Maternal and neonatal outcomes among pregnant women with cardiovascular disease in the Philippines: a retrospective cross-sectional study from 2015–2019

Frederick Berro Riveraa, John Vincent Magalonga, Ourlad Alzeus Tantengcob, Gerard Francis Mangubatd, Mary Grace Villafuertec and Annabelle Santos Volgmane

aDepartment of Medicine, University of the Philippines-Philippine General Hospital, Manila, Philippines; bCollege of Medicine, University of the Philippines Manila, Manila, Philippines; cDivision of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of the Philippines - Philippine General Hospital, Manila, Philippines; dDepartment of Medicine, Southern Philippines Medical Center, Davao City, Philippines; eDepartment of Cardiology, Rush University Medical Center, Chicago, IL, USA

ABSTRACT

Purpose: Several studies link maternal cardiovascular disease (CVD) to maternal and fetal morbidity and mortality. This study describes the profile of maternal, obstetric, and neonatal outcomes among pregnant women with CVD in a tertiary hospital in the Philippines. It identifies the clinical and sociodemographic variables associated with these outcomes.

Materials and Methods: A single-center, retrospective analysis of pregnant women admitted for delivery at the Philippine General Hospital from 2015 to 2019 was performed. Of these patients, pregnant women with CVD were identified as the cohort for this study. Data on clinical and sociodemographic factors, maternal major adverse cardiovascular events, neonatal adverse clinical events, and obstetric complications were collected. Logistic regression analysis was performed to determine the odds ratio for the risk factors for small-for-gestational-age (SGA) babies and preterm birth.

Results: Among 30,053 delivery admissions in the Philippine General Hospital from 2015 to 2019, 293 (0.98%) pregnant women had CVD. Of the CVDs present in this cohort, congenital heart diseases (n = 119, 40.6%) were the most common, followed by rheumatic heart disease (n = 109, 37.2%). Maternal adverse events were rarely observed. Four women experienced symptomatic arrhythmias, two presented with worsening heart failure, three experienced thromboembolic events, and one had cerebrovascular infarction. There was no reported maternal death, cardiac arrest, shock, or acute renal failure. The majority (69.3%) of the women included in the study were delivered by spontaneous vaginal delivery and assisted vaginal delivery by vacuum or forceps; however, a significant portion of these women had undergone cesarean section. Almost all the study cohort delivered live births, with most neonates being delivered at 37–38 weeks gestational age (83.6%) and only 16.0% born preterm. However, a significant portion, a third of the neonates, were classified as having low birth weight. Conditions associated with preterm birth were low educational attainment, previous history of early neonatal death, maternal low ejection fraction, and abnormal maternal left ventricular geometry. The conditions associated with SGA babies were high gravidity and parity, a history of abortion/stillbirth, a history of previous cesarean section delivery, low ejection fraction, a history of multiple gestations, and higher BMI.

Conclusion: In this cohort study, adverse maternal outcomes were rarely observed. CVD in pregnancy is associated with an increased risk of preterm birth and SGA babies. We identified certain maternal conditions and sociodemographic factors associated with these outcomes. Despite having CVD, our study cohort had no mortality from the pregnancy.

1. Introduction

The maternal mortality rate in the Philippines has been steadily declining from 160 per 100,000 live births in 2000 to 121 per 100,000 live births in 2020. Despite the aggressive implementation of maternal health programs in the country, it is still far from achieving the maternal mortality reduction target in the Sustainable Development Goals of the United

CONTACT Frederick Berro Rivera frederick.berro.rivera@gmail.com Department of Medicine, University of the Philippines - Philippine General Hospital, Manila, 1000 Philippines

Supplemental data for this article is available online at https://doi.org/10.1080/14767058.2022.2076590.
Nations [1]. Many unmet maternal healthcare needs still need to be addressed to improve the maternal mortality rate in the Philippines. Although hemorrhage and hypertensive disorders remain the top causes of maternal mortality, maternal morbidity and mortality can significantly be directly attributed to cardiovascular diseases (CVD) during pregnancy and delivery [2]. The prevalence of CVD in pregnancy is estimated to be 1% to 4% in all pregnancies worldwide, and this number continues to rise because of the increasing number of women with congenital heart disease (CHD) reaching childbearing age; increasing maternal age, and the rising incidence of cardiovascular risk factors such as diabetes mellitus, hypertension, and preeclampsia [2,3]. The cases of CHD continue to overtake rheumatic heart disease (RHD) as the leading cause of CVD in pregnant women in developed countries [4]. However, RHD is still prevalent among pregnant patients in developing countries [5].

Maternal CVD was also associated with poor neonatal outcomes [6–8]. The most common adverse neonatal outcomes were preterm birth and small-for-gestational-age birth weight [6]. However, other complications such as respiratory distress syndrome, intracranial or cerebral intraventricular hemorrhage, and fetal death were also observed [8,9]. Pregnant women with cardiomyopathy and pulmonary hypertension had the highest association with prematurity and SGA. Neonates born to mothers with CVD also had longer lengths of stay in the hospital [6].

In the Philippines, there is a lack of data describing the specific profile and needs of pregnant women with CVD. They remain primarily underdiagnosed, and even when detected, there are limited resources and professional expertise. There is minimal data examining Filipino gravidocardiac patients’ characteristics and the determinants of maternal and fetal outcomes of pregnant women with CVD. Thus, care for pregnant mothers with concomitant cardiac problems in the Philippines has become more challenging. This study describes the characteristics of these pregnant women with CVD (excluding hypertensive disorders of pregnancy) in the Philippines. It determines the sociodemographic, obstetric, and clinical profile of pregnant women with CVDs and their association with significant maternal, obstetric, and neonatal adverse events.

