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Delivery outcomes in women with congenital heart disease: results from the Cuban National Programme for pregnancy and heart disease

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Abstract

Objective: To inform on delivery outcomes achieved in congenital heart disease (CHD) patients by the Cuban National Programme for pregnancy and heart disease.

Methods: Single-centre retrospective study on a prospectively collected cardiac pregnancy database at a tertiary referral hospital (January 2000–May 2017). Primary outcomes: pregnancy duration, outcome, maternal/fetal complications.

Results: Four hundred sixty-seven pregnancies in 462 recorded cases reached third trimester. Median age: 25 (21–29) years. Patients presented in NYHA class I (97%, $n = 453$) or II (3%, $n = 14$), 6% ($n = 27$) had arrhythmias, 1% ($n = 4$) had co-morbidities, 1% ($n = 4$) had impaired left ventricular function. There were 464 singleton pregnancies and 3 twin pregnancies. Of the singleton pregnancies, one resulted in stillbirth (0.2%). The rest were live births ($n = 463$), median weight 3200 (2900–3421) grams. Median pregnancy duration: 39.1 (38.6–40) weeks. Caesarean rate: 34% ($n = 156$). All twin pregnancies ($n = 3$) resulted in live births ($n = 6$) via caesarean section, of median weight 2710 (2458–2850) grams and median pregnancy duration 37 (36–38) weeks. Maternal cardiovascular complications (< 0.5%, $n = 2$), and obstetric complications (14%, $n = 67$) did not result in any mortality. Small-for-gestational-age was the commonest neonatal complication (10%, $n = 48$), with zero mortality. Three neonates (1%) had CHD. Post-delivery maternal NYHA functional status: class I in 84% ($n = 393$), class II in 16% ($n = 73$), and class III in one patient (< 0.5%).

Conclusion: In middle-income countries management of CHD pregnancies according to existing guidelines can achieve good maternal and fetal outcomes.

Keywords: Congenital heart disease, Pregnancy, Delivery outcomes, Cuba

Introduction

Due to developments in cardiac surgery and congenital cardiology, women with congenital heart disease (CHD) are now consistently reaching adulthood [1]. CHD has since become one of the most common types of heart disease in pregnancy [2], and represents a significant cause of morbidity to the gravid patient, as well as a risk

of mortality [3, 4]. In the developed world, high-risk pregnant CHD patients should have access to tertiary Adult Congenital Heart Disease (ACHD) centres [5, 6]. Conversely, little is known about pregnancy outcomes for women in low and middle-income countries [3]. This article seeks to address this gap in the literature, examining and updating the delivery outcomes achieved in CHD patients managed by the Cuban National Programme for pregnancy and heart disease [7, 8].

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Complications in CHD pregnancies and risk assessment

Complications arising from a CHD pregnancy can be broadly divided into three main categories: maternal cardiac complications, obstetric complications and fetal complications. Studies have estimated the incidence of cardiac complications at 10–13% in the CHD population [9–11]. Amongst these, heart failure and arrhythmias were identified as the most common [12]. In terms of obstetric complications, CHD pregnancies are associated with a higher rate of thromboembolism than in the general population (1:50 vs 1:1000–2000) [11]. Whilst overall rates of pregnancy-related hypertensive disorders are broadly similar to that of the healthy population (8.7% vs 8%), the incidence of pre-eclampsia and pregnancy induced hypertension can vary widely depending on the specific CHD examined. Lastly, it is estimated that 30% of fetuses experience complications [13], and women with CHD are more likely to have a spontaneous miscarriage or therapeutic abortion [14]. Further complications include an increased risk of premature birth above background, growth restriction and stillbirth [4, 9, 15–17], perhaps going some way in explaining why fetal mortality rates are four times higher in CHD pregnancies [13]. Overall, maternal mortality is not particularly high for most types of CHD, however rates of morbidity remain much higher in CHD patients and their offspring than in the general population [2].

