

# The Impact of Maternal Congenital Heart Disease on Pregnancy Outcomes in Malta -A Retrospective Study

Maryanne Caruana<sup>1</sup>, Miriam Gatt<sup>2</sup>, Oscar Aquilina<sup>1</sup>, Charles Savona Ventura<sup>3</sup>, Victor Grech<sup>4</sup>, Jane Somerville<sup>1</sup>

- 1. Department of Cardiology, Mater Dei Hospital, Msida MSD 2090, Malta
- 2. Directorate for Health Information and Research, Gwardamangia, Malta
- 3. Department of Obstetrics and Gynaecology, University of Malta, Msida MSD 2090, Malta
- 4. Department of Paediatrics, Mater Dei Hospital, Msida MSD 2090, Malta

#### Corresponding author:

Dr. Maryanne Caruana, Cardiac Catheterisation Suite, Department of Cardiology, Mater Dei Hospital, Msida MSD 2090, Malta E-mail: caruana.maryanne@gmail.com

# **Highlights**

#### **Background**

Most female patients with congenital heart disease (CHD) are becoming pregnant. Maternal CHD can have a negative impact on mother and foetus. This is the first study investigating pregnancy outcomes in Maltese grown-up congenital heart disease (GUCH) patients and one of few to compare these with outcomes in women without heart disease.

Known GUCH pregnancies for the period of 2007-2014 were extracted from our database (GUCH cohort) and cardiovascular outcomes retrieved from hospital notes. A control cohort of 540 pregnancies in women without cardiovascular disease was generated through twenty-fold random matching based on subject age from among all pregnancies in Maltese nationals for the same 8-year period. Obstetric and offspring outcomes were compared between the two cohorts.

The GUCH cohort consisted of 27 pregnancies in 24 women. Cardiovascular complications occurred in only 1/27 (3.7%) pregnancies. Elective Caesarean sections were commoner (29.6% vs. 15.4%) and unassisted vaginal deliveries less frequent (51.9% vs. 64.6%) in the GUCH cohort (p=0.02). Obstetric complication rates were similar. GUCH women had smaller babies (median 3030g vs. 3230g; p=0.045) and showed a trend towards more small-for-gestational age babies (18.5% vs. 8.4%; p=0.08) and congenital malformations (7.4% vs. 2.4%; p=0.06).

# **Conclusions**

Despite the potential adverse effects of maternal CHD on mother and foetus, most pregnancies are uncomplicated and outcomes comparable to those in women without heart disease, particularly if baseline clinical status is good. Based on our findings, it is being proposed that prospective mothers be counselled about the possibility of having smaller infants.

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# Introduction

Advances in the management of congenital heart disease (CHD) have led to most patients reaching child-bearing age, with an increasing number of such women becoming pregnant. [1] The physiological changes that occur during pregnancy, including increases in blood volume, heart rate and cardiac output, represent an added cardiovascular burden which may

be poorly tolerated by women with CHD, especially those with haemodynamically significant residua.[2] Such pregnancies are also at higher risk of neonatal complications.[3,4] Three main tools have been proposed for risk stratification of maternal cardiovascular complications among women with heart disease.[5] The CARPREG score [4] and modified World Health Organisation (WHO) classification [6,7] can be applied to women

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with both CHD and acquired heart disease (AHD), while the ZAHARA score [8] is designed specifically for women with CHD. CARPREG and ZAHARA scores consider the maternal clinical cardiac status to calculate risk of cardiovascular complications. In the modified WHO classification, pregnancies are classified into four risk groups based on specific heart lesions, with maternal risk ranging from very low in WHO class I to extremely high and warranting advice against pregnancy in class IV.[6,7]