2. Methods

This study utilized a retrospective cross-sectional study design conducted at the University of the Philippines-Philippine General Hospital, a premier tertiary hospital and national referral center. We included pregnant women after 24 weeks of gestation with diagnosed CVD who were treated during the time surveyed who either had a live birth, miscarriage, or stillbirth. These women were identified from the patient registry of the Division of Maternal and Fetal Medicine, Department of Obstetrics and Gynecology, from January 2015 to December 2019. Women suffering from other medical conditions that can independently affect the pregnancy, such as renal failure, liver disease, pulmonary disease, and severe anemia, were excluded. Due to the more significant number of women affected by these cases, women with hypertensive disorders of pregnancy (gestational hypertension, preeclampsia, and eclampsia) were excluded from this study.

The sample size computation was modeled after the study of Liu et al. [10] using G*Power 3.1.9.2 statistical software; the computed sample size was \( n = 122 \) with a 5% significance level and 80% power. Twenty percent of the patient records in the sample size calculated were included to account for missing and miscoded patient records data. Thus, the minimum sample size was set to \( n = 147 \).

The records of these women were screened for inclusion and exclusion criteria, and all eligible patients were included for analysis. Data was collected through manual chart review and was encoded directly in a protected electronic worksheet for calculation. For confidentiality, data were anonymized using coding per patient. No names or case numbers were extracted. The study was approved by the Institutional Review Board of the Philippine General Hospital.

Descriptive analysis of the pregnant women’s characteristics was determined. Measures of central tendency such as mean and standard deviation were computed for numerical variables such as the age of mother, age of gestation, and the number of pregnancies, while categorical variables such as occupation and educational level, civil status, living in the province or the urban city were summarized into frequency distribution/percentages. Tests of association were done using a t-test to compare two means for quantitative variables and Chi-square for qualitative variables. Logistic regression analysis was used for the risk factors of small-for-gestational-age (SGA) and preterm birth. The odds ratio (95% CI) was computed to measure the association, and \( p \)-values of less than 0.05 are statistically significant.
3. Results

3.1. Sociodemographic and clinical characteristics of pregnant women with CVD

Among 30,053 delivery admissions to the Philippine General Hospital from 2015 to 2019, 293 (0.98%) pregnant women had CVD. These 293 women formed the cohort for this study. The average age of these women was 26.6 years; mostly single (n = 198, 67.6%) and were living in the urban setting such as in the National Capital Region (n = 189, 64.5%) and Region IVA (n = 53, 18.1%). Most of these women were unemployed (n = 196, 66.9%), and most (n = 229 78%) completed at least secondary education. The women included in the study were mostly nonsmokers (n = 252, 86.0%), nonalcoholic beverage drinkers (n = 232, 79.2%), and denied any history of illicit drug use (n = 265, 90.4%) (Table 1).

The clinical characteristics of the study cohort are listed in Table 2. Most of the study cohort had no other comorbidities (n = 189, 64.5%). Of those with comorbidities, diabetes (n = 20, 6.8%) and thyroid diseases (n = 10, 3.4%) were the most common. The mean systolic and diastolic blood pressures on admission were within normal limits. Most of the women were minimally symptomatic (New York Heart Association (NYHA) Class I) (n = 190, 64.9%), although a number presented as NYHA Class II with dyspnea on ordinary activity (n = 63, 21.5%). Only a minority presented with an advanced presentation of symptomatic heart failure (NYHA Class III and IV). Only about 52.2% of the pregnant women with CVD were seen by the

| Sociodemographic characteristics | Frequency | Relative frequency (%) |
|----------------------------------|-----------|------------------------|
| Age (years)                      | N = 293   |                        |
| Range                            | 13–42     |                        |
| Mean 26.6                        |           |                        |
| Civil status                     |           |                        |
| Single                           | 198       | 67.6%                  |
| Married/ common law              | 93        | 31.7%                  |
| Widowed/separated                | 1         | 0.3%                   |
| Not specified                    | 1         | 0.3%                   |
| Region                           |           |                        |
| National capital region          | 189       | 64.5%                  |
| Region IVA (Cavite)              | 53        | 18.1%                  |
| Region IVA (Laguna)              | 21        | 7.2%                   |
| Region IVA (Rizal)               | 5         | 1.7%                   |
| Region III (Bulacan)             | 10        | 3.4%                   |
| Rest of Luzon                    | 7         | 2.4%                   |
| Visayas                          | 6         | 2.1%                   |
| Mindanao                         | 2         | 0.7%                   |
| Occupation                       |           |                        |
| Unknown                          | 29        | 9.9%                   |
| White collar jobs                | 29        | 9.9%                   |
| Blue collar jobs                 | 39        | 13.3%                  |
| Unemployed                       | 196       | 66.9%                  |
| Educational attainment           |           |                        |
| College graduate                 | 54        | 18.4%                  |
| Vocational school graduate       | 25        | 8.5%                   |
| High school graduate             | 150       | 51.2%                  |
| Elementary graduate              | 45        | 15.3%                  |
| Unable to finish elementary      | 6         | 2.1%                   |
| Unknown                          | 13        | 4.4%                   |
| Service/Accommodation            |           |                        |
| Charity or with subsidy from the government | 260     | 88.7%                  |
| Pay or private                   | 32        | 10.9%                  |
| Unknown                          | 1         | 0.3%                   |
| Smoking history                  |           |                        |
| Nonsmoker                        | 252       | 86.0%                  |
| Former smoker                    | 12        | 4.1%                   |
| Current smoker                   | 5         | 1.7%                   |
| Unknown                          | 24        | 8.2%                   |
| Alcoholic history                |           |                        |
| Nonalcoholic                     | 232       | 79.2%                  |
| Moderate/occasional              | 36        | 12.3%                  |
| Unknown                          | 25        | 8.5%                   |
| Illicit drug use                 |           |                        |
| No illicit drug use              | 265       | 90.44%                 |
| (+) history of illicit drug use  | 3         | 1.02%                  |
| Unknown                          | 25        | 8.53%                  |
Table 2. Clinical characteristics of pregnant women with cardiovascular diseases admitted to the Philippine General Hospital.

