Predictors for Complications in Pregnant Women with Heart Disease, a Retrospective Study

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Objective: Evaluate the CARPREG score in predicting cardiac, obstetric, and neonatal complications in pregnant women with heart disease.

Material and Method: This was a retrospective study between 2002 and 2011 at a tertiary care center and included 175 pregnant women with heart disease. Maternal and neonatal outcomes were assessed using Cardiac in Pregnancy Score (CARPREG), which included NYHA-class, systolic ejection fraction, left ventricular obstruction, and history of cardiac events.

Results: Rheumatic heart disease (n = 116, 66.3%) was the predominant cardiac problem. CARPREG score was 0, 1, >1 in 65.1%, 24.6%, and 10.3% pregnancies, respectively. Maternal cardiac events occurred in 27.4%. CARPREG score ≥1 was associated with an increased rate of cardiac events [odds ratio (OR) 6.76, 95% confidence interval (CI) 3.26 to 14.01]. Fetal complications occurred 24.4%. Neonatal birth weight <2,500 g was associated with CARPREG score ≥1 (OR 2.57, 95% CI 1.29 to 5.11).

Conclusion: Maternal cardiac events can be predicted using CARPREG risk index. In Thai population, rheumatic heart disease was the most frequent form of cardiac problems in pregnant women.

Keywords: Pregnancy, Heart disease, Complication, CARPREG score, Neonatal outcome

Heart disease is estimated to complicate approximately 1% of all pregnancies[1]. It is found to be a major cause of maternal deaths[2] and adverse fetal outcomes[3]. Treating these high-risk parturients during labor and delivery are challenge for obstetrician and anesthesiologist. Sui et al[4] proposed a risk index, CARPREG score to predict pregnancy outcomes in women with cardiac disease, which was further validated by Khairy et al[5] in a population predominated with congenital heart disease. In Thailand, the majority of pregnant women with cardiac disorder suffer from rheumatic heart disease (RHD)[6].

The purpose of the present study was to find out if Cardiac Disease in Pregnancy (CARPREG) score could predict cardiac, obstetric, and neonatal outcome in pregnant women with heart disease during labor and delivery at a tertiary care hospital in Thailand.

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Material and Method

After the Institutional Research Board (IRB) approval, the medical records of 175 pregnant women between January 2002 and December 2011 with heart diseases that had delivered at ≥28 weeks of gestation under anesthetic assistance were reviewed. Arrhythmias were defined as symptomatic tachyarrhythmia or bradyarrhythmia requiring treatment before pregnancy. Women with isolated mitral valve prolapse (mild or moderate mitral regurgitation) were excluded.

Baseline data collected at the first prenatal visit included age, gestational age, parity, cardiac lesion, New York Heart Association (NYHA) functional class, comorbid conditions, prior surgery/interventions, cyanosis (oxygen saturation <90%), medications, electrocardiography and echocardiography findings. Other variables gained were mode of delivery, anesthetic procedures, hospital, and intensive care unit (ICU) stay.

According to Siu et al[4] cardiac complications were classified as primary, secondary, and total events. The following symptoms were rated by experienced therapists as primary events (I) pulmonary edema

(chest radiograph or crackles over more than one-third of posterior lung fields), (II) sustained symptomatic tachy- or bradyarrhythmia requiring treatment, (III) stroke, (IV) cardiac arrest or (V) cardiac death. Secondary events included (I) need for invasive cardiac interventions during pregnancy or within 6 months after delivery, (II) non-sustained arrhythmia requiring therapy or (III) decline in ≥2 NYHA functional classes.

Obstetric complications included non-cardiac death, pregnancy-induced hypertension (PIH) defined as increase of systolic (>30 mmHg) and diastolic (>15 mmHg) blood pressure or postpartum hemorrhage (PPH) defined as blood loss >500 mL for vaginal delivery or >1,000 mL for cesarean delivery, which required transfusion or was accompanied by a drop in hemoglobin >20 g/L.

Neonatal complications were defined as premature birth (less than 37 weeks gestation), small-for-gestational-age birth weight (<10th percentile), respiratory distress syndrome, intraventricular hemorrhage, fetal death (>20 weeks gestation), neonatal death (within 28 days after birth).

