnancy, while this is rarely, if ever, seen in the general population.

Foetal outcome

Of the 1321 pregnancies, foetal outcome was unknown in 43 pregnancies; 23 twins were born and therefore outcome data were

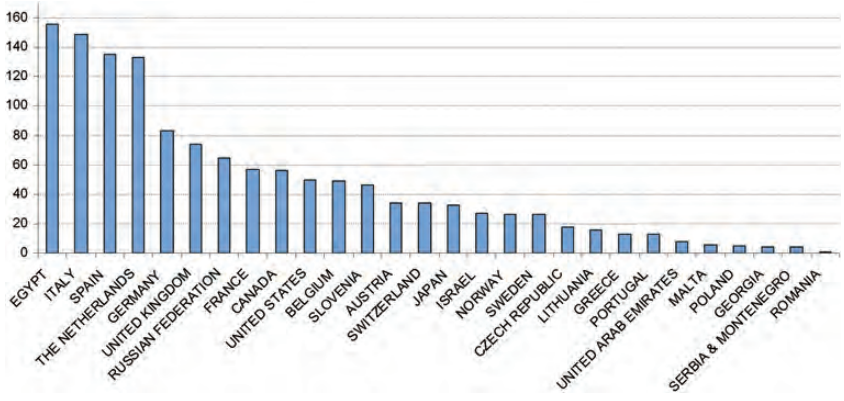

Figure 1 Inclusion per country. Pregnant patients with structural heart disease included between 2007 and 2011.

Table 1 Baseline characteristics for women with structural heart disease, compared with the normal pregnant population and per subgroup

	Normal	Reg (*n* = 1321)	*P*-value	CHD (*n* = 872)	VHD (*n* = 334)	CMP (*n* = 88)	IHD (*n* = 25)	*P*-value
Mean age in years (range)[a]	30 (12–62)	30 (16–53)	0.93	29.6 (16–45)	30.3 (18–53)	30.7 (18–43)	37.3 (24–47)	<0.001
Prior cardiac intervention[b] (%)	<0.5	54	<0.001	66	34	6.8	44	<0.001
Nulliparous (%)[a]	44	50	<0.001	55	38	46	28	<0.001
NYHA class								<0.001
NYHA class 1		70		76	58	56	64	
NYHA class 2		25		21	33	32	28	
NYHA class 3		3.1		1.3	6.8	8.0	0.0	
NYHA class 4		0.3		1.5	7.4	8.0	0.0	
WHO categories								<0.001
WHO 1		18		26	3.9	0.0	0.0	
WHO 2		39		38	47	26	0.0	
WHO 3		38		33	42	56	96	
WHO 4		4.0		2.1	7.4	10.2	4.0	
Hypertension (%)[c]	7	6.7	0.75	6.2	4.5	12.5	36	<0.001
Current smoker (%)[a]	10	3.3	<0.001	3.3	1.8	5.7	12	0.022
Diabetes (%)[d]	1.8	1.6	<0.001	1.1	2.4	2.3	8.0	0.034
Complaints of heart failure (%)	0	11	<0.001	6.7	20	15	0.0	<0.001
Any medication (%)[e]	2	28	<0.001	20	39	55	72	<0.001
Beta-blocker[b] (%)	<0.5	15	<0.001	10	15	44	48	<0.001
ACE-inhibitor[b] (%)	<0.5	3.7	<0.001	1.4	4.5	17	28	<0.001
Anticoagulation[b] (%)	<0.5	10	<0.001	5.7	21	13	28	<0.001

P-value comparison between CHD, VHD, CMP, and IHD, if significant one of the groups is different compared with at least one other group. CHD, congenital heart disease; VHD, valvular heart disease; CMP, cardiomyopathy; IHD, ischaemic heart disease; NYHA, New York Heart Association; WHO, World Health Organisation categories.
Normal data were used from:
[a]EURO-PERISTAT.[20]
[b]Drenthen *et al.*[6]
[c]Cutler *et al.*[21]
[d]Lawrence *et al.*[22]
[e]Hameed *et al.*[7]

available for 1301 babies. Foetal mortality (>22 weeks or 500 g) was observed in 1.7% of pregnancies, of which 62% were intrauterine foetal death without further information, 21% were clearly due to the maternal condition, and 17% were because of structural foetal abnormalities. The cause of neonatal mortality was severe neonatal abnormalities (four), premature birth (two), bronchopneumonia (one), and sudden death (one). CHD was reported in 29 of the 829 (3.5%) children born to women with CHD. Six of them had the same congenital defect as their mother (two ASD, two VSD, and two Marfan syndrome). In addition, two patients with coarctation had a child with a hypoplastic left heart syndrome.