| Clinical characteristics                                                                 | Frequency N = 293 | Relative frequency (%) |
|--------------------------------------------------------------------------------------------|-------------------|------------------------|
| Comorbidities                                                                             |                   |                        |
| No known comorbidities                                                                    | 189               | 64.5%                  |
| With known comorbidities                                                                  | 53                | 18.1%                  |
| Unknown                                                                                   | 51                | 17.4%                  |
| Specific comorbidities                                                                     |                   |                        |
| Diabetes                                                                                  | 20                | 6.8%                   |
| Chronic hypertension                                                                      | 5                 | 1.7%                   |
| Thyroid disorders                                                                          | 10                | 3.4%                   |
| Allergies                                                                                 | 6                 | 2.1%                   |
| Bronchial asthma                                                                          | 6                 | 2.1%                   |
| Antiphospholipid antibody syndrome                                                         | 6                 | 2.1%                   |
| Stroke (prior to current pregnancy)                                                        | 2                 | 0.7%                   |
| Connective tissue diseases                                                                | 2                 | 0.7%                   |
| Polycystic ovarian syndrome                                                                | 2                 | 0.7%                   |
| Chronic venous insufficiency                                                               | 1                 | 0.3%                   |
| Psoriasis                                                                                 | 1                 | 0.3%                   |
| Pulmonary tuberculosis                                                                    | 1                 | 0.3%                   |
| Systolic blood pressure on admission (mmHg) mean                                           | 115.64 ± 15.67    |                        |
| Diastolic blood pressure on admission (mmHg) mean                                          | 77.82 ± 10.46     |                        |
| New York Heart Association (NYHA) functional classification                                |                   |                        |
| Class I                                                                                   | 190               | 64.9%                  |
| Class II                                                                                  | 63                | 21.5%                  |
| Class III                                                                                 | 6                 | 2.0%                   |
| Class IV                                                                                  | 1                 | 0.3%                   |
| Unknown                                                                                   | 33                | 11.3%                  |
| Previous hospitalization for heart failure                                                 | 4                 | 1.4%                   |
| Previous intubation or respiratory failure                                                 | 0                 | 0%                     |
| Seen by cardiology service prior/during pregnancy                                         | 153               | 52.2%                  |
| No                                                                                        | 43                | 14.7%                  |
| Unknown/not mentioned                                                                     | 97                | 33.1%                  |
| Had a 2D echocardiogram done and documented during pregnancy                              | 77                | 26.3%                  |
| General classification of cardiac conditions                                               |                   |                        |
| Rheumatic heart disease                                                                    | 109               | 37.2%                  |
| Congenital heart disease                                                                   | 119               | 40.6%                  |
| Cardiomyopathies                                                                          | 11                | 3.8%                   |
| Ischemic heart disease                                                                     | 2                 | 0.7%                   |
| Others/ unspecified                                                                        | 93                | 31.7%                  |
| Specific cardiac lesions (congenital heart disease)                                        |                   |                        |
| Patent ductus arteriosus                                                                   | 39                | 13.3%                  |
| Ventricular septal defect                                                                  | 30                | 10.2%                  |
| Atrial septal defect                                                                       | 19                | 6.5%                   |
| Tetralogy of Fallot                                                                        | 2                 | 0.7%                   |
| Coarctation of aorta                                                                       | 1                 | 0.3%                   |
| Specific cardiac lesions (valvular lesions)                                               |                   |                        |
| Mitral valve prolapse                                                                      | 20                | 6.8%                   |
| Mitral stenosis                                                                            | 22                | 7.5%                   |
| Mitral regurgitation                                                                       | 62                | 21.2%                  |
| Aortic stenosis                                                                            | 5                 | 1.7%                   |
| Aortic regurgitation                                                                       | 20                | 6.8%                   |
| Tricuspid regurgitation                                                                    | 51                | 17.4%                  |
| Tricuspid stenosis                                                                         | 1                 | 0.3%                   |
| Pulmonic stenosis                                                                          | 3                 | 1.0%                   |
| Pulmonic regurgitation                                                                     | 34                | 11.6%                  |
| Previously documented arrhythmias or ECG changes                                          |                   |                        |
| With previously known arrhythmia/ECG changes                                               | 24                | 8.2%                   |
| Without previously known arrhythmias                                                       | 269               | 91.8%                  |
| Specific arrhythmias                                                                       |                   |                        |
| Atrial fibrillation, atrial flutter                                                        | 5                 | 1.7%                   |
| Heart block (atrioventricular block), unspecified                                          | 5                 | 1.7%                   |
| Unspecified tachy/brady/dysrhythm                                                         | 7                 | 2.4%                   |
| Sick sinus syndrome                                                                        | 1                 | 0.3%                   |
| Wolff parkinson white pattern                                                              | 1                 | 0.3%                   |
| Benign ECG changes                                                                         | 5                 | 1.7%                   |
| Peripartum cardiomyopathy                                                                  | 4                 | 1.4%                   |
| Pulmonary hypertension (on treatment)                                                      | 1                 | 0.3%                   |
| Use of cardiac medications                                                                |                   |                        |
| Not on medications                                                                         | 174               | 59.4%                  |
| Unknown                                                                                   | 40                | 13.7%                  |
| Taking cardiac medications                                                                | 79                | 27.0%                  |

(continued)
cardiology service at least once before or during pregnancy. Furthermore, only 26.3% of these patients had a documented 2D echocardiogram done during pregnancy.

