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ORIGINAL ARTICLE



Maternal cardiac disease and perinatal outcomes in a single tertiary care center

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ABSTRACT

Objective: Maternal mortality in the U.S. has increased, with a substantial contribution from maternal cardiac disease. As a result of improved childhood survival, more women with congenital heart disease are reaching reproductive age leading to a growing high-risk obstetric population. We sought to determine the obstetrical and neonatal outcomes of women with maternal cardiac disease, including acquired cardiovascular disease and congenital heart disease.

Methods: We studied a retrospective cohort study of women that delivered from 2008 to 2013 ($N = 9026$). Singleton pregnancies without preexisting conditions were established as the unexposed group for this study. Maternal and neonatal outcomes were compared between the unexposed group ($N = 7277$) and women exposed to maternal (acquired or congenital) cardiac disease ($N = 139$) as well as only congenital heart disease ($N = 85$). Statistical comparisons used univariate/multivariable logistic and linear regression analysis controlling for confounders with $p < .05$ and 95% confidence intervals indicating statistical significance.

Results: Pregnancies complicated by maternal cardiac disease were associated with increased odds of preterm birth (<34 weeks, <37 weeks), intrauterine growth restriction (IUGR), need for assisted vaginal delivery, maternal ICU admission, and prolonged maternal hospitalization (>7 d). Neonatal outcomes including small for gestational age and Apgar score <7 at 5 min were increased in the pregnancies complicated by maternal cardiac disease. When pregnancies complicated by congenital heart disease were analyzed as a sub-group of the cohort, the results were similar. There were increased odds of preterm birth (<37 weeks), early-term delivery, need for assisted vaginal delivery, and prolonged hospitalization. Neonatal outcomes were only significant for small for gestational age.

Conclusion: We observed that in a select cohort of pregnancies complicated by maternal cardiac diseases (acquired or congenital), there were significant increases of adverse perinatal outcomes. Therefore, a multidisciplinary approach including maternal-fetal medicine specialists, cardiologists, obstetric anesthesia, and dedicated ancillary support is imperative for optimal care of this high-risk obstetrics population.

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Introduction

Maternal mortality in the United States has increased, with a substantial contribution from maternal cardiac disease. About 1–4% of pregnancies in the United States are affected by cardiovascular afflictions annually [1], representing the principal cause of mortality among pregnant and postpartum women in the United States (4.23 maternal deaths per 100,000 live

births) [2]. Because of the complex physiologic, genetic, and anatomical problems faced by these women, the American College of Cardiology, the American Heart Association, and the American College of Obstetricians and Gynecologists have recommended that all women with moderate or complex congenital heart disease receive obstetric care in a regional center with expertise in Adult Congenital Cardiology and

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Maternal-Fetal Medicine [3]. Despite the risks, most women with congenital and acquired cardiovascular disease can expect to carry a pregnancy successfully.

Congenital cardiac anomalies are the most common birth defects in humans, occurring in roughly 1% of all live births [4]. Technical advances in surgical, interventional, and medical care over the last 40 years have led to a remarkable increase in survival, and the majority of patients born today with congenital heart disease are now expected to reach adulthood. In the United States and other developed countries, there are now more adults with congenital heart disease than there are children with congenital heart disease [5,6]. One of the major medical challenges facing this new population of patients is the issue of reproductive health. Women with congenital heart disease are experiencing longer life expectancy and now more commonly reach reproductive age. In fact, recent studies have shown that from 2000 to 2010, the rate of pregnancies complicated with congenital heart disease increased from 6.4 to 9.0 per 10,000 delivery hospitalizations [7]. As the number of pregnancies complicated with congenital heart disease have increased so have the already elevated rates of maternal morbidity and mortality in the United States [8].

Major adaptations to the maternal cardiovascular system occur during normal pregnancy. Systemic blood volume and stroke volume increase considerably in the third trimester and during labor and delivery. These changes are essential to meet the increased metabolic demands of pregnancy. With regards to the maternal cardiac output, a major impact is seen at the time of birth and immediately after delivery, with an increase of CO by 30–50% and significant autotransfusion of blood well over 500 cc. Women without heart disease adapt to these changes without difficulty [9]. Failure to accommodate these changes may be the first sign of unrecognized heart disease [3]. Maternal arrhythmias, heart failure, and thromboembolic events are common complications in pregnancy in cardiac disease populations [1]. We have previously reported the association of pregnancies complicated with maternal arrhythmias and increased odds of intrauterine fetal growth restriction, as well as an association with placental abruption [10].