Malta has a population of around 425,000 and the main religion is Roman Catholic.[9] Termination of pregnancy is illegal up to the time of writing of this manuscript. Malta's health care system is funded through taxation and national insurance, and specialised services, including a dedicated service for grownups with congenital heart disease (GUCH) are provided in one main teaching hospital. Obstetric data covering all deliveries to residents and non-residents taking place on the Maltese islands is collected and administered by the National Obstetric Information System (NOIS), which was launched by the Department of Health Information and Research in 1999.[10] There has been a trend of increasing maternal age over the past decade, with the 30-34 years' age bracket being the one with most reported deliveries (36.3%) in 2015. There were 3544 reported deliveries in women of Maltese nationality in 2015, 92.7% of all babies were born at term and the average birth weight was 3217g. Two maternal deaths were reported in the last decade.[10]

The overall incidence of CHD in Malta has been reported at around 0.8%, which is similar to that in other European countries. [11] Virtually all congenital cardiac surgery on children and adults born in Malta is carried out in overseas tertiary referral centres, in the United Kingdom, through a reciprocal National Health Service agreement. A number of structural cardiac interventions are carried out locally by visiting specialists. A GUCH service was initiated in the late 1990s and expanded considerably over the last decade. It includes a specific service for the provision of preconceptual counselling to female patients who want to get pregnant and for their management during pregnancy through close collaboration with obstetricians and anaesthetists.

The aims of this retrospective study were (a) to describe maternal outcomes among women with CHD in Malta and (b) to investigate the potential impact of maternal CHD on obstetric and offspring outcomes through comparison with reported outcomes in agematched women with no history of cardiovascular disease in the general Maltese population.

# Methods

All known pregnancies in women of Maltese nationality with CHD for the 8-year period 2007 - 2014 were retrieved from our institutional database ("GUCH pregnancy cohort"). Baseline characteristics, cardiac events and obstetric and offspring outcomes for these women were obtained retrospectively from hospital paper notes and digital investigation reports. An individual twenty-fold random matching based on subject age was performed out of all 29,349 pregnancies in Maltese women with no documented cardiovascular disease as collected by NOIS for the same study period. This generated the age-matched control cohort of 540 pregnancies referred to in the manuscript as "non-CVD pregnancy cohort". NOIS pregnancy entries for women of non-Maltese nationality were excluded primarily to

avoid any bias related to potentially differing epidemiological and/or genetic characteristics, as well as due to the possibility of their medical data leading up to the index pregnancy being incomplete. Maltese pregnancies with incomplete obstetric and/or offspring outcome data were also excluded during the matching process.

The term "tachyarrhythmias" refers to any symptomatic sustained and non-sustained tachyarrhythmia and excludes incidental asymptomatic atrial/ventricular ectopy. Ventricular and valvular function was based on echocardiographic findings and follows international guidelines.[12] Left ventricular systolic dysfunction is defined as an ejection fraction <55% and right ventricular systolic dysfunction is defined as a tricuspid annular plane systolic excursion (TAPSE) <16mm and fractional area change <35%. Aortic outflow tract obstruction is referred to as moderate if peak velocity is 3.0-3.9m/s and mean pressure drop is 25-40mmHg and severe if peak velocity is 34.0m/s and mean pressure drop is >40mmHg. Pulmonary outflow tract obstruction is defined as moderate if peak velocity is 3.0-4.0m/s and severe if >4.0m/s. Mitral regurgitation is defined as more than mild if proximal isovelocity surface area (PISA) is >0.4cm and vena contracta >0.3cm. Aortic regurgitation is defined as more than mild if pressure half time is <500ms and vena contracta is >0.3cm. Pulmonary regurgitation is referred to as severe if pressure half-time is <100ms and colour flow Doppler origin of the regurgitant jet is from the bifurcation of the branch pulmonary arteries. Severity of tricuspid regurgitation is based mostly on visual assessment.