In this study population, CHD \( (n = 119, 40.6\%) \) were more common than RHD \( (n = 109, 37.2\%) \), and ischemic CVD was rare \( (0.7\%) \). Of those with known CHD, the most common abnormalities were patent ductus arteriosus (PDA), ventricular septal defect (VSD), and atrial septal defect (ASD). Mitral valve involvement was the most common valvular lesion: 21.2% with mitral stenosis, 7.5% with mitral regurgitation, and 6.8% with mitral valve prolapse. Other lesions were also noted, such as tricuspid regurgitation \( (17.4\%) \), pulmonic regurgitation \( (11.6\%) \), and aortic regurgitation \( (6.8\%) \).

Electrocardiographic (ECG) changes and established arrhythmias were also seen in some gravidocardiac women. Unspecified arrhythmias and ECG changes that are usually clinically insignificant were common. Most patients were not on any cardiac medication \( (n = 174, 59.4\%) \). Patients taking cardiac medications before pregnancy were diagnosed with CHD ad RHD. The most common medications were digoxin, beta-blockers, loop diuretics, and ACE inhibitors as maintenance medications before pregnancy.

### 3.2. Obstetric characteristics of pregnant women with CVD

Table 3 shows that women in the study had average gravidity of two and parity of one. Most women gave birth to their first child before they are 30 years old. Most of these women had no history of preterm births, previous abortions, stillbirths, or cesarean births. Only about half of these women completed the minimum recommended eight prenatal care visits based on World Health Organization (WHO) 2016 recommendation.

### 3.3. Echocardiographic characteristics in pregnant women with CVD

The echocardiographic characteristics of this study cohort are presented in Table 4. Most of the cohort had no 2D echocardiogram done or available in their charts \( (n = 216, 73.7\%) \) during the pregnancy period. Most of those patients with available 2D echocardiogram results \( (81.8\%) \) had ejection fraction \( >50.0\% \). Only two women had a 30.0% or less low ejection fraction. Most patients had normal LV geometry. Concentric left ventricular hypertrophy \( (n = 12) \) was less common than eccentric hypertrophy \( (n = 17) \), and only four women had hypokinesia or wall motion abnormalities on their 2D echocardiogram. In eight patients, right ventricular changes (enlargement, dilatation) were also present. Regurgitant lesions, primarily mitral regurgitation, tricuspid regurgitation, and pulmonic regurgitation were most common. Mitral stenosis was present in 16.0%. Patients commonly had more than one valvular abnormality. One patient was documented to have a mechanical heart valve. PDA, VSD, and ASD were the most common congenital heart defects seen in the 2D echocardiogram. Contrary to valvular lesions, congenital lesions usually occur singly; however, especially in advanced disease, concomitant valvular lesions may be seen. Pulmonary arterial hypertension was seen in about 25.0% of patients with a 2D echocardiogram.

### 3.4. Maternal outcomes

Table 5 shows the maternal outcomes in this study. In this cohort, adverse outcomes were rarely observed. Four women experienced symptomatic arrhythmias, three of which were near-fatal (ventricular tachycardia). Two presented with worsening heart failure during pregnancy. The other adverse outcomes were one cerebrovascular event (stroke) and three thromboembolic events (DVT, PE). There was no reported
maternal death, cardiac arrest, shock, or acute renal failure. Two patients needed intubation, and two required ICU admission.

The majority (69.3%) of the cohort delivered by spontaneous vaginal delivery and assisted vaginal delivery (vacuum or forceps). A significant portion of these women had undergone abdominal delivery (primary cesarean section), mostly done for emergent indications: particularly for non-reassuring fetal status and dystocia. Only a few experienced abdominal deliveries for worsening maternal conditions. Most women had blood loss of less than 500 ml; however, blood loss of >1000 ml was about three times more common among those who underwent abdominal delivery than spontaneously or assisted vaginal delivery.

### 3.5. Neonatal outcomes

Table 6 shows the neonatal outcomes found in this study. Most of the study cohort delivered live births, with two having an early neonatal death. Most neonates being delivered at 37–38 weeks gestational age (83.6%) and only 16.0% born preterm. The proportion of preterm births among these patients was...
Table 5. Maternal Outcomes of Pregnant Women with Heart Diseases in the Philippine General Hospital from 2015 to 2019.