Cardiac Disease in Pregnancy (CARPREG) score was assigned one point for each of the following variables (I) prior cardiac event (heart failure, transient ischemic attack, or stroke before pregnancy), (II) baseline NYHA functional class > II or cyanosis, (III) left heart obstruction (mitral valve area <2 cm², aortic valve area <1.5 cm² or peak left ventricular outflow tract gradient >30 mmHg), (IV) reduced systemic ventricular systolic function (ejection fraction <40%). The sum of predictor points (maximum scores of four) was used to predict maternal and neonatal events.

Statistical analysis

Data analysis was performed using SPSS (IBM, Armonk, NY, USA) version 17. Descriptive statistics were presented as mean ± standard deviation (SD), median (minimum, maximum) or number (%). Chi-square test, Fisher's exact tests were applied for comparing data when appropriate and displayed as odds ratios (OR) and 95% confidence intervals (95% CI). A p-value <0.05 was considered statistically significant.

Results

During the past 10 years, with 86,939 deliveries at authors' institution, cardiac diseases were found to complicate 651 (0.75%) pregnancies.

Anesthetic procedures were performed in 218 (33.5%) women. Of these in 175 cases, complete data were available, being analyzed in the present study. Six women had repeated pregnancies. One had twin pregnancy.

Maternal baseline characteristics and distribution of cardiac lesions are shown in Table 1. Most patients (81.7%) were 18 to 35 years old. Main cardiac diagnosis (66.3%) was rheumatic heart disease (RHD), mainly mitral valve dysfunction (65.5%). Septal defects were the most frequent congenital lesions (35, 77.8%). Sixty-seven (38.3%) women had cardiac interventions before pregnancy, including shunt ligation (n = 23), percutaneous balloon valvulotomy (n = 19), and valve replacement (n = 25). Anemia was the major problem (35; 81.4%) in women with associated medical diseases (43; 24.6%). Seventy-four (42.3%) women were on cardiac medications such as diuretics, digoxin, anticoagulant, antiplatelet, and antiarrhythmic drugs. At the first antenatal visit, 140 (80.0%) women were classified NYHA class I and 35 (20.0%) NYHA class II.

Maternal complications were summarized in Table 2. Primary cardiac events were observed in 33 (18.9%) women, 90.9% of them with acquired, 9.1% with congenital heart disease (CHD). Pulmonary edema was the most frequent event (18.3%). There

Table 1. Baseline maternal and disease characteristics

Characteristics	Total (n = 175)
Age (year)	29.3±5.75
Primigravidas	81 (46.3%)
NYHA functional class	
Class I	140 (80.0%)
Class II	35 (20.0%)
CARPREG score	
0	114 (65.1%)
1	43 (24.6%)
>1	18 (10.3%)
Acquired heart disease	130 (74.3%)
Single valve involvement	81 (62.4%)
Multiple valve involvement	35 (26.9%)
Cardiomyopathy	12 (9.2%)
Arrhythmia	2 (1.5%)
Congenital heart disease	45 (25.7%)
Non-cyanotic	43 (95.6%)
Cyanotic	2 (4.4%)

Values are mean ± SD or the number (%)
CARPREG = cardiac disease in pregnancy
NYHA = New York Heart Association

were five maternal deaths; two of them had severe pulmonary hypertension, one caused by Eisenmenger's syndrome and one by moderate pulmonary regurgitation. Two more deaths due to postpartum myocardial failure occurred in a mother with cardiomyopathy from severe mitral regurgitation and another one with moderate pulmonary hypertension from patent ductus arteriosus. Another woman with severe mitral stenosis (MS) and, severe aortic regurgitation having mitral plus aortic valve replacement (MVR, AVR) at the first postpartum day died from cardiac tamponade.

There were 37 secondary cardiac events. Six women who had no previous cardiac procedure needed urgent intervention. Four of them had percutaneous balloon mitral valvulotomy at 22 to 27 weeks of gestational age, another one at seven weeks postpartum. Deterioration of NYHA class (≥2 classes) occurred in 33 women (18.9%). Obstetric complications were found in 29 (16.6%) cases with pregnancy-induced hypertension prevailing (13.7%).