Because of the high risk of complications in pregnancy and delivery, the importance of preconception counselling and appropriate risk stratification cannot be overstated. Preconception counselling should begin in adolescence, and should take place in a tertiary centre experienced in both the care of ACHD patients and high-risk pregnancies. Advice provided varies on a case-by-case basis, but should generally include guidance on appropriate contraception methods, a medication review and an appropriate assessment of the maternal cardiovascular risk that would be sustained in pregnancy [5, 6]. Three risk calculators have been validated to provide reliable information in this regard: the modified World Health Organisation (mWHO) classification of pregnancy risk [18], the CARPREG risk score [9] and the ZAHARA risk score [4]. Of these, the most effective is the mWHO classification of pregnancy risk, which is based primarily on the type and severity of the maternal heart defect [10].

The management of delivery in CHD patients

Guidelines on the management of delivery in CHD pregnancies have become more widely available in recent years. Pregnant women considered high-risk (mWHO class III–IV) should always give birth in a tertiary care centre where an appropriate multi-disciplinary team (MDT) can be called upon [5, 6]. Members of the MDT

will usually include an experienced obstetrician, a cardiologist, a neonatologist and an anaesthetist [19]. Spontaneous vaginal delivery is considered the preferred option for most CHD patients. Exceptions to this include an obstetric indication and/or a small number of high-risk cardiac conditions, where the Valsalva manoeuvre during active second stage may cause potentially detrimental haemodynamic changes [6, 19]. Indications for caesarean section (CS) include patients on oral anticoagulants going into preterm labour, Marfan's syndrome and other aortopathies with a fragile aorta, and the presence of acute intractable heart failure [6]. However, most guidance in this regard lacks definitive evidence, and relies instead on expert opinion.

Managing CHD pregnancies in low and middle-income countries

CHD expertise can be much more difficult to access in low and middle-income countries. In Latin America, exceptions to this rule are found in Mexico, Brazil and Cuba, where contrary to the norm, such care is available to the population [20–22]. The Cuban National Programme for heart disease in pregnancy remains the most established of these, having been in existence for close to 20 years.

It operates under the umbrella of the Institute of Cardiology and Cardiovascular Surgery in Havana, and has its base at the Hospital of Obstetrics and Gynaecology “Ramon Gonzalez Coro”, also based in Havana. As a national service, patients are referred via regional coordinators, and are assessed by the team of two consultant cardiologists and an obstetrician working for the Programme. Those deemed of sufficiently high-risk (mWHO criteria class II–III, III and IV) [18] are managed by the team for the duration of their pregnancy. Patients with pregnancies deemed class I and II are referred back to their regional hospital, with remote support available from the team where necessary. Pregnancies managed by the team in Havana are reviewed at 20–22 weeks, at 28–29 weeks, 34 weeks and at term. A cardiovascular management plan for delivery is made for each patient; following birth mothers remain under observation for at least 5 days. Post-discharge, they attend a follow-up appointment with a member of the team within 6 weeks.

However, even within established services such as the Cuban Programme, care provided can differ from that offered in high-income countries. A scarcity of resources and expertise, as well as long travel distances to access services and cultural, socioeconomic and ethnic differences in the populations served can all influence health-care outcomes for the CHD patient. Hence, there is a need to update and clarify the outcomes achieved for these patients in these services; the following analysis seeks to provide some such clarity.

Materials and methods

Study design and patient population

This was a retrospective single-centre study conducted on a prospectively collected cardiac pregnancy database at a tertiary referral hospital. The research protocol was approved by the local Institutional Review Board. Verbal informed consent was obtained for all participants in the study; written informed consent was not deemed necessary by the Review Board. The database comprised data from 1st January 2000 to 15th May 2017, and included a record of patients admitted under the Programme at its base in the Hospital of Obstetrics and Gynaecology “Ramon Gonzalez Coro” over this period. Data were collected on discharge using both obstetric and medical records, and anonymised at the point of collection, hence it was not usually possible to identify patients who presented to the Service in subsequent pregnancies.

