Archives of Gynecology and Obstetrics (2019) 300:1613–1619
https://doi.org/10.1007/s00404-019-05350-2

MATERNAL-FETAL MEDICINE

Precipitating factors and maternal and neonatal outcomes of heart failure in pregnancy: a retrospective analysis in a large tertiary hospital in China, 2012–2017

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Received: 13 April 2019 / Accepted: 15 October 2019 / Published online: 28 October 2019

Abstract

Purpose To investigate the precipitating factors of heart failure (HF) and to investigate the maternal and neonatal outcomes in pregnant women with HF.

Methods We reviewed the medical records of pregnant women with HF who were treated at West China Second University Hospital between September 2012 and September 2017. We recorded baseline characteristics, onset and treatment of HF, comorbidities, modes of delivery, and maternal and fetal mortality and morbidity. Chi-square tests or Fisher's exact tests were used to explore the comorbidities in different subgroups.

Results Seventy pregnant women with HF were identified. The most common pregnancy-specific conditions were severe preeclampsia (36/70, 51.43%) and multiple pregnancies (16/70, 22.86%). The most common nonpregnancy-specific conditions were lung infections (34/70, 48.57%) and cardiac problems (25/70, 35.71%). Sixty patients (85.71%) developed HF during pregnancy. Sixty-seven pregnancies (95.71%) ended in cesarean section. Three maternal deaths (4.29%) from HF were recorded. Of the 87 fetuses, three fetuses (3.45%) ended in miscarriages and stillbirth occurred in 5.75% of fetuses. The mean birth weight of a neonate was 2174.49 ± 609.57 (817–3430) g. There were eight neonatal deaths (8/79, 10.13%). The incidence of lung infection ($P = 0.031$) or cardiac problems ($P = 0.044$) differs between patients with NYHA classes II and patients with NYHA classes III/IV. The incidence of lung infection ($P = 0.006$) was also different in patients with prenatal HF and patients with postpartum HF.

Conclusion Peripartum HF is associated with high maternal and neonatal morbidity and mortality. Hypertensive disorders in pregnancy, lung infections, and cardiac problems are most common precipitating factors of HF in pregnancy.

Keywords Pregnancy · Heart failure · Comorbidities · Mortality · Morbidity

Introduction

Pregnancy is characterized by significant increases in both cardiac output and blood volume, which stress on the heart mostly during the 32nd to 34th gestational weeks, at the time of labor, and after delivery [1]. Although these changes are well tolerated in healthy women, women with a known heart problem or with an underlying heart disease may suffer severe adverse consequences such as heart failure (HF), which is defined as the onset of symptoms and signs secondary to abnormal cardiac function [2]. Reported precipitating factors of HF during pregnancy include congenital or acquired structural heart disease, arrhythmia, infections, hypertensive disorders, anemia, and thyroid- related disorders [3].

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Despite high rates of maternal and neonatal morbidity and mortality associated with HF during pregnancy, there is little information in the literature on this subject. In our present study, we retrospectively reviewed and analyzed onset and treatment of HF, comorbidities, modes of delivery, and maternal and fetal mortality and morbidities in 70 pregnant women with HF treated in our institution in west China over a 5-year period.

Materials and methods

This retrospective study was approved by the Institutional Review Board of West China Second University Hospital. We reviewed the medical records of pregnant women who were admitted and delivered at West China Second University Hospital, a tertiary referral center, between September 2012 and September 2017. Based on discharge diagnosis, seventy pregnant women with HF were identified by searching the hospital record database. Data were collected through review of electronic medical records and telephone interview. Informed consent was obtained from all individual participants included in the study.

Baseline characteristics were reviewed, including age, gravidity, parity, place of residence, body weight and height, type of cardiac disease, previous cardiac surgery or medication, and gestational weeks at delivery. New York Heart Association (NYHA) class was assigned at admission. The comorbidities such as hypertension, preeclampsia, eclampsia, thyroid-related disorders, and multiple pregnancies were also recorded in the current study.