| Maternal obstetric outcomes                      | Frequency $N = 293$ | Relative frequency (%) |
|--------------------------------------------------|----------------------|------------------------|
| Mode of Delivery for Current Pregnancy           |                      |                        |
| Spontaneous vaginal delivery                     | 86                   | 29.4%                  |
| Assisted vaginal delivery (vacuum, forceps)      | 117                  | 39.9%                  |
| Abdominal delivery/cesarean section              | 88                   | 30.0%                  |
| Unknown                                          | 2                    | 0.7%                   |
| Indication of Abdominal Deliveries ($n = 88$)    |                      |                        |
| Nonreassuring fetal status                       | 26                   | 20.5%                  |
| Dystocia/ dysfunctional labor                     | 24                   | 27.3%                  |
| Worsening maternal status                        | 7                    | 8.0%                   |
| Repeat cesarean section                          | 23                   | 26.1%                  |
| Unknown                                          | 5                    | 5.7%                   |
| Others                                           | 3                    | 3.4%                   |
| Estimated maternal blood loss                    |                      |                        |
| $\geq 1000cc$                                    | 33                   | 11.3%                  |
| 501 to 999cc                                    | 23                   | 7.8%                   |
| $\leq 500cc$                                     | 201                  | 68.6%                  |
| Unspecified                                      | 36                   | 12.3%                  |
| Adverse maternal outcomes                        |                      |                        |
| Live births                                      | 291                  | 99.3%                  |
| Still births/ abortions                          | 0                    | 0                      |
| Unknown                                          | 2                    | 0.7%                   |
| Gestational age                                  |                      |                        |
| By LMP (mean, in days)                           | 266.5 ± 16           |                        |
| By pediatric aging (mean, in weeks)              | 37.7 ± 1.8           |                        |
| Classification by pediatric aging                |                      |                        |
| Preterm (<37 weeks)                              | 47                   | 16.0%                  |
| Term (37–41 weeks)                               | 245                  | 83.6%                  |
| Post-term (≥42 weeks)                            | 0                    | 0                      |
| Unclassified                                     | 1                    | 0.4%                   |
| Birth Weight, in grams (mean)                    | 2722 ± 512           |                        |
| Birth weight classification (WHO)                |                      |                        |
| Extremely low birth weight (<1000 g)             | 0                    | 0                      |
| Very low birth weight (<1500 g)                  | 5                    | 1.7%                   |
| Low birth weight (1500–2500 g)                   | 92                   | 31.4%                  |
| Normal (2500–4000 g)                             | 193                  | 65.9%                  |
| Macrosomia (>4000 g)                             | 2                    | 0.7%                   |
| Unknown                                          | 1                    | 0.3%                   |
| Specific major adverse cardiac outcomes           |                      |                        |
| Worsening/decompensated heart failure            | 2                    | 0.7%                   |
| Acute pulmonary edema                            | 0                    | 0                      |
| Venous thromboembolism (DVT and PE)              | 3                    | 1.0%                   |
| Acute myocardial infarction                      | 0                    | 0                      |
| Near-fatal/ symptomatic arrhythmia               | 4                    | 1.4%                   |
| Stroke/cerebrovascular events                    | 1                    | 0.3%                   |
| Aortic dissection                                | 0                    | 0                      |

DVT: deep venous thrombosis; ICU: intensive care unit; PE: pulmonary embolism; RRT: renal replacement therapy.

Table 6. Neonatal outcomes of pregnant women with heart diseases in the Philippine General Hospital from 2015 to 2019.

| Neonatal outcomes                        | Frequency $N = 293$ | Relative frequency (%) |
|------------------------------------------|----------------------|------------------------|
| Live births                              | 291                  | 99.3%                  |
| Still births/ abortions                   | 0                    | 0                      |
| Unknown                                  | 2                    | 0.7%                   |
| Gestational age                          |                      |                        |
| By LMP (mean, in days)                    | 266.5 ± 16           |                        |
| By pediatric aging (mean, in weeks)       | 37.7 ± 1.8           |                        |
| Birth Weight, in grams (mean)             | 2722 ± 512           |                        |
| Birth weight classification (WHO)         |                      |                        |
| Extremely low birth weight (<1000 g)      | 0                    | 0                      |
| Very low birth weight (<1500 g)           | 5                    | 1.7%                   |
| Low birth weight (1500–2500 g)            | 92                   | 31.4%                  |
| Normal (2500–4000 g)                      | 193                  | 65.9%                  |
| Macrosomia (>4000 g)                      | 2                    | 0.7%                   |
| Unknown                                  | 1                    | 0.3%                   |
| Adverse neonatal outcomes                 |                      |                        |
| Neonatal prematurity                      | 47                   | 16.0%                  |
| Neonatal ICU admission                    | 51                   | 17.4%                  |
| Neonatal intubation/ acute respiratory failure | 0                  | 0                      |
| Early neonatal death                      | 2                    | 0.7%                   |

ICU: intensive care unit; LMP: last menstrual period; WHO: World Health Organization.
comparable to the national average as of 2019 (15 in 1000 live births). Most neonates had been classified as having normal birth weight, and the overall mean birth weight still falls within the normal range. However, a significant portion, accounting for a third of the neonates, were classified as having low birth weight. Around 17.4% of neonates born from gravido-cardiac mothers were admitted neonatal intensive care unit. However, only two neonates have been reported to have died (higher than the national average of 0.1%), and none of these neonates were intubated. These two neonatal mortalities were born from women with congenital heart disease and rheumatic heart disease.

### 3.6. Risk factors for preterm birth and SGA neonates

We found a significant association between preterm birth and SGA neonates and certain sociodemographic and clinical factors of the study cohort, such as highest educational attainment ($p = .009$), previous history of early neonatal death ($p = .046$), ejection fraction classification ($p = .036$), and LV geometry ($p = .049$) were associated with preterm births among pregnant women with CVD from 2015 to 2019 (Supplementary Table 1).

In patients with CVD admitted from 2015 to 2019, gravidity ($p = .032$), parity ($p = .041$), history of abortion/stillbirth ($p = .047$), history of previous cesarean section ($p = .019$), ejection fraction classification ($p = .02$), history of multiple gestation ($p = .011$), weight ($p = .001$), and BMI ($p = .012$) were associated with SGA neonates (Supplementary Table 2).

Multiple logistic regression analysis was used to determine the strength of association and measured the odds ratio of the sociodemographic and clinical risk factors with poor neonatal outcomes. The maternal level of education was significantly associated with preterm birth ($p$-value of 0.025) (Table 7). Those patients who did not finish elementary were 30 times more likely to have a preterm birth than those who finished college. On the other hand, only the maternal weight during pregnancy was significantly associated with the occurrence of SGA neonates ($p = .0289$). A unit increase in the mother’s weight decreased the risk of SGA infants (OR = 0.93) (Table 8).