Thirty-five women (20.0%) delivered vaginally, spontaneously in 11 (31.4%) and instrument assisted in 24 (68.6%) cases; epidural anesthesia was performed in 33 patients, two of them with combined spinal epidural block. Patients with cesarean section (n = 140) had general (42.1%), spinal (33.6%), epidural

Table 2. Cardiac, obstetric, and neonatal events

	Total (n = 175[a])
Cardiac events[b]	48 (27.4%)
Primary	33 (18.9%)
Pulmonary edema	32 (18.3%)
Symptomatic arrhythmia	7 (4.0%)
Stroke	1 (0.6%)
Cardiac arrest	5 (2.9%)
Cardiac death	5 (2.9%)
Secondary	37 (21.1%)
Change in NYHA by ≥2	33 (18.9%)
Need for urgent cardiac procedures	6 (3.4%)
Obstetric events[b]	29 (16.6%)
Pregnancy-induced hypertension	24 (13.7%)
Postpartum hemorrhage	5 (2.9%)
Neonatal events[b]	43 (24.4%)
Premature birth	29 (16.5%)
Small for gestational age	17 (9.7%)
Respiratory distress syndrome	5 (2.8%)
Neonatal death	1 (0.6%)

Values are the number (%)
NYHA = New York Heart Association
[a] n = 176 for neonatal complications (1 twin neonates)
[b] At least one of the following

(20.0%), or combined general plus epidural anesthesia (4.3%) respectively.

Neonatal outcomes are summarized in Table 2. There were 43 (24.4%) neonatal complications with premature birth (<37 weeks gestation) being the predominant event (29, 16.5%). Five neonates were born at <32 weeks' gestation without relevant complication. There was one death in a vaginally delivered premature infant (28 week; 940 g) due to respiratory distress syndrome.

Six women with CHD and 30 women with acquired heart disease were classified NYHA class III/IV at delivery, required cesarean section more often compared to NYHA class I/II (91.7% vs. 77.0%, $p = 0.05$), the indication being heart disease in 51.5% and 10.1% ($p<0.001$), respectively. The requirement for general anesthesia was higher in these patients (72.2% vs. 22.3%, $p<0.001$). Furthermore, there were more fetal complications (47.2% vs. 18.7%, $p<0.001$), more low birth weight (<2.5 kg) newborns (44.4 vs. 22.3%, $p = 0.008$), longer hospital stays (12 ds vs. 8 ds, $p = 0.004$), and more ICU stays (66.7% vs. 12.9%, $p = 0.016$) in patients with NYHA class III/IV compared I/II. However, obstetric complications were similar in both groups.

CARPREG score was 0, 1, >1 in 114 (65.1%), 43 (24.6%), and 18 (10.3%) pregnancies, respectively. There were no patients with scores >2 in the present study. The estimated risk of primary cardiac events in pregnancies with 0, 1, and >1 points was 0%, 35%, and 95%, respectively. All five cardiac deaths occurred in pregnancies with risk score ≥1. Primary, secondary, and total cardiac events were associated with CARPREG score (Table 3). CARPREG score ≥1 was associated with increased rate of cardiac events. The score was not predictive for other obstetric or neonatal outcome parameters, except neonatal birth weight <2,500 g (score ≥1; OR 2.57, 95% CI 1.29-5.11, $p = 0.006$). Cesarean sections were mainly performed in general anesthesia (score ≥1; OR 6.7, 95% CI 2.94-15.29, $p<0.001$).