This study was designed to determine if women with cardiac disorders with or without congenital heart disease are at an increased odds of adverse perinatal outcomes compared to women without cardiac disorders. Establishing outcomes among these patients may help to identify risk factors or disease features associated with adverse outcomes that might represent important information in the management of these

complicated pregnancies with the ultimate goal to improve perinatal outcomes.

Materials and methods

This was a retrospective cohort study of women that received multidisciplinary care and delivered from 2008 to 2013 ($N=9026$) at the University of California, San Francisco. The Institutional review board from the Committee on Human Research at the University of California, San Francisco approved the study.

In 2008, the University of California, San Francisco Pregnancy and Cardiac Treatment (PACT) team was founded. The team is a multidisciplinary group consisting of maternal-fetal medicine and genetic specialists, obstetricians, cardiologists, anesthesiologists, and nurse practitioners. The PACT team meets formally once per month to discuss the specifics of the management of individual patients. The group has kept a record of all patients with maternal cardiac disease including patients with congenital heart disease. Maternal cardiac disease was defined as those having acquired or congenital cardiovascular disease (including valvular, cardiomyopathy, or arrhythmia) diagnosed before or during pregnancy. Women with congenital heart disease include those with defects in the structure of the heart or great vessels present at birth. University of California, San Francisco also maintains a perinatal database of all patients delivered. We compared patients cared for in the PACT program to a group unexposed to cardiac disease. Inclusion criteria for the unexposed and cardiac groups were as follows: singleton pregnancies with no history of preexisting medical conditions (hematological, pulmonary, gastrointestinal, endocrine, renal, rheumatological, oncological, or neurological disorders). Maternal and neonatal outcomes were compared between the unexposed group ($N=7277$) and women exposed to any maternal cardiac diseases ($N=139$). Subsequently, we compared maternal and neonatal outcomes between the unexposed group and women specifically with congenital heart disease ($N=85$). Maternal characteristics and pregnancy information were collected. The perinatal database is maintained with daily chart review by trained abstractors to ensure proper information gathering and to minimize missing data. The database was additionally reviewed by trained physicians for quality assurance.

We studied maternal and neonatal outcomes between women with a diagnosis of cardiac disease with and without congenital heart disease, as compared to the unexposed group. Obstetric outcomes of interest included mode of delivery, intrauterine fetal demise,

preeclampsia, intrauterine growth restriction (IUGR, defined as estimated fetal weight for gestational age $\leq$ 10th percentile), clinical chorioamnionitis, PPRM, postpartum hemorrhage (defined as estimated blood loss >500 ml after vaginal delivery or >1000 ml after cesarean delivery), need for blood transfusion, clinical diagnosis of placental abruption, and intensive care unit (ICU) admission. Neonatal outcomes included gestational age at delivery, preterm birth less than 37 weeks, birth weight, NICU admission, 5-min Apgar < 7 , and small for gestational age (SGA). We analyzed the data for composite maternal outcomes which included a diagnosis of preeclampsia, IUGR, intrauterine fetal demise, and placental abruption, and for neonatal composite outcomes which included preterm birth, SGA, 5-min Apgar < 7 , umbilical artery pH < 7.0 , and NICU admissions. Statistical comparisons were conducted using univariate and multivariable logistic and linear regression analysis controlling for potential confounders. Potential confounders were selected based on established clinical significance, these include maternal age, parity, race, ethnicity, gestational diabetes, and history of chronic hypertension. We defined statistical significance if $p < .05$ or if the 95% confidence interval did not include unity. Statistical analysis was performed using STATA v11.0 (StataCorp, College Station, TX).

Results

Our study demographics are presented in Table 1. We first analyzed pregnant women with the diagnosis of cardiac disease, including congenital heart disease.

Subsequently, we addressed a separate cohort including only pregnancies complicated by congenital heart disease.

Maternal cardiac disease

From our cohort, 7,416 patients met the inclusion criteria, of which 139 had maternal cardiac disease. Utilizing a multivariable analysis controlling for confounders previously specified, we found that women with maternal cardiac diseases were more likely to have a spontaneous and medically indicated preterm birth, IUGR, small for gestational age, and an Apgar score less than 7 at 5-min when compared with the unexposed group (Table 2). For patients with maternal cardiac disease, cesarean delivery rates were not different from the unexposed group nor were indications for cesarean section, but they were more likely to undergo an operative vaginal delivery (Tables 2 and 3). There were no differences in the rates of preterm rupture of membranes, fetal demise, chorioamnionitis, or postpartum hemorrhage in the maternal cardiac disease group (Table 2). However, they were more likely to undergo a preterm and early-term delivery. Mothers with maternal cardiac disease had a longer hospital stay (Table 2). Among the patients with maternal cardiac disease, only 2 (1.4%) required admission to the intensive care unit.