The outcomes compared between the subjects in the two study cohorts were based on those collected by NOIS. Obstetric outcomes studied were threatened abortion, threatened premature labour, antepartum haemorrhage, placenta praevia, placental abruption, suspected intrauterine growth retardation (IUGR), maternal infections, hypertensive diseases of pregnancy, gestational diabetes, need for hysterectomy within 24 hours of delivery, retained placenta, severe haemorrhage (defined as blood loss of 1 litre in 2 hours), need for blood transfusion, dystocia and maternal death. Offspring outcomes studied were number of offspring per pregnancy, offspring gender, pregnancy duration, prematurity (pregnancy duration < 37 weeks), smallfor-gestational age (SGA) births (birth weight <10th centile for gestational age), birth weight, presence of congenital malformations diagnosed at birth and occurrence of stillbirths and neonatal death. Informed consent was obtained from all participants. The study protocol was approved by the University of Malta Research Ethics Committee and conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

# Statistical methods

Categorical variables were analysed using Chi-squared tests. Fisher's Exact test was applied in the case of smaller sample sizes. Shapiro-Wilk test applied to numerical variables (pregnancy duration and birth weight) showed a non-normal distribution. Subsequently, Mann-Whitney *U* test was used for comparison of these variables between the two study cohorts. Analyses were performed using SPSS 21 (IBM® SPSS® 21, SPSS Inc., Chicago IL, USA). All statistical analyses were two-sided and statistical significance was defined as p≤0.05.



# Results

The GUCH pregnancy cohort consisted of 27 pregnancies in 24 women, with 9 pregnancies belonging to modified WHO class I, 15 pregnancies to modified WHO class II/II-III and 3 pregnancies to modified WHO class III (Table 1). Maternal baseline characteristics are summarised in Table 2. Repaired tetralogy of Fallot was the commonest congenital heart lesion, featuring in 6/27 (22.2%) GUCH pregnancies. Mean maternal age was  $27.44 \pm 5.24$  years (range 15-41 years). All women were in New York Heart Association (NYHA) class I prior to the index pregnancy and none had cyanosis at baseline. Three patients were on cardiac medications prior to pregnancy: two women were on aspirin and one patient was on warfarin. Only one patient - a case of atriopulmonary (AP) Fontan surgery for tricuspid atresia - had a history of prior arrhythmias in the form of sustained atrial flutter needing direct current cardioversion in the past. Complete echocardiographic data was available for 23/27 GUCH pregnancies. In all these cases, there was good systemic ventricular function at baseline. One patient had moderate congenital aortic stenosis (AS) and another patient had moderate right ventricular outflow tract obstruction (RVOTO) at branch pulmonary artery level but no patients had severe outflow tract obstruction.

Cardiac events and cardiac medication use in pregnancy in the GUCH cohort is summarised in Table 3. Cardiac events were uncommon with only one patient, with a history of tricuspid atresia and atriopulmonary (AP) Fontan surgery, developing paroxysmal atrial arrhythmias and heart failure. The same patient was also the only one to require antiarrhythmic therapy, low-dose diuretics and anticoagulation during pregnancy. Two other women, one with total cavopulmonary connection (TCPC) and one with recent percutaneous closure of an atrial septal defect (ASD) remained on low-dose aspirin during pregnancy.

Tables 4 and 5 summarise the results of comparison of obstetric and offspring outcomes respectively. There were no significant differences in the frequency of pregnancy and delivery-related complications between the two cohorts. Unassisted vaginal delivery was the commonest mode of delivery in both cohorts, however it was less common among subjects in the GUCH cohort (GUCH 51.9% vs. non-CVD 64.6%). Conversely, elective pre-labour Caesarean section was employed more frequently among women in the GUCH cohort (8/27; 29.6%) when compared to those in the non-CVD cohort (83/540; 15.4%). Four of the 8 Caesarean sections (50%) in the GUCH pregnancy cohort were performed for cardiac indications, 3/8 (37.5%) had obstetric indications and one was performed based on patient preference. Instrumental delivery was used for 2/27 (5.4%) GUCH pregnancies and for 20/540 (3.7%) non-CVD pregnancies. The differences in delivery methods between the two cohorts were statistically significant (p=0.02). There were more premature births in the GUCH cohort (11.1% vs. 4.1%) though this difference did not reach statistical significance (p=0.11). Overall pregnancy duration in the two cohorts was not significantly different (median duration GUCH 38 weeks vs. non-CVD 39 weeks; p=0.14). Women in the GUCH cohort gave birth to significantly smaller babies (median birth weight: GUCH 3030g vs. non-CVD 3230g; p=0.045) and showed a trend towards having more SGA babies (GUCH 18.5% vs. non-CVD 8.4%; p=0.08). There was also a trend towards more frequent congenital malformations among offspring born to GUCH women (7.4% vs. 2.4%; p=0.06).