### 4. Discussion

In this cohort of patients, there was a 0.98% prevalence of pregnant patients with CVD admitted for delivery to the Philippine General Hospital. This finding is similar to previous studies, which showed that CVDs complicate 1-4% of pregnancies and account for 16% of maternal mortality during pregnancy [11]. Our CVD cohort had an equal distribution of CHD and RHD. Mitral valve involvement was the most common valvular lesion: 21.2% with mitral stenosis, 7.5% with mitral regurgitation, and 6.8% with mitral valve prolapse. Tricuspid regurgitation was present in 17.4% of pregnant patients, 11.6% had pulmonic regurgitation,
and 6.8% had aortic regurgitation. Our results agreed with previous studies showing mitral valve lesions were the most common valvular lesion among pregnant patients with valvular heart disease [12–14]. The advancement in the medical and surgical treatments for CHD resulted in an increased life expectancy for these patients allowing them to reach childbearing age [13]. This has contributed to the increase in pregnant patients with CHD. However, RHD remains highly prevalent in pregnant women due to its endemicity in several countries. RHD is most common in developing countries [15,16]. Despite being a preventable disease, the prevalence of RHD remains high in developing countries like the Philippines [17,18]. The most common valvular lesions of our patients with RHD include mitral, tricuspid, and pulmonic regurgitation. The European Registry on Pregnancy and Heart Disease also reported that mitral regurgitation was one of the most common valvular pathologies in pregnant women with CVD [19]. A previous study showed that women with aortic and pulmonic regurgitation are at low risk for cardiac complications during pregnancy [20]. Additionally, mixed valvular disease in RHD can lead to poorer maternal outcomes than a pure valvular disease of similar severity [21]. Further investigation may focus on this sub-population to estimate its actual burden in the Philippines.

Diabetes was the most common comorbidity in our cohort of pregnant patients with CVD, which is not surprising since there is a high burden of diabetes in the Philippines, approximately 7.1% in adults between 20 and 79 years old. Diabetes significantly increases the risk of long-term morbidity and mortality due to cardiovascular disease (9–11). The prevalence of gestational diabetes mellitus was also reported at 14% in the Philippines (8). This comorbidity further increases the risk of maternal and neonatal complications among Filipino pregnant patients with CVD.

We did not observe any maternal mortality in the patients included in this study. Most of the patients included in this study had a baseline NYHA class of I or II, only six with NYHA class III, and one patient with NYHA class of IV. Baseline NYHA class is a significant determinant of maternal and fetal outcomes [19,22,23]. However, due to the limitations in the number of pregnant patients with baseline NYHA class III and IV in our study, we could not perform statistical analysis to determine its association with maternal and fetal outcomes. Madazli et al. reported that maternal morbidity and cesarean delivery rates were significantly higher in the NYHA stage III-IV group compared to NYHA class I-II [22]. Our study showed that pregnancy was generally safe in women with CVD with a baseline NYHA class I or II. Specific congenital lesions increase the risk of maternal morbidity. Severe maternal CHD also increases the risk of maternal morbidity and mortality. In our study, most pregnant patients had less severe lesions, such as patent ductus arteriosus and ventricular septal defects, which may explain the low maternal morbidity in this study [24].

Approximately 27.0% of pregnant women with CVD in this study required medications before their

| Table 8. Association of sociodemographic and clinical risk factors small gestational age. |
|---------------------------------|-----|-----|-----|-----|-----|
| Sociodemographic and clinical risk factors | OR  | Lower | Upper | p-value |
| Weight in kg | 0.93 | 0.88 | 0.99 | .0289* |
| BMI | 1.09 | 0.93 | 1.27 | .2765 |
| Gravidity | 0.93 | 0.41 | 2.12 | .8613 |
| Parity | 1.04 | 0.45 | 2.39 | .9229 |
| History of previous abortion/still birth | Ref | | | |
| Unknown history of previous abortions/stillbirths | 2.86 x 10^5 | 0.00 | | .9994 |
| With history of previous abortions/stillbirths | 1.42 | 0.34 | 6.04 | .6324 |
| History of previous cesarean | Ref | | | |
| No history of previous cesarean | 1.73 | 0.10 | 31.11 | .7087 |
| with history of previous cesarean | 0.32 | 0.09 | 1.15 | .0798 |
| History of multiple gestation | Ref | | | |
| Unknown history of multifetal gestation | 3.99 x 10^5 | 0.00 | | .9992 |
| With history of multifetal gestation | 0.00 | 0.00 | | .9996 |
| Ejection fraction (EF) classification | Ref | | | |
| Unknown EF classification | | | | |
| LVEF <40% | 3.07 | 0.47 | 19.89 | .2389 |
| LVEF 41%–49% | 46.40 | 0.00 | | .9996 |
| LVEF >50% | 1.07 | 0.52 | 2.19 | .8547 |

*p-value < .05 is statistically significant; BMI: body mass index.
pregnancy and did not have 2D echocardiography done during their pregnancy. The lack of available healthcare services for diagnosing CVD could be why it remains one of the leading causes of maternal mortality and morbidity in developing countries [25]. Moreover, managing patients with CVD require multispecialty care from cardiologists, obstetricians, maternal-fetal medicine doctors, and neonatologists [4]. The low number and unequal distribution of these specialists in the Philippines also serve as a challenge in diagnosing and treating pregnant patients with CVD. Currently, there are only 247 maternal-fetal medicine specialists in the Philippines taking care of all the high-risk pregnancy patients, including those with CVD. The lack of multispecialty care services and the lack of epidemiologic and clinical studies on pregnancy outcomes for this set of patients may serve as a roadblock to adequately managing and preventing adverse effects in pregnant patients with CVDs.