The time of occurrence, medication ways, and treatments of peripartum HF were recorded. Clinical signs of HF included dyspnea, NYHA class III or class IV, orthopnea, and rales [4]. Diagnosis of HF was done by the cardiologist through the history taken, physical examination, and auxiliary examinations. During HF, patient evaluation was performed by a multidisciplinary team, consisting of obstetricians, cardiologists, and intensive care (ICU) physicians. Complete general physical, cardiovascular, electrocardiography (ECG), transthoracic echocardiography, oxygen saturation, and obstetric examinations were performed. When the cardiac function deteriorated, NYHA class was assigned again. Laboratory investigations, such as N-terminal BNP, myocardial enzyme, hemoglobin, and other biological indices were examined. Positive inotropic agents (such as Cedilanid and Milrinone) were used to increase contractility of the heart. Morphine and diuretics (such as hydrochlorothiazide and furosemide) were used to reduce heart load. Mask oxygen inhalation or tracheal intubation was administrated to improve oxygenation. Arterial, central venous, and/or pulmonary artery monitoring was performed to optimally manage the mother. Hemodynamic measurements and blood gas analyses were carried out in all cases during treatment. Antibiotic prophylaxis was provided for endocarditis prophylaxis.

Modes of delivery and anesthesia way were documented. We also recorded whether or not the prophylactic operations for preventing postpartum hemorrhage (such as uterine artery ligation, B-Lynch saturation, and Bakri balloon tamponade) were performed.

Patients and their neonates were followed up for 6 weeks after delivery. Fetal and neonatal complications included miscarriage (spontaneous fetal loss before 20 gestational weeks, stillbirth (fetal death at or after 20 gestational weeks), prematurity (< 37 gestational weeks), small for gestational age (SGA) birth weight (< 10th percentile), or neonatal death (death within 28 days after birth).

The data were analyzed using SPSS version 20.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics for nominal data were expressed as absolute numbers and percentages. Continuous variables with normal distribution were presented by mean ± standard deviation (SD). Medians (range) were computed for continuous variables with non-normal distribution. Chi-square tests or Fisher's exact tests were used to explore the comorbidities in different subgroups. *P* values < 0.05 were considered statistically significant.

Results

From September 2012 to September 2017, 55,235 pregnant women were admitted and delivered at our institution and 70 patients (0.13%, 70/55, 235) developed HF. The mean maternal age of these 70 patients was 29.46 ± 5.54 (17–43) years old. Forty patients (40/70, 57.14%) came from rural areas, and 28 patients (28/70, 40.00%) had no regular care. Fifty-two patients (52/70, 74.29%) were transferred to our hospital due to acute HF or other severe maternal complications. Most of the patients were primiparas and had NYHA class III or class IV on admission. Fifty-two patients (52/70, 74.29%) were transferred to ICU during treatment, and most of them were transferred after delivery. The left ventricular ejection fraction (LVEF) was 48.00 ± 11.21%. The hemoglobin was 90.50 ± 28.64 g/L. The median value of BNP was 9457.00 pg/ml (725.00–32,456.00). The time of hospital stay was 10.59 ± 5.03 days (4–25 days). Baseline characteristics of all the women in the study are shown in Table 1.

We classified the comorbidities in pregnant women with HF as pregnancy-specific conditions and nonpregnancy-specific conditions. The most common pregnancy-specific conditions were severe preeclampsia (36/70, 51.43%), multiple pregnancies (16/70, 22.86%), intrahepatic cholestasis in pregnancy (ICP) (8/70, 11.43%), gestational diabetes mellitus (GDM) (5/70, 7.14%), placental abruption (3/70, 4.29%), and premature rupture of membrane (PROM) (1/70, 1.43%).