# **Discussion**

Maternal CHD is traditionally associated with poorer pregnancy outcomes, mainly through increased risk of cardiac events in the mother and complications in the foetus.[6] Neonatal complication rates of 20-28% and neonatal mortality of 1-4% have been reported among women with all forms of heart disease.[3,4,8,13,14] The commonest reported complications are premature births, small-for-gestational-age birthweights and respiratory distress syndrome. The maternal predictors of neonatal events are baseline NYHA class >II or cyanosis, maternal left heart obstruction, smoking during pregnancy, multiple gestation, use of oral anticoagulation during pregnancy and the presence of a mechanical valve prosthesis. [6] Hypertensive diseases of pregnancy and postpartum haemorrhage (PPH) are the commonest obstetric complications reported in women with heart disease.[3,13] Contrary to maternal and neonatal complications, the reported experience with obstetric complications is more variable. Whereas the CARPREG investigators found coarctation of the aorta as an independent predictor for pregnancy-induced hypertension and use of antiocoagulants in the peripartum period and cyanosis as independent predictors for PPH [4], the ZAHARA investigators found no such associations in their cohort.[8]

Adverse maternal cardiac events were only observed in one of the 27 GUCH pregnancies (3.7%) in our cohort, with the same patient developing symptomatic paroxysmal atrial arrhythmia as well as heart failure. This pregnancy was the one with the highest predicted risk in our cohort (CARPREG risk = 27%; ZAHARA risk = 70%; modified WHO class III). Arrhythmias and heart failure have been consistently reported as the commonest maternal cardiovascular complications.[3,4,8,15] Our cardiac event rate of 3.7% is lower than what has been reported in most large studies concentrating on pregnancy in women with CHD, where cardiac event rates ranged from 4% to 25%.[1,3,5,8,13,16,17] Although this finding is reassuring, it should be interpreted with caution as it is likely to be, at least partly, due to fewer women with more complex forms of CHD and poorer baseline cardiac status in the Maltese GUCH cohort when compared to other studies referred to earlier. In fact, both CARPREG and ZAHARA risk scores for the 23/27 patients in the Maltese GUCH cohort with complete pre-pregnancy echocardiographic data were low, with an overall CARPREG mean risk of 6.91 ± 6.34% (median 5%) and an overall ZAHARA mean risk of 8.25 ± 13.89% (median 2.9%). Similarly, only three pregnancies occurred in women considered to be at high risk of maternal cardiac complications by modified WHO classification, with all other pregnancies being in lower risk categories (Table 1).

The commonest primary cardiac lesion in our series was tetralogy of Fallot (TOF) (6/27 in 6 patients; 22.2% pregnancies), followed by coarctation of the aorta (4/27 in 3 patients; 14.8% pregnancies). No maternal cardiac events were reported in either of these groups. RV dysfunction and/or moderate to severe PR have been reported as the main risk factors for cardiac complications in pregnancies in women with TOF.[6,18-20] All our TOF patients had undergone complete repair in infancy or early childhood. Although two women had moderate pulmonary regurgitation



Table 1.