Discussion

The proportion of pregnant women with heart diseases have remained relatively constant for several decades, the incidence reported between 0.25 and 3.1%[7-11]. The authors found an incidence of 0.75%. The prevalence of pregnancies complicated by rheumatic heart disease (RHD) has decreased in developed countries. However, in developing countries the incidence of RHD is still higher than congenital

Table 3. Outcomes associated with CARPREG score

Outcomes	Score		Crude OR (95% CI)	p-value
	0 (n = 114)	≥1 (n = 61)		
Primary cardiac events (n = 33)	7.9%	39.3%	7.57 (3.23, 17.76)	<0.001
Secondary cardiac events (n = 37)	10.5%	41.0%	5.90 (2.69, 12.96)	<0.001
Total cardiac events (n = 48)	14.0%	52.5%	6.76 (3.26, 14.01)	<0.001
Obstetric events (n = 29)	14.9%	19.7%	1.40 (0.62, 3.16)	0.52
Neonatal events (n = 43)	20.2%	32.8%	1.93 (0.96, 3.90)	0.07
Birth weight <2,500 g (n = 47)	20.2%	39.3%	2.57 (1.29, 5.11)	0.006
GA for CS (n = 65)	33.0%	76.7%	6.70 (2.94, 15.29)	<0.001

CARPREG = cardiac disease in pregnancy; GA = general anesthesia; CS = cesarean section

heart disease (CHD) with 88% and 66.3%[9] respectively, mitral valve being predominantly affected[9,10]. In the present study, septal defects were the most frequent form of CHD (77.8%), which is similar to the report of Bhatla et al (62.5%)[9]. Patients in the present study were mainly NYHA class I/II, more than reported by Bhatla et al (80.2%)[9] or Sawhney et al (77.4%)[10].

The authors observed cardiac events in 27.4% of all cases, comparable to the results of other studies with high rate of RHD[9,12]. The rate is higher compared to studies conducted in populations predominated by CHD[4,13-17], with the exception of one report[5]. The most frequent primary cardiac event in authors' and other studies[4,5,13,16,17] was pulmonary edema. Patients in the present study were NYHA class I/II at the first antenatal visit, 18.9% of them deteriorating to ≥2 functional classes, which is comparable to 22.7% in a similar study population[9]. The rate was higher compared to reports in populations with mainly CHD[4,5].

Previously, Sui et al[4] validated CARPREG score 0, 1 and >1 points being associated with cardiac event rates of 4%, 31% and 69%, respectively, compared to authors' rates of 14%, 41.9% and 77.8%, respectively. Though their patients predominantly had CHD compared to RHD in the present study, their results can be applied to authors' findings. A higher score is associated with a higher rate of primary, secondary, and total cardiac events.

Compared to Sui et al[4], the rate of pregnancy-induced hypertension was higher (13.7% vs. 4%), whereas the incidence of postpartum hemorrhage was comparable (2.9% vs. 3.2%). CARPREG score did not predict these events.

In the present study, 33.5% of pregnant women with heart disease received anesthetic care, compared to 80% in the study of Goldszmidt et al[11].

In the present study 66.7% of the women performed instrumental assisted vaginal delivery, most of them receiving epidural analgesia in order to avoid stress response in these high-risk cardiac patients. Cesarean section rate was 27.5%, being below authors' institution's overall rate of 37.9% and the 52.2% reported by Langesaeter et al[18]; it is clinically indicated in high-risk, deteriorating patients[19]. In 22.1% of patients in the present study, cardiac event was the indication for cesarean section compared to only 2.6% in the study of Goldszmidt et al[11]. Compared to others[11,18], authors performed more general anesthesia (44.8% vs. 9.3%, respectively) particularly in patients with hemodynamic instability, intractable heart failure or inability to tolerate the supine position, most of them were NYHA class III/IV. However, Goldszmidt et al[11] and Langesaeter et al[18] preferred regional anesthesia for high-risk patients (80%, 86.4%, respectively). CARPREG score was associated with the choice of anesthesia: general anesthesia was most often performed in patients with score ≥1.

Maternal heart disease is associated with an increased risk of fetal complications[6,20]. The authors found 24.4% of these complications, which was similar (20-27.8%) to other studies[4,5,14].

The perinatal outcome in patients with RHD depends on functional cardiac status of the mother, with worsened outcome especially in NYHA class III/IV[9,10]. In fact the authors observed more neonatal complications and low birth weight (<2,500 g) in patients with NYHA class III/IV compared to NYHA class I/II. RHD patients who underwent corrective valve interventions prior to pregnancy or during peripartum period had better maternal and fetal outcomes, which was in accordance to other studies[9,10]. Therefore, these procedures have

to be considered when indicated. Regarding neonatal outcome CARPREG score only predicted birth weight <2,500 g.