Congenital heart disease

When we analyzed the cohort of pregnancies complicated only by maternal congenital heart disease, we

Table 1. Cohort demographics characteristics.

Patient characteristics	Unexposed N = (7277)	Congenital heart disease N = (85)	
	N(%)	N(%)	N(%)
Maternal age in years			
Age less than 35	4735 (65.1%)	96 (69.1%)	63 (74%)
Age 35 or greater	2534 (34.9%)	43 (30.9%)	22 (26%)
Pre-pregnancy BMI			
Normal-BMI < 25	4011 (64.1%)	62 (55.9%)	35 (56%)
Overweight- $25 \leq \text{BMI} < 30$	1465 (23.4%)	27 (24.3%)	18 (29%)
Obese-BMI ≥ 30	779 (12.5%)	22 (19.8%)	10 (16%)
Gravida			
Mean ($\pm$ SD)	2.3 ($\pm$ 1.6)	2.6 ($\pm$ 1.7)	2.2 ($\pm$ 1.7)
Para			
Mean ($\pm$ SD)	0.7 ($\pm$ 1.0)	0.8 ($\pm$ 1.1)	0.6 ($\pm$ 1.1)
Race/Ethnicity			
Single race-White	3318 (45.6%)	67 (48.2%)	41 (48%)
Single race-Black	687 (9.4%)	14 (10.1%)	6 (7%)
Single/Mult race-Latina	971 (13.3%)	22 (15.8%)	17 (20%)
Single race-Asian/Pacific Islander	1296 (17.8%)	18 (12.9%)	8 (9%)
Other (Native, Mult, other)	1005 (13.8%)	18 (12.9%)	13 (15%)
Diabetes gestational			
No	6745 (92.7%)	129 (92.8%)	78 (92%)
Yes	531 (7.3%)	10 (7.2%)	7 (8%)
Chronic hypertension			
No	6939 (95.4%)	123 (88.5%)	79 (93%)
Yes	337 (4.6%)	16 (11.5%)*	6 (7%)

* $p < .0001$ from chi square.

found different outcomes compared to maternal cardiac disease overall. We found a difference in distribution with regards to the rate of medically indicated preterm births or IUGR (Table 2). Univariate and multivariate analysis showed a difference in the outcomes of interest such as rate of preterm birth before 37 weeks, early term delivery, operative vaginal delivery, SGA, and prolonged maternal hospitalization (>7 d). In the congenital group, the infants were more likely to be SGA but not identified prenatally as IUGR. Patients with congenital heart disease were more likely to undergo an operative vaginal delivery (Table 2). However, there were no differences in the rate of cesarean deliveries or indications for the procedure compared to the unexposed group (Tables 2 and 3). No differences in the rates of preterm

rupture of membranes, chorioamnionitis, or postpartum hemorrhage were observed between the congenital heart disease and unexposed groups. Importantly, early preterm delivery (less than 34 weeks) was not different when compared to the unexposed group. These patients were more likely to undergo a late preterm or early-term delivery. There were no fetal demises reported in the congenital group. None of the patients with congenital heart disease required ICU care (Table 2).

Discussion

Our study illustrates the need for a multidisciplinary approach to pregnancies complicated by maternal

Table 2. Perinatal outcomes in maternal cardiac disease or congenital heart disease alone compared to unexposed group.