Our results showed that almost 83.6% of women with CVD completed pregnancy until term delivery. This percentage was significantly higher than a previous study conducted in the Philippines, which showed that 68% of gravidocardiac patients delivered a term live birth fetus [26]. Most patients with CHD, especially those with mild forms of CHD, could conceive and carry a pregnancy to term [27]. A previous study conducted in Vietnam also showed a high term delivery rate (95.42%) among pregnant patients with CVD [8].

Our cohort's most common adverse neonatal outcomes were preterm birth (16.0%) and low birth weight (33.1%). Our study revealed that educational attainment was associated with preterm birth among gravidocardiac patients. Patients with lower levels of education were 30 times more likely to have a preterm birth than those who could finish college. Previous studies have shown the association between levels of education and the risk of preterm birth [28–30]. The educational gradient in preterm birth among pregnant patients with CVD might be explained by socioeconomic status and access to high-quality healthcare. Those who finished college may have better jobs and access to antenatal care with multispecialty services. In mothers with RHD, poor antenatal outcomes were associated with a lack of antenatal care [31].

Our study showed that advanced maternal age was not associated with preterm birth and SGA baby among pregnant patients with CVD. Advanced maternal age among pregnant patients without CVD increased the risk of adverse neonatal outcomes [32,33]. However, previous studies showed that women with CVD had a higher risk of preterm birth and giving birth to an SGA baby at all maternal ages [34,35]. They did not find a higher risk of adverse neonatal outcomes among women with CVD >35 years than women with CVD ≤35 years [34,35]. The presence of maternal CVD and other comorbidities may have leveled the risk of adverse neonatal outcomes among these mothers regardless of maternal age.

Moreover, higher educational attainment also encourages better health behaviors such as birth spacing, decreasing the risk of preterm birth [36]. Lastly, our study revealed that a higher maternal weight during pregnancy reduced the risk of small gestational age infants. Previous studies showed that gestational weight gain was positively associated with a decreased prevalence of underweight children. The surplus of energy and nutrients may protect the fetuses from intrauterine growth restriction and SGA [37,38].

This study has several limitations that should be considered when interpreting the results of this study. 1) This study was only limited to one tertiary hospital in the Philippines; however, the Philippine General Hospital is the largest tertiary care hospital in the Philippines and receives patients from different parts of the country; 2) this is a retrospective cross-sectional study, and may not be used to explain cause and effect for the risk factors for adverse pregnancy outcomes identified in this study; 3) only 77 (26.3%) patients had 2D echocardiogram available during their pregnancy and this limited our analysis on the echocardiographic characteristics the pregnant patients with CVD. Nevertheless, this is the most extensive cross-sectional study in the Philippines on the maternal and fetal outcomes in Filipino pregnant patients with CVD.

5. Conclusion

Our study observed a 0.98% prevalence of maternal CVD among pregnant patients admitted for delivery in the Philippine General Hospital. Almost 83.6% of pregnant women with CVD completed pregnancy until term delivery. This study's most common adverse neonatal outcomes include preterm birth (16.0%) and low birth weight (33.1%). Low educational attainment, previous history of early neonatal death, low ejection fraction, and abnormal LV geometry was associated with preterm birth. High gravidity and parity, history of abortion/stillbirth, previous cesarean delivery, low ejection fraction, history of multiple gestations, and lower BMI were associated with increased risk of SGA babies.
Author contributions

**CRediT roles:** Frederick B. Rivera MD: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Writing - original draft; Writing - review & editing; John Vincent Magalond MD: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Writing - original draft; Writing - review & editing; Ourlad Alzeus Tantengco BSc: Data curation; Formal analysis; Investigation; Methodology; Validation; Writing - review & editing; Mary Grace M. Villafuerte MD: Conceptualization; Data curation; Methodology; Validation; Writing - review & editing; Gerard Francis Mangubat, MD: Statistical analysis; Annabelle Santos Volgman MD: Review & editing.

Disclosure statement

The authors state no conflicts of interest regarding this study.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Frederick Berro Rivera [http://orcid.org/0000-0001-9100-0724]
Ourlad Alzeus Tantengco [http://orcid.org/0000-0002-4535-8837]

References

[1] World Health Organization. Regional Office for the Western Pacific. Sustainable development goals (SDGs) [N/A]: Goal 3. Target 3.1[N/A]: By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births [Internet]. Manila PP - WHO Regional Office for the Western Pacific 2016. Available from: http://iris.wpro.who.int/handle/10665.1/12775.

[2] Elkayam U, Goland S, Pieper PG, et al. High-risk cardiac disease in pregnancy: part I. J Am Coll Cardiol. 2016;68(4):396–410.

[3] Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. J Am Coll Cardiol. 2018;71(21):2419–2430.

[4] Adam K. Pregnancy in women with cardiovascular diseases. Methodist Debakey Cardiovasc J. 2017;13(4):209–215.

[5] Carapetis JR, Steer AC, Mulholland EK, et al. The global burden of group a streptococcal diseases. Lancet Infect Dis. 2005;5(11):685–694.

[6] Owens A, Yang J, Nie L, et al. Neonatal and maternal outcomes in pregnant women with cardiac disease. J Am Heart Assoc. 2018;7(21):e009395.

[7] Marshall WH, V Gee S, Lim W, et al. Maternal and fetal outcomes in pregnant women with pulmonary hypertension: the impact of left heart disease. Int J Cardiol Congenit Heart Dis. 2022;8:100354.