Baseline data collected included: demographics (age, province of origin), CHD diagnosis/diagnoses, presence of significant co-morbidities, New York Heart Association (NYHA) functional status class I-IV prior to pregnancy, and baseline ECG and echocardiography results.

Study outcomes and follow-up assessment

The primary data outcomes recorded were: duration of pregnancy, outcome of pregnancy and any maternal or fetal complications experienced. Additional labour outcomes recorded included: mode of delivery, indication for caesarean section, birthweight, gestational age at delivery, fetal gender and the use of oxytocin in induction or augmentation of labour (data on the use of tocolytics in the third stage of labour were not collected). Small-for-gestational-age was defined as a baby born with a birth weight less than the 10th centile. Intrauterine growth restriction was defined as an estimated fetal weight less than the 10th centile based on ultrasound based centiles calculated using Hadlock’s formula. Maternal complications data were further classified into cardiovascular and obstetric. Following delivery, further maternal outcomes recorded included: post-partum NYHA functional class, heart failure, resting oxygen saturations (if abnormal: < 92%), arrhythmias requiring a permanent pacemaker.

Results

A total of 501 cases were identified. Of these, 487 had follow-up outcomes available at the time of analysis, and so were included in the study. Of the 487 cases, 7 (1.4%) were a repeat pregnancy, bringing the total number of recorded pregnancies analysed to 495. Out of 495 pregnancies, 27 (5%) were terminated on or before 22 weeks gestation, with one (0.2%) additional pregnancy terminated at 26 weeks. Overall, 467 pregnancies were further

evaluated. Pregnancies from women who had more than one pregnancy, were treated independently.

The baseline characteristics of the 467 CHD pregnancies managed at the Hospital “Ramon Gonzalez Coro” are described in Table 1. Overall, the median age at pregnancy was 25 (21–29) years. While all Cuban provinces were represented in the study population, most of the cases originated from Havana (71%). Patients had a wide variety of congenital heart defects (Table 1). Six cases involved a mWHO IV classed cardiac lesion, where pregnancy is contraindicated [18]. All cases presented in NYHA class I (97%, $n = 453$) or II (3%, $n = 14$), 6% ($n = 27$) had arrhythmias, 1% ($n = 4$) reported a significant co-morbidity, and 1% ($n = 4$) had impaired systemic ventricular function.

There were 464 singleton pregnancies and 3 twin pregnancies (Table 2). Of the singleton pregnancies, one pregnancy resulted in stillbirth (0.2%), with the rest resulting in live births (99.8%, $n = 463$), at a median duration of gestation of 39.1 (38.6–40) weeks and a median birth weight of 3200 (2900–3421) grams. Sixty-seven percent of cases ($n = 308$) resulted in a vaginal delivery, with caesarean section rates of 34% ($n = 156$). Oxytocin was used in 98 (21%) deliveries before the third stage. In 77 deliveries (79%) this was for induction, and in 21 cases (21%) this was for augmentation. Indications for caesarean delivery were divided into cardiovascular indications and obstetric indications. Cardiovascular indications existed in 19% of cases ($n = 30$). All six women with mWHO class IV disease were delivered by caesarean section: five were for cardiac reasons and one was performed for obstetric reasons at 41 weeks gestation. Only one of the five women with WHO Class IV disease was delivered preterm (32 weeks gestation), and this was for cardiac reasons. All twin pregnancies ($n = 3$) resulted in live births ($n = 6$), at a median duration of gestation of 37 (36–38) weeks, and a median birth weight of 2710 (2458–2850) grams. All twins were born via caesarean section.

Maternal cardiovascular complications did not result in mortality. One patient developed an arrhythmia, and a further one severe mitral insufficiency. The most prevalent maternal obstetric complication was gestational diabetes, which was present in 8% ($n = 36$) of pregnancies. This was followed by gestational hypertension in 2% of pregnancies ($n = 11$), haemorrhage (1%, $n = 4$), and uterine atony (1%, $n = 4$). Additionally, there were reported cases of pre-eclampsia (< 0.5%, $n = 2$), endometritis (< 0.5%, $n = 2$), sepsis (< 0.5%, $n = 2$), and uterine rupture (< 0.5%, $n = 1$).