Perinatal outcomes compared to unexposed group <i>Logistic regression model (unless otherwise indicated)</i>	Maternal cardiac disease		Congenital heart disease	
	MV logistic aOR (95 CI) ^a	<i>p</i>	MV logistic aOR (95 CI) ^a	<i>p</i>
Preeclampsia with and without severe features – <i>ref:</i> <i>Absence of preeclampsia</i>	0.73 (0.38–1.41)	.3451	0.75 (0.31–1.78)	.5130
Medically indicated preterm delivery – <i>ref:</i> term delivery <i>and spontaneous preterm delivery</i>	2.83 (1.59–5.05)	.0004	1.60 (0.63–4.08)	.3276
Preterm delivery at less than 34 weeks – <i>ref:</i> delivery at or <i>more than 34 weeks</i>	2.48 (1.33–4.62)	.0041	1.71 (0.68–4.32)	.2533
Preterm delivery at less than 37 weeks – <i>ref:</i> delivery at or <i>more than 37 weeks</i>	2.35 (1.54–3.58)	<.0001	1.88 (1.06–3.32)	.0312
Early term delivery between 37 and 38 weeks ^b – <i>ref:</i> <i>delivery at or more than 39 weeks</i>	2.25 (1.59–3.19)	<.0001	2.99 (1.93–4.63)	<.0001
Intrauterine growth restriction (IUGR) – <i>ref:</i> no IUGR <i>detected on US</i>	2.32 (1.15–4.67)	.0187	2.10 (0.82–5.38)	.1240
Small for gestational age <10%ile based on birth weight – <i>ref:</i> birth weight at or above 10%ile	1.61 (1.02–2.55)	.0429	2.13 (1.24–3.65)	.0061
Preterm rupture of membranes- <i>ref:</i> absence of PROM	1.16 (0.39–3.42)	.7900	1.62 (0.48–5.44)	.4400
Fetal demise – <i>ref:</i> live birth	0.88 (0.13–6.04)	.9000	<i>no fetal demises were observed in this group</i>	
Chorioamnionitis – <i>ref:</i> absence of chorioamnionitis	0.92 (0.44–1.91)	.8300	1.42 (0.67–3.00)	.3600
Postpartum hemorrhage – <i>ref:</i> no postpartum hemorrhage	1.17 (0.79–1.73)	.4300	1.15 (0.70–1.91)	.5700
Cesarean Delivery – <i>ref:</i> all vaginal deliveries	1.30 (0.88–1.92)	.1819	1.40 (0.86–2.28)	.1740
Operative Vaginal Delivery – <i>ref:</i> spontaneous vaginal delivery	3.92 (2.55–6.02)	<.0001	4.47 (2.69–7.43)	<.0001
Apgar score at 5-minute less than 7 – <i>ref:</i> Apgar of 7 or <i>higher</i>	1.94 (1.10–3.43)	.0218	1.47 (0.68–3.17)	.3251
NICU admission – <i>ref:</i> Well baby nursery	1.09 (0.70–1.68)	.7020	1.08 (0.63–1.84)	0.7763
Maternal hospital length of stay (LOS)(<i>linear regression model</i>)	2.10 (1.59–2.61)	<.0001	1.57 (0.94–2.20)	<.0001

^aAdjusted for maternal age, parity, race, ethnicity, gestational diabetes, and chronic hypertension.

^bEarly term is defined as 37 0/7–38 6/7 weeks of gestation.

Table 3. Mode of delivery in maternal cardiac disease or congenital heart disease alone compared to the unexposed group.

Mode of delivery	Unexposed <i>N</i> = (7277)	Maternal cardiac Disease <i>N</i> = (139)		Congenital heart disease <i>N</i> = (85)	
	<i>N</i> (%)	<i>N</i> (%)	<i>p</i> *	<i>N</i> (%)	<i>p</i> *
Delivery method			<.0001		<.0001
Spontaneous vaginal delivery	5061 (69.6%)	69 (49.6%)		38 (45%)	
Operative vaginal delivery	619 (8.5%)	31 (22.3%)		23 (27%)	
Cesarean delivery	1595 (21.9%)	39 (28.1%)		24 (28%)	
Indication for cesarean			1.000		1.000
Other indications for cesarean	1315 (82.4%)	32 (82.1%)		20 (83%)	
Intolerance of labor/Non-reassuring fetal heart rate tracing	280 (17.6%)	7 (17.9%)		4 (17%)	
			0.3491		0.7435
Other indications for cesarean	1182 (74.1%)	32 (82.1%)		19 (79%)	
Failed induction/Failure to progress	413 (25.9%)	7 (17.9%)		5 (21%)	
			0.9343		0.6740
Other indication for cesarean	1238 (77.6%)	31 (79.5%)		20 (83%)	
Elective repeat cesarean	357 (22.4%)	8 (20.5%)		4 (17%)	

**p* from chi square or *t*-test. *p* values from chi square tests are for overall difference when there are more than 2 level.

cardiac diseases with and without congenital heart disease. These results support similar findings made by other groups [3,11–13]. As presented in the results section, there is substantial evidence of increased odds of adverse perinatal outcomes in this selective population. Cardiovascular disease is increasingly recognized as a leading cause of pregnancy-related morbidity and mortality [14]. In fact, data from the state of California demonstrated that cardiovascular disease was the most common cause of pregnancy-related death, with the mortality rate for African American women being nearly 10 times higher, and women who died were more likely to be obese [15]. This highlights the importance of individualized multidisciplinary care as not all maternal cardiac disease patients are the same.

Our study further showed that pregnancies complicated by maternal cardiac conditions tend to have a higher risk for maternal complications such as preterm birth, both medically indicated or spontaneous at < 34 weeks or < 37 weeks, operative vaginal delivery (vacuum/forceps), prolonged hospitalization (> 7 d), and ICU admission. Interestingly, with regards to neonatal outcomes we observed increased odds of IUGR, Apgar score < 7 by 5 min, and SGA.