[8] Manh TN, Van NB, Le TH, et al. Pregnancy with heart disease: Maternal outcomes and risk factors for fetal growth restriction. Int J Environ Res Public Health. 2019;16(12):2075.

[9] Khairy P, Ouyang DW, Fernandes SM, et al. Pregnancy outcomes in women with congenital heart disease. Circulation. 2006;113(4):517–524.

[10] Liu H, Xu J, Zhao X, et al. Pregnancy outcomes in women with heart disease. Chin Med J (Engl). 2010;123:2324–2330.

[11] Ramlas Khan KP, Johnson MR, Roos-Hesselink JW. Pregnancy and cardiovascular disease. Nat Rev Cardiol. 2020;17(11):718–731.

[12] Tsiaras S, Poppas A. Mitral valve disease in pregnancy: outcomes and management. Obstet Med. 2009;2(1):6–10.

[13] Nanna M, Stergiopoulos K. Pregnancy complicated by valvular heart disease: an update. J Am Heart Assoc. 2014;3:1–18.

[14] van Hagen IM, Thorne SA, Taha N, et al. Pregnancy outcomes in women with rheumatic mitral valve disease. Circulation [Internet]. 2018;137(8):806–816.

[15] Carapetis JR. Rheumatic heart disease in developing countries. N Engl J Med. 2007;357(5):439–441.

[16] Watkins DA, Johnson CO, Colquhoun SM, et al. Global, regional, and national burden of rheumatic heart disease, 1990–2015. N Engl J Med. 2017;377(8):713–722.

[17] Alimurung MM. Heart disease in the Philippines. Am J Cardiol. 1962;10:362–366.

[18] Carapetis JR. Rheumatic heart disease in Asia. Circulation. 2008;118(25):2748–2753.

[19] Roos-Hesselink JW, Ruys TPE, Stein JI, on behalf of the ROPAC Investigators, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European society of cardiology. Eur Heart J. 2013;34(9):657–665.

[20] Pfaller B, Dave Javier A, Grewal J, et al. Risk associated with valvular regurgitation during pregnancy. J Am Coll Cardiol. 2021;77(21):2656–2664.

[21] French KA, Poppas A. Rheumatic heart disease in pregnancy: global challenges and clear opportunities. Circulation. United States. 2018;137(8):806–819.

[22] Madazli R, Sâl V, Çift T, et al. Pregnancy outcomes in women with heart disease. Arch Gynecol Obstet. 2010;281(1):29–34.

[23] Anwar AD, Winarno GNA, Anggraeni EN. Correlation between risk or severity of heart failure and outcome of pregnancy. IJGM. 2020;16(12):2075.

[24] Hardee I, Wright L, McCracken C, et al. Maternal and neonatal outcomes of pregnancies in women with congenital heart disease: a meta-analysis. J Am Heart Assoc. 2021;10(8):e017834.

[25] Puspa Pitaloka C, Secka A, Ermawati E, et al. Characteristics shifting of heart disease in pregnancy: a report from low Middle-income country. J Public Health Res. 2021;10(4):2137.

[26] Maranian AP, Supe MGS. Factors associated with clinical outcomes of gravidocardiac patients. Book of
[27] Canobbio MM, Warnes CA, Aboulhosn J, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American heart association. Circulation. 2017;135(8):e50–e87.

[28] Morgen CS, Bjørk C, Andersen PK, et al. Socioeconomic position and the risk of preterm birth—a study within the Danish national birth cohort. Int J Epidemiol. 2008;37(5):1109–1120.

[29] Cantarutti A, Franchi M, Monzio Compagnoni M, et al. Maternal’s education and the risk of several neonatal outcomes: an evidence from an Italian population-based study. BMC Pregnancy Childbirth. 2017;17(1):221.

[30] Jansen PW, Tiemeier H, Jaddoe VW, V, et al. Explaining educational inequalities in preterm birth: the generation R study. Arch Dis Child Fetal Neonatal Ed. 2009;94(1):F28–34.

[31] Liaw J, Walker B, Hall L, et al. Rheumatic heart disease in pregnancy and neonatal outcomes: a systematic review and meta-analysis. PLoS One. 2021;16(6):e0253581.

[32] Ciancimino L, Laganà AS, Chiofalo B, et al. Would it be too late? A retrospective case-control analysis to evaluate maternal-fetal outcomes in advanced maternal age. Arch Gynecol Obstet. 2014;290(6):1109–1114.

[33] Fuchs F, Monet B, Ducruet T, et al. Effect of maternal age on the risk of preterm birth: a large cohort study. PLoS One [Internet]. 2018;13(1):e0191002–e0191002.

[34] Kloster S, Andersen A-MN, Johnsen SP, et al. Advanced maternal age and risk of adverse perinatal outcome among women with congenital heart disease: a nationwide register-based cohort study. Paediatr Perinat Epidemiol. 2020;34(6):637–644.

[35] Furenäs E, Eriksson P, Wennerholm U-B, et al. Effect of maternal age and cardiac disease severity on outcome of pregnancy in women with congenital heart disease. Int J Cardiol. 2017;243:197–203.

[36] Weitzman A. The effects of women’s education on maternal health: evidence from Peru. Soc Sci Med. 2017;180:1–9.

[37] Britto RPdA, Florêncio TMT, Benedito Silva AA, et al. Influence of maternal height and weight on low birth weight: a cross-sectional study in poor communities of northeastern Brazil. PLoS One. 2013;8(11):e80159.

[38] Li C, Zhu N, Zeng L, et al. Effect of maternal pre-pregnancy underweight and average gestational weight gain on physical growth and intellectual development of early school-aged children. Sci Rep. 2018;8(1):12014.