Within the cohort of live births, being small-for-gestational-age was the commonest complication (10%, $n = 48$). Preterm birth affected 5% of pregnancies (23 singleton, 1 twin), and intrauterine growth restriction was noted in 3% of pregnancies (12

Table 1 Baseline characteristics

	CHD pregnancies (n = 467)
Age (years) ^a	25 (21–29)
Province of origin, n (%)	
Pinar del Rio	12 (3)
Artemisa	28 (6)
Havana	330 (71)
Mayabeque	20 (4)
Matanzas	15 (3)
Cienfuegos	3 (1)
Villa Clara	2 (< 0.5)
Sancti Spiritus	4 (1)
Ciego de Avila	7 (1)
Camaguey	8 (2)
Las Tunas	6 (1)
Granma	12 (3)
Holguin	7 (1)
Santiago de Cuba	3 (1)
Guantanamo	6 (1)
Isla de la Juventud	3 (1)
Other (Venezuela)	1 (< 0.5)
Diagnosis, n (%)	
mWHO I	333 (71)
Atrial Septal Defect (ASD) - repaired	33 (7)
Atrial Septal Defect (ASD) - unrepaired	57 (12)
Atrioventricular Septal Defect (AVSD) - repaired	3 (1)
Atrioventricular Septal Defects (AVSD) - unrepaired	3 (1)
Bicuspid aortic valve	5 (1)
Other	29 (6)
Patent Ductus Arteriosus (PDA) - repaired	7 (1)
Patent Ductus Arteriosus (PDA) - unrepaired	17 (4)
Pulmonary stenosis - repaired	11 (2)
Pulmonary stenosis (mild-moderate) - unrepaired	52 (11)
Ventricular Septal Defect (VSD) - repaired	3 (1)
Ventricular Septal Defect (VSD) - unrepaired	113 (24)
mWHO II	81 (17)
Coarctation of the aorta - repaired	26 (6)
Coarctation of the aorta (mild-moderate) - unrepaired	14 (3)
Tetralogy of Fallot - repaired	41 (9)
mWHO III	47 (10)
Aortic stenosis	2 (< 0.5)
Congenitally corrected Transposition of the Great Arteries (cTGA)	2 (< 0.5)
Ebstein's anomaly	14 (3)

Table 1 Baseline characteristics (*Continued*)

	CHD pregnancies (n = 467)
Fontan	3 (1)
Pulmonary regurgitation (mild – moderate) - unrepaired	4 (1)
Pulmonary stenosis (severe) -unrepaired	5 (1)
Sub-aortic stenosis - repaired	3 (1)
Sub-aortic stenosis – unrepaired	9 (2)
Transposition of the Great Arteries (TGA) – arterial switch	5 (1)
mWHO IV	6 (1)
Pulmonary Hypertension	4 (1)
Severe coarctation of the aorta - unrepaired	2 (< 0.5)
Co-morbidities	
Yes	4 (1)
No	463 (99)
Functional status at the start of pregnancy, n (%)	
I	453 (97)
II	14 (3)
III	0 (0)
IV	0 (0)
Arrhythmias, n (%)	
Yes	27 (6)
No	440 (94)
Left ventricular function, n (%)	
Normal (> 55%)	463 (99)
Impaired (< 55%)	4 (1)

Baseline data collected on 467 CHD pregnancies managed by the Programme 2000–2017. ^aAge was only available for 463 patients. Continuous data is presented as median (interquartile range)

singleton). Four women were delivered preterm due to concerns about cardiac function (three at 32 completed weeks and one at 34 completed weeks gestation), and all four women were delivered by caesarean section.