Type of heart disease

Clear differences were found in maternal and foetal outcome by type of heart disease (*Table 3*). Maternal mortality was highest in patients with CMP (2.4%), and also heart failure and ventricular arrhythmias were seen more often in these patients. CS rate was highest in patients with IHD or CMP, while post-partum haemorrhage occurred more often in patients with VHD. Of the women who had post-partum haemorrhage, 58% were receiving oral anticoagulants compared with 9% in the patients without post-partum haemorrhage. Pregnancy duration was shorter and neonatal death rate higher in patients with IHD compared with the other groups.

WHO categories

A strong correlation with cardiac, obstetric, and foetal outcome was found. In particular, maternal hospital admission, heart failure, CS, and post-partum haemorrhage were clearly different between the different WHO categories and also birth weight and pregnancy duration showed clear differences (*Table 4*).

Developed vs. developing countries

Though any between-group comparison is very fragile since the size of the populations was grossly unbalanced, significant differences were found: maternal mortality was 3.9 vs. 0.6%

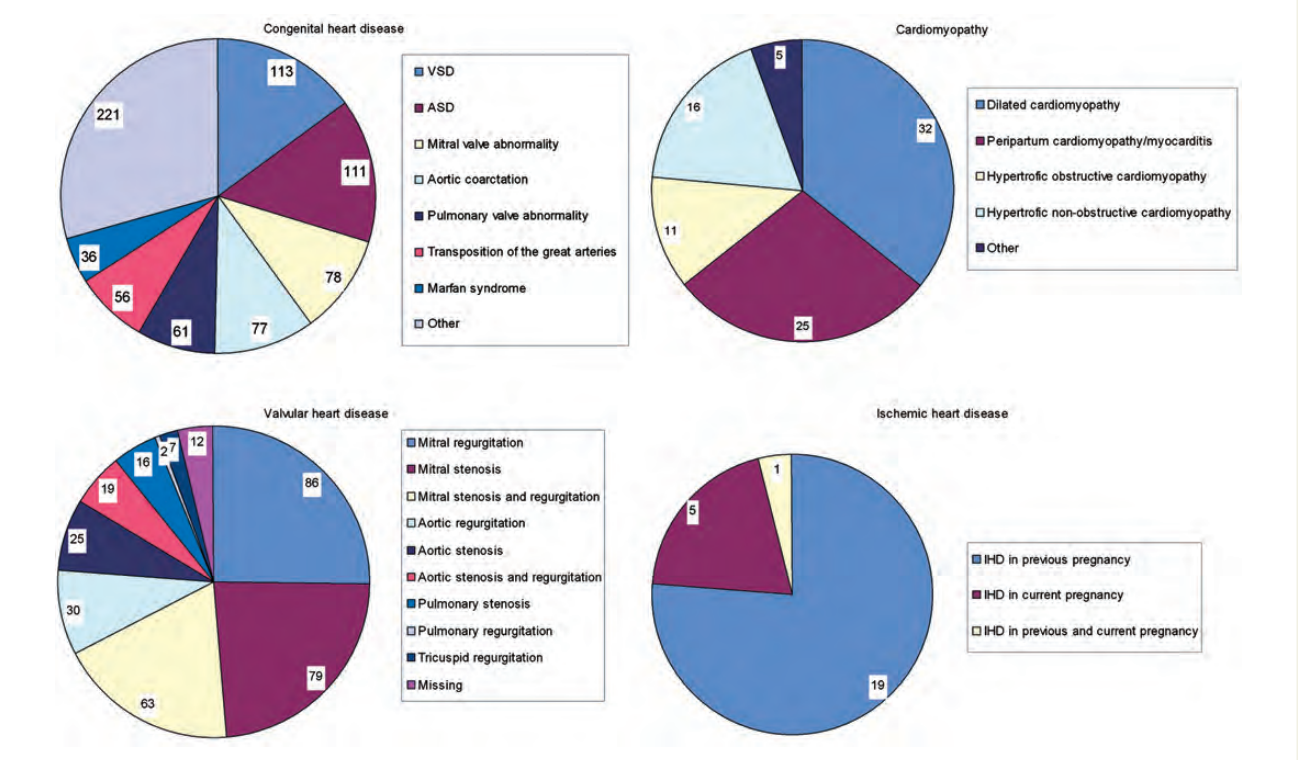

Figure 2 Cardiovascular diagnosis per subgroup.