Modified WHO class I (n=9)					
Repaired ASD	3 (11.1%)	Repaired PDA	3 (11.1%)		
Repaired PS	1 (3.7%)	Repaired TAPVD	1 (3.7%)		
Repaired pAVSD	1 (3.7%)				
Modified WHO class II / II-III (n=15)					
Repaired CoA	4 (14.8%)	Unoperated VSD	1 (3.7%)		
Repaired TOF	6 (22.2%)	SAS	3 (11.1%)		
Congenital AS	1 (3.7%)				
Modified WHO class III (n=3)					
Fontan-type palliation	2 (7.4%)	TGA-Mustard	1 (3.7%)		

Congenital heart lesions in the 27 GUCH pregnancies divided by modified WHO classification of maternal cardiovascular risk [6,7]. Abbreviations:

ASD = atrial septal defect;

VSD = ventricular septal defect;

PDA = patent ductus arteriosus;

CoA = coarctation of the aorta;

TOF = tetralogy of Fallot;

PS = pulmonary stenosis;

TAPVD = total anomalous pulmonary venous drainage;

SAS = subaortic stenosis;

TGA = transposition of great arteries; AS = aortic stenosis; pAVSD = partial atrioventricular septal defect: WHO = World Health Organisation

(PR) and one had severe PR, all 6 patients were asymptomatic and all had normal right ventricular (RV) function at baseline. All three coarctation patients in our cohort had undergone surgical repair, and none had significant residua or hypertension prior to pregnancy. Consequently, they were all at low risk of aortic rupture and cerebral aneurysm rupture, which are the maternal complications mostly reported in this patient group.[6]

Three women went through a high-risk pregnancy: one patient with atrial switch (Mustard repair) for transposition of the great arteries (TGA) and two patients with Fontan-type palliation. Our only atrial switch patient had good systemic RV function, no significant TR and no previous arrhythmias, putting her in a more advantageous position for a good maternal outcome.[6,21-23] Both women with Fontan palliation had good NYHA status, retained ventricular function and no significant atrioventricular valve regurgitation at baseline, all factors considered favourable with this type of circulation.[6] However, a previous history of atrial arrhythmias requiring treatment and a possibly less efficient type of Fontan circuit (classical Fontan with right atrium to pulmonary artery conduit) in the patient with AP Fontan resulted in a difference in occurrence of cardiac events between the pregnancies.[24] Thus, even when assessed by cardiac lesion, most of our patients tolerated pregnancy without maternal complications, largely because their anatomy and function at baseline put them at the more favourable end of the spectrum.

Our study is one of few in the literature to compare pregnancy outcomes in GUCH patients with those in contemporary women without heart disease from the same population.[1,14,17,25]

Table 2.

	Number of pregnancies (%)
(a) Clinical characteristics (N = 27)	
Cyanosis	0 (0)
NYHA functional class I	27 (100)
History of atrial arrhythmias	1 (3.7)
History of ventricular arrhythmias	0 (0)
Permanent pacemaker / ICD in situ	0 (0)
History of congestive heart failure	0 (0)
(b) Cardiac medications (N = 27)	
Antiplatelets	2 (7.4)
Oral anticoagulant	1 (3.7)
Antiarrhythmics	0 (0)
Antihypertensive agent	0 (0)
Diuretics	0 (0)
(c) Echocardiographic parameters (N = 23)*	
Systemic ventricular dysfunction	0 (0)
Subpulmonary ventricular dysfunction	0 (0)
Moderate aortic outflow tract obstruction	1 (4.3)
Severe aortic outflow tract obstruction	0 (0)
Moderate pulmonary outflow tract obstruction	1 (4.3)
Severe pulmonary outflow tract obstruction	0 (0)
More than mild mitral regurgitation	0 (0)
More than mild aortic regurgitation	0 (0)
More than mild tricuspid regurgitation	0 (0)
More than mild pulmonary regurgitation	3 (13)

Maternal baseline cardiac characteristics for the 27 pregnancies in the GUCH cohort.