Following delivery, 4 singleton babies had a low Apgar score (1%) (three at term and one preterm). Further complications present in neonates included neonatal jaundice (1%, 3 singleton babies), meconium aspiration syndrome (< 0.5%, 1 singleton baby), hypoxia (< 0.5%, 1 singleton baby), and respiratory depression (< 0.5%, 1 singleton baby). Congenital malformations were found in 5 singleton babies (1%). Three (1%) had congenital cardiac defects (unrelated to the mother) and 2 (< 0.5%) had other congenital malformations. Following birth and up to 6 weeks of age, there were no reported neonatal deaths.

Post-natal maternal cardiovascular outcomes are summarised in Table 3. At 6 weeks follow-up, NYHA functional status was class I in 84% ($n = 393$) of cases,

Table 2 Pregnancy outcomes

	Singleton CHD pregnancies (n = 464)	Twin CHD pregnancies (n = 3)
Duration of pregnancy (weeks)	39.1 (38.6–40.0)	37 (36–38)
Outcome of pregnancy		
Live birth	463 (99)	6 (100)
Stillbirth	1 (< 1)	0 (0)
	Live births (n = 463)	Live births (n = 6)
Birth weight (gr)	3200 (2900–3421) ^a	2710 (2458–2850)
Mode of delivery, n (%)		
Vaginal	308 (66)	0 (0)
Caesarean section	156 (34)	6 (100)
Indications for caesarean, n (%)		
Cardiovascular indication	30 (19)	0 (0)
Obstetric indication	126 (81)	3 (100)
Maternal cardiovascular complications, n (%)		
Mitral insufficiency	1 (< 0.5)	0 (0)
Arrhythmia	1 (< 0.5)	0 (0)
Maternal obstetric complications, n (%)		
Gestational diabetes	35 (8)	1 (33)
Gestational hypertension	11 (2)	0 (0)
Pre-eclampsia	2 (< 0.5)	0 (0)
Thromboembolism	0 (0)	0 (0)
Haemorrhage	4 (1)	0 (0)
Haematoma	2 (< 0.5)	0 (0)
Endometritis	2 (< 0.5)	0 (0)
Uterine rupture	1 (< 0.5)	0 (0)
Uterine atony	3 (1)	1 (33)
Sepsis	2 (< 0.5)	0 (0)
Neonatal complications		
Acute fetal distress	18 (4)	0 (0)
Preterm birth	22 (5)	2 (33)
Intrauterine growth restriction	12 (3)	0 (0)
Small for gestational age	48 (10) ^a	0 (0)
Low Apgar score	4 (1)	0 (0)
Hypoxia	1 (< 0.5)	0 (0)
Respiratory depression	1 (< 0.5)	0 (0)
Meconium aspiration syndrome	1 (< 0.5)	0 (0)
Neonatal jaundice	3 (1)	0 (0)
Congenital cardiac defects	3 (1)	0 (0)
Other fetal malformations	2 (< 0.5)	0 (0)
Post-natal mortality	0 (0)	0 (0)

Pregnancy outcomes for 467 CHD pregnancies managed by the Programme 2000–2017. ^aBirth weight and consequently small-for-gestational-age results were only available for 462 neonates. Continuous data is presented as median (interquartile range)

Table 3 Maternal cardiovascular outcomes at six-week follow-up

	CHD pregnancies (n = 467)
Functional status, n (%)	
I	393 (84)
II	73 (16)
III	1 (< 0.5)
IV	0 (0)
Arrhythmias requiring a permanent pacemaker, n (%)	1 (< 0.5)
Severe mitral insufficiency	1 (< 0.5)

Follow-up maternal cardiovascular outcomes for 467 CHD pregnancies managed by the Programme 2000–2017

class II in nearly 16% ($n = 73$) and class III in a further case (< 0.5%). Additionally, one patient (< 0.5%) developed an arrhythmia requiring a permanent pacemaker and another developed a severe mitral insufficiency (< 0.5%).