Table 2 Maternal mortality in women with structural heart disease

Diagnosis	NYHA class	Medication used before pregnancy	Developing/ Developed	Age (years)	When	Reason	Foetal outcome
Mitral stenosis	2	None	Developing	23	35 weeks	Cardiogenic shock	−
Mitral stenosis and regurgitation	1	Antiplatelets	Developed	42	Delivery (CS)	Heart failure and sudden cardiac death	+
Mitral regurgitation	1	None	Developing	21	2 weeks pp	Heart failure	−
Mechanical mitral valve	1	Antiplatelet, Vit K	Developing	29	12 weeks	Severe bronchopneumonia	−
Dilated Cardiomyopathy	1	None	Developed	32	5 weeks pp	Cardiogenic shock	++
Cardiomyopathy after anthracycline	2	LMWH	Developed	27	22 weeks pp	Arterial thrombus of solo kidney	+
Tricuspid regurgitation	1	UFH	Developing	19	1 week pp	Right-sided heart failure	_
Eisenmenger syndrome (ASD, VSD)	2	None	Developed	29	1 week pp	Acute hypoxia after CS	+
Atrial septal defect	1	Vit K	Developing	30	1 week pp	Septic shock	+
Mitral stenosis and regurgitation	1	None	Developing	25	6 weeks pp	Sepsis	−
Pulmonary atresia	2	Diuretics, LMWH, antiplatelets	Developed	36	1 week pp	Anoxic cerebral event, brain death	+
Mitral stenosis and regurgitation	2	Digoxin, Vit K	Developing	29	1 week pp	Brain stem embolization	+
Pulmonary stenosis	1	Atenolol, antiplatelets	Developed	21	Delivery (CS)	Sudden cardiac death during CS	+

LMWH, low-molecular-weight heparin; Vit K, vitamin K antagonist; pp, post-partum; +, foetal survival; ++, twin survival; −, foetal death.

Table 3 Outcome and complications per diagnosis for women with structural heart disease, compared with the normal pregnant population and per subgroup

	Normal	Reg ($n = 1321$)	*P*-value	CHD ($n = 872$)	VHD ($n = 334$)	CMP ($n = 88$)	IHD ($n = 25$)	*P*-value
Maternal mortality (%)[a]	0.007	1.0	<0.001	0.5	2.1	2.4	0.0	0.031
Maternal hospital admission (%)[b]	2	26	<0.001	20	38	33	28	<0.001
Cardiac								
Heart failure (%)[b]	0	12	<0.001	8.0	18	24	8.0	<0.001
Supraventricular arrhythmias (%)[c]	<0.5	0.9	<0.001	0.7	3.0	1.1	0.0	0.025
Ventricular arrhythmias (%)[c]	<0.5	2.0	<0.001	1.6	0.6	11	0.0	<0.001
Obstetrics complications								
Pregnancy-induced hypertension (%)[d]	2.5	2.4	0.93	2.3	2.4	3.4	4.0	0.61
(pre-)Eclampsia (%)[d]	4	3.3	0.23	2.2	3.9	11	4.0	0.001
Caesarean section (%)[a]	23	41	<0.001	38	42	58	60	0.001
Post-partum haemorrhage (%)[e]	5	2.9	<0.001	2.4	5.1	0.0	0.0	0.021
Foetal								
Apgar score <7 (%)[a]	1	10	<0.001	6.5	15	18	24	<0.001
Preterm birth <37 weeks (%)[a]	8	15	<0.001	13	16	30	36	<0.001
Foetal death (%)[a]	0.35	1.7	<0.001	0.5	3.9	4.5	4.0	<0.001
Neonatal death (%)[a]	0.4	0.6	0.27	0.6	0.3	1.1	4.0	0.13
Mean birth weight (g)[f,g,h]	3190	3010	<0.001	3056	2959	2878	2662	0.001
Pregnancy duration (weeks)[a]	40	38	<0.001	38	38	37	36	<0.001

P-value comparison between CHD, VHD, CMP, and IHD, if significant one of the groups is different compared with at least one other group.
Normal data were used from: [a]EURO-PERISTAT,[20] [b]Hutcheon,[23] [c]Hameed *et al.*,[7] [d]Drenthen *et al.*,[6] [e]Oyelese and Ananth.,[24] [f]Ferrazzani *et al.*,[25] [g]Jaddoe *et al.*,[26] [h]Ahrari *et al.*[28]

($P < 0.001$), respectively, and foetal death 6.5 vs. 0.9% ($P < 0.001$) (*Table 5*).

Discussion

In this large contemporary international prospective registry of 1321 patients with structural heart disease or IHD, the incidence of cardiac and neonatal complications was, as expected, found to be much higher than in the normal pregnant population and maternal mortality was more than 100 times higher than in the background population. However, clear distinctions could be made between the different types of heart disease and between the outcomes in developed vs. developing countries. The use of caesarean delivery was higher than in the normal population (41 vs. 23%) with a large variation between countries.