Abbreviations:

ICD = implantable cardioverter-defibrillator;

NYHA = New York Heart Association

There were significantly more deliveries by Caesarean section and fewer normal vaginal deliveries in our GUCH cohort, which compares to the reported literature.[1,14,17,25] There was no excess of obstetric complications in our GUCH pregnancy cohort when compared to non-CVD women (Table 4). These findings are similar to those reported in the Canadian study by Siu et al [14], the German study by Hrycyk et al [25] and those stemming from the Registry Of Pregnancy And Cardiac disease (ROPAC).[17] Conversely, in their nationwide U.S. study from 2015, Thompson et al found the odds of several obstetric complications, including gestational diabetes, preterm labour, placental abruption and postpartum haemorrhage, to be significantly higher among delivery hospitalisations for women with CHD.[1]

Overall, neonatal outcomes in our GUCH cohort were good and, in the main, not significantly worse than those in the non-CVD cohort. Although there was a higher rate of premature

<sup>\*</sup> Complete echocardiographic data was available for 23/27 pregnancies.



Table 3.

	Number of pregnancies (%)
Cardiac events	1 (3.7)
Heart failure	1 (3.7)+
Atrial arrhythmias requiring treatment	1 (3.7) +
Ventricular arrhythmias requiring treatment	0 (0)
Thromboembolic events	0 (0)
Infective endocarditis	0 (0)
Need for urgent percutaneous / surgical intervention	0 (0)
Cardiac medications used during pregnancy	
Antiplatelets	2 (7.4)
Low-molecular weight heparin	1 (3.7)*
Antiarrhythmic agent/s	1 (3.7)*
Diuretic	1 (3.7)*
Antihypertensive agent	0 (0)

Cardiac events and need for cardiac medication use during pregnancy in the 27-patient GUCH pregnancy cohort

Table 4.

Complication	GUCH pregnancies	Non-CVD pregnancies	p value
Threatened abortion	1/27 (3.7%)	28/540 (5.2%)	1.00
Threatened premature labour	0/27 (0%)	13/539 (2.4%)	1.00
Antepartum haemorrhage	0/27 (0.0%)	9/540 (1.7%)	1.00
Placenta praevia	0/27 (0.0%)	2/539 (0.4%)	1.00
Placental abruption	0/27 (0.0%)	3/540 (0.6%)	1.00
Suspected IUGR	2/27 (7.4%)	28/539 (5.2%)	0.65
Infections	0/27 (0%)	32/540 (5.9%)	0.39
Gestational hypertension	0/27 (0.0%)	37/540 (6.9%)	0.24
Pre-eclampsia/ eclampsia	0/27 (0.0%)	3/540 (0.6%)	1.00
Gestational diabetes	0/27 (0%)	25/539 (4.6%)	0.62
Hysterectomy within 24hrs	0/27 (0%)	0/540 (0%)	/
Retained placenta	0/27 (0%)	3/540 (0.6%)	1.00
Haemorrhage (1I in 2hrs)	0/27 (0%)	0/540 (0%)	/
Blood transfusion	0/27 (0%)	2/539 (0.4%)	1.00
Dystocia	0/27 (0%)	1/540 (0.2%)	1.00
Maternal death	0/27 (0%)	0/540 (0%)	/

Comparison of obstetric complications between GUCH and non-CVD cohorts

Abbreviations:

IUGR = intrauterine growth retardation

Table 5.

Outcome	GUCH pregnancies	Non-CVD pregnancies	p value*
Singleton pregnancy	26/27 (96.3%)	527/540 (97.6%)	0.50
Male infant gender	14/27 (51.9%)	292/540 (54.1%)	0.82
Pregnancy duration (weeks)+	38 (range 36 - 41)	39 (range 22 - 41)	0.14
Premature birth§	3/27 (11.1%)	22/537 (4.1%)	0.11
Small for gestational age§	5/27 (18.5%)	45/537 (8.4%)	0.08
Birth weight (grams)#	3027 (2821, 3232) [3030]	3212 (3168, 3256) [3230]	0.045
Congenital malformations	2/27 (7.4%)	13/540 (2.4%)	0.06
Still births / neonatal deaths	0/27 (0%)	5/540 (1%)	1.00