Discussion

Overall, the study identified 467 pregnancies (464 singleton, 3 twin). The median age at pregnancy in the study population (25 years), is similar to that reported in studies of high-income countries (26–30 years) [4, 10, 23]. Some provinces in Cuba appear to be significantly overrepresented (e.g. Havana) compared to others (e.g. Santiago de Cuba), even when accounting for differences in population density (see Fig. 1). To some extent this can be explained by the dual function the Hospital “Ramon Gonzalez Coro” plays as both the national referral centre for the management of high-risk CHD pregnancies, and also the regional centre for lower risk CHD pregnancies. Nevertheless, the relatively low rate of cases seen in some Cuban provinces compared to others (particularly to the capital) could indicate that patients further afield are not being appropriately referred to the programme, may be unwilling to travel to the capital for monitoring, or are remaining undiagnosed and are therefore not being referred.

Regarding pregnancy outcomes, the live birth rate (99%) is particularly encouraging, with neonatal mortality rates approximately four times lower than have been reported elsewhere for CHD pregnancies [10, 11]. However, it is important to note that the study population was mixed in the level of risk the pregnancies presented; a significant proportion of cases were classified as low-risk. Overall, 89% of our cohort were in the mWHO class I-II category, where pregnancy would be considered to pose either no risk or a small increased risk of maternal mortality, or moderate increase in mortality [10]; 97% of women in our cohort had a NYHA functional score of I at the start of pregnancy. Whilst this reflects the ACHD survivor population that would be

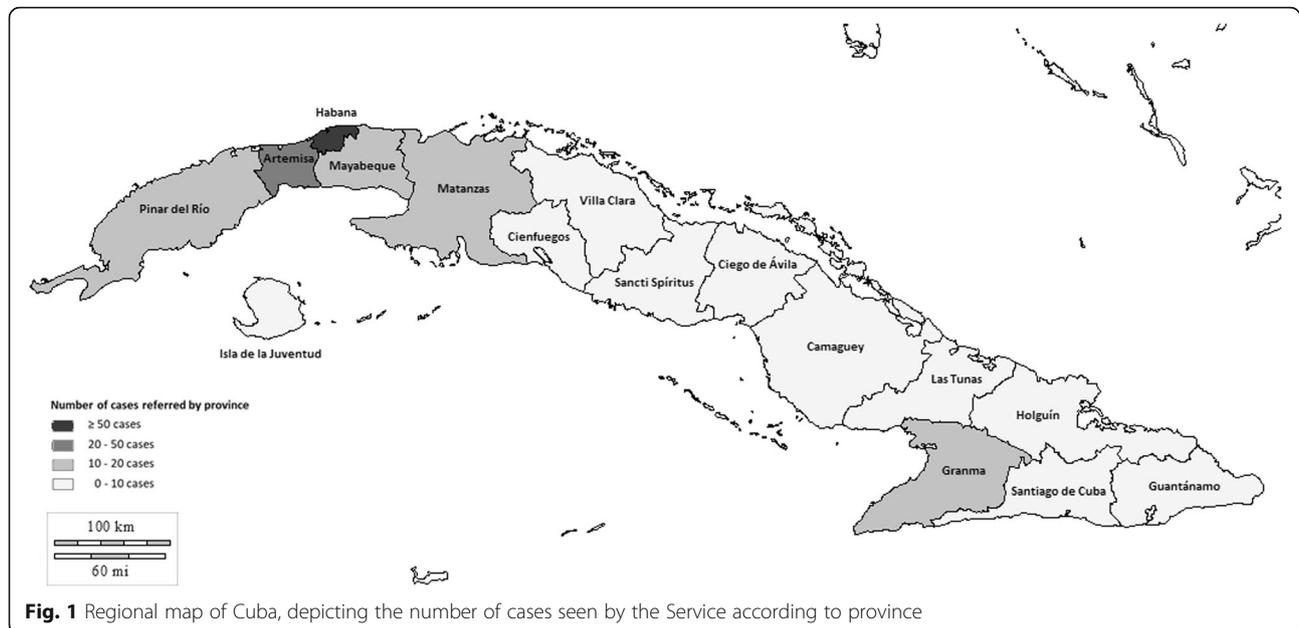


Fig. 1 Regional map of Cuba, depicting the number of cases seen by the Service according to province