Congenital heart disease

This was the largest subgroup in the registry and its outcomes were relatively good compared with other subgroups. Most of these patients were diagnosed and treated long before pregnancy and nowadays have pre-pregnancy counselling; as a consequence, they are better prepared for pregnancy. The high rate of successful prior cardiac corrective surgery, favourable baseline NYHA class, and low use of medication are all factors which are likely to have contributed to the relatively favourable outcomes. However, even in this group with relatively good outcome CS rates were higher and mean birth weight was lower than in the background population.[27] The recent ESC guidelines advocate spontaneous onset of labour with vaginal delivery for most CHD patients. However, this is not based on hard data and clearly needs further investigations. It is possible that doctor's decision was the main reason for the high number of CSs. Premature birth was reported in 13% of our CHD patients, which is slightly lower than the 16% reported in a previous literature review, but higher than the 8% found in the normal population.[6] The prematurity in this group is likely to have been influenced in part by the decision to perform elective CS but nevertheless, prematurity in any context must be taken seriously as it has the potential to influence neonatal outcome adversely.

Valvular heart disease

Patients with VHD were often not known to have heart disease before pregnancy, and many patients were in NYHA classes II and III before pregnancy. As expected, mitral stenosis and/or regurgitation were the most common lesions (63%), while aortic valve disease occurred in 23%. Patients with VHD had a higher maternal mortality rate than patients with CHD. Heart failure was the most frequently observed maternal complication as was also found earlier by Hameed *et al.*[7] and recorded in 18% of cases. In 38%, hospital admission was necessary and supraventricular arrhythmias were more common than in other patient subgroups. Furthermore, post-partum haemorrhage was encountered more often,

Table 4 Outcome and complications per WHO categories for severity of heart disease

	WHO 1 (*n* = 241)	WHO 2 (*n* = 514)	WHO 3 (*n* = 504)	WHO 4 (*n* = 53)	*P*-value
	241	514	504	53	
Maternal mortality (%)	0.4	0.6	1.5	4.0	0.035
Maternal hospital admission (%)	13	18	36	66	<0.001
Cardiac					
Heart failure (%)	1.2	5.6	19	57	<0.001
Supraventricular arrhythmias (%)	0.4	1.4	1.4	3.8	0.13
Ventricular arrhythmias (%)	1.7	0.8	3.4	1.9	0.068
Obstetrics complications					
Pregnancy-induced hypertension (%)	1.7	3.1	2.4	0.0	0.91
(pre-)Eclampsia (%)	2.1	2.9	3.4	3.8	0.32
Caesarean section (%)	27	37	49	60	<0.001
Post-partum haemorrhage (%)	0.0	1.2	5.2	11	<0.001
Foetal					
Apgar score <7 (%)	4.1	10	11	17	0.001
Preterm birth <37 weeks (%)	8.7	15	17	30	<0.001
Foetal death (%)	0.4	0.6	2.8	5.7	0.001
Neonatal death (%)	1.2	0.4	0.4	0.0	0.24
Birth weight (g)	3109	3074	2925	2735	<0.001
Pregnancy duration (weeks)	39	38	38	37	<0.001

P-value comparison between WHO 1, WHO 2, WHO 3, and WHO 4, if significant one of the groups is different compared with at least one other group.

probably associated with the use of anticoagulant therapy. The way that this high incidence of complications relates to the diagnosis of VHD, the country of residence, and the time they present for the first time (before or during pregnancy) will be investigated in more depth when more patients have been included in the registry.

Cardiomyopathy

In the 88 patients with CMP, the pre-pregnancy NYHA class was even worse than in the patients with VHD. Furthermore, maternal mortality, heart failure, and ventricular arrhythmias occurred more often than in any other group. Currently, the numbers are limited, making it impossible to correct for ejection fraction and type of CMP. As the registry is still ongoing, we expect this analysis will be possible in the future. Until now, no European studies have reported on the prognosis for women with PPCM. In South Africa, case series have demonstrated that mortality rates have slowly improved over time but rates of mortality within 6 months of delivery remain as high as 10%. Our study shows that more attention needs to be paid to this group. A dedicated registry for patients with PPCM will start within the ESC-EURObservational Research Programme.