Comparison of offspring outcomes between pregnancies in the two study cohorts

- + Pregnancy duration is expressed as median followed by range in weeks
- § Rates of premature birth and small for gestational age babies (<10th centile for gestational age) are expressed as percentages out of all live births
- # Birth weight is expressed as mean with 95% confidence intervals followed by median in square brackets.
- Statistically significant differences are shown in bold

births in our GUCH cohort (11.1% vs. 4.1%), this difference did not reach statistical significance (p=0.11). Furthermore, the lowest pregnancy duration observed was only 36 weeks and there were no cases of severe prematurity. This contrasts with the observations made by other studies where higher rates of premature births in GUCH pregnancies [4,26], as well as significantly more premature births when compared to women without heart disease, were reported.[14,17] However, it should be noted that some of these studies included other forms of heart disease apart from CHD and had a higher proportion of women with a less favourable baseline maternal status and thus a higher propensity for poorer neonatal outcomes.

The main difference in offspring outcomes observed between patient and control cohorts related to significantly smaller babies born to women with CHD (median birth weight GUCH 3030g vs. non-CVD 3230g; p=0.045). There was also a trend towards more babies being small-for-gestational age in the GUCH cohort (18.5% vs. 8.4%; p=0.08). This observation has been documented by several other studies.[17,25,27] Maternal cyanosis and poor cardiac output are recognized as the main risk factors for foetal growth restriction and lower birth weights.[27] The fact that, on the whole, our GUCH cohort consisted of women with good saturations and satisfactory cardiac output at baseline, and that use of medications linked with IUGR was minimal, suggests that there might be other less well-recognized factors coming into play to interfere with foetal growth in mothers with CHD. It could also be argued that the "cardiologist's definition" of good cardiac output based on imaging and functional status might not necessarily translate into equally good uteroplacental flow.

<sup>+\*</sup> The only patient to develop significant cardiac events during pregnancy and to require anticoagulation, antiarrhythmic therapy and a diuretic was a patient with atriopulmonary Fontan for tricuspid atresia.



### Limitations

The small Maltese GUCH population and the even smaller numbers of female patients that became pregnant during the study period, which in themselves are an inevitable consequence of the small size of the country, represent the main limitation of this study. It is possible that some women with CHD of mild complexity who were not under regular specialist follow-up and were deemed to be at very low risk in pregnancy might have delivered in private centres and thus failed to be included due to lack of documentation in hospital records. Notwithstanding, the fact that most Maltese deliveries on the islands take place in state-run hospitals irrespective of maternal or obstetric risk makes it likely that missed GUCH pregnancies were few and that only women with mild or trivial lesions were selected out. A further limitation is the retrospective nature of the study which resulted in some patients having incomplete data, though this was limited to few patients who were not under regular specialist clinical follow-up. The comparison of outcomes between GUCH and non-CVD cohorts relied on outcomes routinely collected by NOIS. Because NOIS only captures pregnancies that end in the birth of a baby of ≥22 completed weeks, comparison of miscarriage rates could not be performed.

# **Conclusions**

Although pregnancy in the presence of maternal CHD can be of higher risk to mother and foetus, our findings reinforce the fact that, with careful preconceptual counselling and close monitoring by a specialist team of cardiologists, obstetricians and anaesthetists, pregnancy outcomes can be comparable to those in women without heart disease. The presence of maternal CHD appears to predispose to lower infant birth weight, even in women with less complex disease and good baseline functional status. While risk-predicting tools are a helpful guide, advice to prospective mothers needs to be tailored to the individual patient's case, taking into account not only the woman's functional status but also the services and infrastructure of the institution where the pregnancy will be followed and delivery performed so as to ensure safety at all stages.[28] Finally, large multi-centre collaborations like the European Society of Cardiology's ROPAC [29] which also include data about follow-up after pregnancy, will help shed more light on the long-term impact that pregnancy could have on cardiac function in women with CHD, particularly in an era where access to assisted reproductive technology, often with use of hormonal therapy and a higher possibility of multiple pregnancies, is increasing in many countries.

# **Declarations of interest:**

The authors declare no conflicts of interest.

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The authors state that they abide by the "Requirements for Ethical Publishing in Biomedical Journals." [30]

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