expected in a middle-income country, it also means live birth outcomes may not be entirely comparable to studies with a greater focus on high-risk CHD pregnancies. The caesarean rate reported for singleton pregnancies (34%) is broadly similar to the rates reported in the literature [4], and lower than the national rate of caesarean sections of 40% in Cuba [24]. The 19% rate of caesarean section rate for cardiac indications may seem high given that the majority of women were mWHOI and II, and could be a reflection of clinician anxiety regarding maternal wellbeing. In Cuba, a previous caesarean section would be an indication for a further caesarean in all subsequent pregnancies, differing from the practice of most Western countries, where vaginal birth after caesarean (VBAC) is now encouraged [25].

Rates of maternal cardiovascular complications are in line with those reported by Drenthen et al [4], but lower than most other studies [9, 11, 16]. Obstetric complications are generally lower than reported elsewhere [4], though rates of gestational diabetes were higher than the general Cuban population (8% vs 5.8% respectively) [26]. Lastly, neonatal adverse outcomes were also consistently lower than reported by others [10, 11]. Rates of neonatal CHD were relatively low [3].

At follow-up, maternal cardiac functional status had decreased in 13% of the cohort. However, given the short-follow up time post-delivery (6 weeks), one must consider the context in which this outcome was measured; the decline in functional status could well be due to non-cardiac reasons, e.g. the normal fatigue experienced when looking after a new-born. It is therefore not possible to establish the long-term effects pregnancy and delivery have had on maternal cardiac function.

Strengths and limitations of the study

This work represents the largest report to date of a cohort of women, with 467 women with congenital cardiac disease who embarked on pregnancy in Cuba. Moreover, we have presented data from a middle-income health-care system as few comparable reports exist in the literature [20–22]. However, owing to the study methodology, it was not possible to reconcile patient data for patients that had a subsequent pregnancy. As such, the analysis was based on individual pregnancy cases managed by the Service as opposed to outcomes based on inter-pregnancy dependent variables. The implications of this are mainly that we have underestimated the deterioration in cardiovascular function with subsequent pregnancies. For example, a woman could have experienced a deterioration in cardiovascular function in her 1st pregnancy, which further decreased in a subsequent pregnancy. However, given that most women had an NYHA score of I at the start of pregnancy, this is unlikely to be the case. Improvements in data linkage systems would enable more precise estimations of the impact of pregnancy on cardiovascular disease and vice versa. The short follow-up time and retrospective nature of the study also restrict the conclusions that can be made, particularly on long-term maternal cardiovascular outcomes following pregnancy for CHD patients.

Conclusion

Pregnancy and labour can cause a significant burden to the abnormal cardiovascular system. In the context of CHD, appropriate risk-stratification measures and clear management strategies developed within a multidisciplinary team remain critical for positive outcomes in both

mother and child. The results of this study serve to demonstrate how, despite resource constraints, CHD patients can be successfully managed in middle-income countries at similar levels to those in more high-income healthcare systems. Nevertheless, the long-term outcomes of pregnancy remain to be established, and present a further avenue of research both in the developed and developing world.

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Availability of data and materials

The datasets generated and/or analysed during the current study can be requested from the authors on reasonable request.

Authors' contributions

JP and PR designed the study and gained institutional approval. RV, JP and PR performed the data collection. CK processed the results and wrote the manuscript. ST, HC, PC, JP and PR reviewed the manuscript. All authors approved the final version prior to submission.

Competing interest

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The research protocol was approved by the local Institutional Review Board. Verbal informed consent was obtained for all participants in the study; written informed consent was not deemed necessary by the Review Board.

Consent for publication

Not applicable.

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