In the cohort of pregnancies complicated by congenital heart disease only, we found evidence of increased adverse perinatal outcomes, although different to maternal cardiac diseases. For instance, the rate of preterm birth and the early term was significantly increased as compared to the unexposed group. The rate of SGA was also significantly higher as compared to the unexposed group. In general, these pregnancies might require a medically indicated early delivery based on maternal condition. As a multidisciplinary approach, it is our practice to recommend an early-term delivery plan in this population, based on maternal cardiac assessment and echocardiogram findings.

We observed that vaginal delivery was successful and appears safe among our cohort of women with cardiac diseases with and without congenital heart disease. These findings are consistent with larger studies and reviews that have suggested that cesarean delivery be reserved for usual obstetric indications as well as those patients with severe heart failure, aortic root dilatation, or aortic dissection [10,13,16]. It is important to highlight that in our cohort we did not observe an increased rate of cesarean section, as in prior studies on congenital heart disease [17]. This could reflect our current practice to offer operative delivery to shorten the second stage of pregnancy and the patient willingness to have a vaginal delivery.

This is in line with updated recommendations of assisted second stage of labor in patients with pre-load-dependent lesions [18,19]. The lack of an increased rate for NICU admission and normal Apgar score (in the congenital heart disease-only group) could be an indication that perhaps this approach has led to successful vaginal deliveries without imposing more risk in maternal health and infant care.

With regards to perinatal surveillance and fetal assessment during pregnancy, our study showed a tendency to have neonates that were SGA. It is important to note that in the whole maternal cardiac disease cohort the rate of IUGR and SGA were significantly elevated, as evidenced in prior studies [17,20]. These findings support the approach of having serial fetal ultrasounds in pregnancies complicated with maternal cardiac diseases with and without congenital heart disease. In addition, pregnancies complicated with maternal congenital heart disease should require a fetal echocardiogram, as they have up to a 10% risk to have offspring affected by congenital heart disease [20]. With regards to maternal comorbidities during pregnancy, hypertension disorders have been associated with pregnancies affected by cardiac disorders. Hypertensive disorders of pregnancy are associated with an increased risk of myocardial infarction and heart failure [3]. Chronic hypertension was observed in the maternal cardiac group (Table 1), but we did not observe an increased rate of pre-eclampsia. Nevertheless, pregnancies complicated by cardiac diseases should be screened early in pregnancy for hypertensive disorders and comorbidities such as GDM [3].

The present study is not without limitations. As is the nature of a retrospective cohort, although minor, missing, or imprecise chart values could have added information bias to the analysis. Furthermore, the PACT patient population is heterogeneous by nature, introducing difficult to control within-group variability. We isolated patients with congenital heart disease to obtain a more homogenous cardiac group. However, in our cohort, there were less than 100 mothers with CHD, limiting the generalizability of these results. Nevertheless, the strength of this study resides in the large database of pregnancies complicated with maternal cardiac disorders being cared for at a single tertiary center with a multidisciplinary team approach along with a rather sizable group unexposed to maternal cardiac disease. Moreover, our current practice to offer earlier induction of labor and operative vaginal delivery to reduce morbidity invariably introduces bias in postnatal outcomes.

With the rising maternal congenital heart disease population reaching reproductive age and women

delaying pregnancy to the fourth and fifth decades of life, there is a palpable necessity for a multidisciplinary approach and a comprehensive medical program. The expanding field of cardio-obstetrics aims to meet this demand by focusing on the prevention, early detection, and management of cardiovascular disease in pregnancy with recommendations on the care of this patient population have been recently published [18,19,21–23]. Outcomes-based on these recommendations have not been published thus far. Our tertiary care center's multidisciplinary team approach includes experts from Cardiology, Maternal-Fetal Medicine, Obstetrics, Anesthesiology, and Nursing. We meet monthly to review plans of care and have a weekly multidisciplinary clinic. The clinic includes all the specialties in one space fostering cross-pollination and discussion of the plan of care with the patient at the center of the discussion. These multidisciplinary discussions are crucial to the risk stratification and plan of care for each pregnancy. This perhaps has allowed our team to provide safe vaginal deliveries and a baseline rate of NICU admissions and fetal demise. Prospective studies are also needed to address in detail different maternal cardiac afflictions and perinatal outcomes.

Disclosure statement

The authors report no conflict of interest. The results of this study were presented at the 3rd international congress on Cardiac Problems in Pregnancy (CPP 2014) in Venice, Italy on February 20–23, 2014.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author, KB. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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