The present study has some limitations. The authors included only patients subjected to anesthetic procedures. Incomplete records led to exclusion, resulting in the possibility of information bias. As a tertiary referral center, authors' hospital may not be represented for other obstetric facilities in this country.

In conclusion, the present study showed that CARPREG risk index could predict maternal cardiac events and neonatal birth weight <2,500 g, but no further outcome parameters, neither for the mother nor for the newborn. Multidisciplinary care including cardiologists, obstetricians, anesthesiologists, and neonatologists can minimize the risks. To gain generally applicable standards, prospective multicenter studies are required.

What is already known on this topic?

Heart disease is found to be a major cause of maternal deaths and adverse fetal outcomes. Cardiac in Pregnancy Score (CARPREG) score, which includes NYHA-class, systolic ejection fraction, left ventricular obstruction and history of cardiac events, was proposed to predict pregnancy outcome in women predominated by congenital heart disease.

What this study adds?

Rheumatic heart disease was the predominant cardiac problem in Thai pregnant women. CARPREG risk index can predict maternal cardiac events in this population. CARPREG score ≥1 was associated with an increased rate of cardiac events and neonatal birth weight <2,500 g.

Potential conflicts of interest

None.

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การศึกษาย้อนหลังถึงปัจจัยที่ใช้ทำนายภาวะแทรกซ้อนในสตรีตั้งครรภ์ที่มีโรคหัวใจ

เสาวภาคย์ จำปาทอง, ชุลีพร สิริทวีสิทธิ์, นุชสโรช เพ็ญไพศิษฎ์, สุวรรณี สุรเศรณีวงศ์, Benno von Bormann, วิทยา ถิฐาพันธ์, สุดตา ปรักกโมดม

วัตถุประสงค์: เพื่อประเมินคะแนน CARPREG ในการทำนายภาวะแทรกซ้อนของระบบหัวใจ ทางสูติกรรม และในทารกของ สตรีตั้งครรภ์ที่มีโรคหัวใจ

วัสดุและวิธีการ: เป็นการศึกษาแบบย้อนหลังในสตรีตั้งครรภ์ที่มีโรคหัวใจ 175 ราย ในช่วงเวลา 10 ปี ระหว่าง พ.ศ. 2545 ถึง พ.ศ. 2554 ณ ศูนย์ตติยภูมิ โดยการใช้คะแนน CARPREG ซึ่งประกอบด้วย ระดับ NYHA การบีบของหัวใจช่วง systolic การอุดกั้นหัวใจห้อง ventricle ซ้าย และประวัติการเกิดเหตุการณ์ของระบบหัวใจ ในการประเมินผลที่เกิดขึ้นต่อมารดาและทารก

ผลการศึกษา: พบโรคหัวใจรูมาติกมากที่สุด 116 ราย คิดเป็นร้อยละ 66.3 พบคะแนน CARPREG 0, 1 และมากกว่าหรือเท่ากับ 1 คิดเป็นร้อยละ 65.1, 24.6 และ 10.3 ของสตรีตั้งครรภ์ตามลำดับ พบภาวะแทรกซ้อนของระบบหัวใจในมารดาคิดเป็นร้อยละ 27.4 คะแนน CARPREG ที่มากกว่าหรือเท่ากับ 1 เกี่ยวข้องกับการเพิ่มขึ้นของภาวะแทรกซ้อนของระบบหัวใจ [odds ratio (OR) 6.76, 95% confidence interval (CI) 3.26 to 14.01] พบภาวะแทรกซ้อนในทารกคิดเป็นร้อยละ 24.4 น้ำหนักทารก แรกเกิดที่น้อยกว่า 2,500 กรัม เกี่ยวข้องกับคะแนน CARPREG ที่มากกว่าหรือเท่ากับ 1 (OR 2.57, 95% CI 1.29 to 5.11)

สรุป: คะแนน CARPREG สามารถใช้ทำนายภาวะแทรกซ้อนของระบบหัวใจในสตรีตั้งครรภ์ได้ ในสตรีตั้งครรภ์ไทยพบโรคหัวใจ รูมาติกมากที่สุด