Ischaemic heart disease

IHD is seldom encountered during pregnancy, although the incidence is increasing, and it was found to be an important contributor to maternal mortality in the British Enquiry 'Saving Mothers Lives'.[9,11,12] In this registry, to date, only 25 patients with IHD have been included. Not surprisingly, this patient group was older at baseline with more risk factors for coronary artery disease. Of the 20 patients who suffered from myocardial infarction prior to pregnancy, only one experienced a new ACS during the current pregnancy. Although these numbers are small, they are encouraging and may positively influence the current practice of cardiologists in counselling these patients. Until now, only case reports on patients becoming pregnant after ACS have been described in the literature. In the five other patients, a 'new' ACS occurred during the current pregnancy; all mothers survived. However, foetal outcome was poor with babies from this group having the greatest proportion of low Apgar scores, preterm deliveries, lowest birth weight, and highest mortality. Whether medication use, smoking, older age, or other factors were the contributors to this unfavourable outcome has to be determined in larger series. Indeed, in some women, the high incidence of preterm deliveries and low birth weight may be the expression of a diffuse vasculopathy causing chronic placental insufficiency.

Developed vs. developing countries

Cultural and social pressures may have a greater influence on the decision to become pregnant in developing countries, meaning that pregnancies occur in a higher risk population than in developed countries. In this study, we found higher maternal mortality and morbidity in developing countries. This is a very complex issue, but if achievable, pre-conception counselling focusing on the severity of the heart disease with a clear statement of the consequences of pregnancy may save lives.

Table 5 Outcome and complications in pregnant patients with heart disease, per IMF Classification of developed vs. developing countries

	Total	Developed ($n = 1136$)	Developing ($n = 185$)	*P*-value
Baseline				
Mean age (range)	30 (12–62)	30 (16–53)	27 (18–45)	<0.001
NYHA class I (%)	70	74	47	<0.001
Type of heart disease				<0.001
Congenital (%)	66	74	18	
Valvular (%)	25	18	72	
Other (%)	9	8	10	
Prior cardiac surgery (%)	54	59	22	<0.001
Medication use before pregnancy (%)	28	26	37	0.002
Nulliparous (%)	50	52	34	<0.001
Outcome				
Maternal mortality (%)	1.0	0.6	3.9	<0.001
Maternal hospital admission (%)	26	23	41	<0.001
Cardiac				
Heart failure (%)	12	11	23	<0.001
Supraventricular arrhythmias (%)	0.9	1.1	2.7	0.07
Ventricular arrhythmias (%)	2.0	2.2	0.5	0.16
Obstetrics complications				
Pregnancy-induced hypertension (%)	2.4	2.5	2.2	0.80
(pre-)Eclampsia (%)	3.3	3.0	4.9	0.18
Caesarean section (%)	41	40	44	0.34
Post-partum haemorrhage (%)	2.9	2.9	2.7	0.88
Foetal				
Apgar score <7 (%)	10	8.7	17	0.001
Preterm birth <37 weeks (%)	15	16	11	0.12
Foetal death (%)	1.7	0.9	6.5	<0.001
Neonatal death (%)	0.6	0.6	0.5	0.90
Birth weight (g)	3010	3027	2899	0.004
Pregnancy duration (weeks)	38	38	38	0.93

P-value comparison between developed and developing.

Future directions

The pregnancy registry will continue to enrol patients over the next few years. This should allow a very large database to accumulate so that with more detailed analysis in larger disease-specific groups, firmer conclusions can be raised on the available data. These conclusions can then be used as the evidence base for improved management plans. Hopefully, these will make pregnancy safer for both mother and baby in this challenging situation.

Study limitations

Although this study describes a large population of patients, subgroup analysis was not performed in detail due to small numbers per group. Differences by diagnosis will exist; therefore, pooling patients is an over-simplification. In addition, the input and quality of data was checked in only 5–10% of cases. In 5% of patients, the data were incomplete. In addition, some centres had much higher volumes than others. Therefore, there may be bias of data. Although most data were collected prospectively (2008–11), pregnancies of 2007 (14% of patients) were included retrospectively. As participation to the registry was voluntary and there may be differences between sites that agreed to participate and those that did not, the registry may not be representative and therefore all conclusions must be drawn with caution. Finally, it was difficult to find a good control population. By including large prospective series from the countries that included most patients, we hope to have provided the best possible information for comparison.

Conclusions

Pregnancy in patients with heart disease results in a maternal mortality of 1%, which is a hundred times higher than in normal pregnant patients. However, clear differences were found in pregnancy

outcomes with respect to the underlying diagnosis and between patients in developed and developing countries. Most patients with adequate counselling and optimal care should not be discouraged and can go safely through pregnancy. The CS rate is high and more research should focus on the optimal mode of delivery for these patients.

Supplementary material

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

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