Table 1 Characteristics of 70 pregnant patients diagnosed with heart failure

Characteristic ($n=70$)	Mean ± SD (range) or median (range) or n (%)
Age (years)	
< 18	2 (2.86%)
18–35	60 (85.71%)
≥ 35	8 (11.43%)
Gravidity	2 (1–7)
Previous parity	0 (0–4)
Height (cm)	157 ± 7.77 (119–172)
Weight (kg)	68.29 ± 12.23 (40–90)
Blood pressure on admission (mmHg)	
Systolic pressure	147.50 ± 29.32 (89–210)
Diastolic pressure	89.89 ± 18.91 (55–135)
Heart rate on admission	106.50 ± 18.12 (70–148)
NYHA class on admission	
II	13 (18.57%)
III	36 (51.43%)
IV	21 (30.00%)
Oxygen saturation on admission (%)	93.38 (49–99)
LVEF on admission (%)	55.40 ± 4.54 (30–73)
Onset of HF	
< 20 weeks	2 (2.86%)
20–27^{+6} weeks	7 (10.00%)
28–31^{+6} weeks	8 (11.43%)
32–36^{+6} weeks	31 (44.29%)
≥ 37 weeks	12 (17.14%)
After delivery	10 (14.29)
Transfer to ICU	52 (74.29%)
Time of hospital stay (d)	10.59 ± 5.03 (4–25)

NYHA class New York Heart Association class; *LVEF* left ventricular ejection fraction; *HF* heart failure; *ICU* intensive care unit

The most common nonpregnancy-specific conditions were lung infections (34/70, 48.57%), cardiac problems (25/70, 35.71%), moderate/severe anemia (16/70, 22.86%), renal failure (7/70, 10%), chronic hypertension (6/70, 85.71%), hyperthyroidism (5/70, 7.14%), and hypothyroidism (4/70, 5.71%). Besides, one patient (1.43%) was diagnosed with cretinism, who was only 115 centimeter in height.

There were 42 cases of hypertensive disorders in pregnancy, and 36 cases (36/42, 85.71%) of them were severe preeclampsia. Among cases of severe preeclampsia, two were preeclampsia superimposed upon chronic hypertension. Four additional cases were chronic hypertension, that is, a total of six patients (6/42, 14.29%) suffered from chronic hypertension before pregnancy. Another two cases were gestational hypertension.

Among 25 patients complicated with cardiac problems, seven cases (7/25, 28.00%) suffered from peripartum cardiomyopathy (PPCM), in which one patient had PPCM and left HF during previous pregnancy 5 years ago. Other cardiac problem included six cases (6/25, 24.00%) of untreated congenital malformations (five valvular disease, one ductus arteriosus, one aortic coarctation), six cases (6/25, 24.00%) of arrhythmia (including intermittent pre-excitation syndrome (IPS), atrioventricular block, bradycardia, and tachycardia), four cases (4/25, 16.00%) of dilated cardiomyopathy, three cases (3/25, 12.00%) of hyperthyroid heart disease, two cases (2/25, 8.00%) of hypertensive heart disease and one case (1/25, 4.00%) of rheumatic heart disease. None patient with congenital heart disease underwent cardiac surgery.

Sixteen cases of HF (16/70, 22.86%) were multiple pregnancy in our study. Eleven cases were in vitro fertilization, and the remaining five were natural pregnancy. Nearly half of the pregnant women with HF suffered lung infection. The patients developed symptoms of pneumonia, including purulent, productive cough, fever, and dyspnea. However, none developed sepsis.

Sixty cases (60/70, 85.71%) developed HF during pregnancy. Mean onset of HF was at 32.67 ± 4.68 gestational weeks. Two cases of HF (2/70, 2.86%) occurred before 20 gestational weeks, 46 cases (46/70, 65.71%) occurred between 20 and 36 + 6 gestational weeks, and 12 cases (12/70, 12.00%) occurred after 37 gestational weeks. Ten cases (10/70, 14.29%) developed HF after delivery. Among these ten cases, nine patients had HF within three days after delivery and one patient developed HF in the fourth day postpartum.

Mean gestational age at delivery was 32.93 ± 4.51 gestational weeks. Two cases (2/70, 2.86%) had miscarriages due to severe acute left HF at 17 and 18 gestational weeks, respectively. Fifty-four cases (54/70, 77.14%) were premature deliveries, and 14 cases (14/70, 20.00%) were term deliveries. All premature deliveries were induced because of severe maternal complication.

Sixty-seven pregnancies (67/70, 95.71%) ended in cesarean section (CS). CS was performed under general anesthesia or combined spinal epidural anesthesia. A preventive antibiotic was given. Preventive procedures to avoid postpartum hemorrhage were performed in 29 cases (29/67, 43.28%) during CS, including 17 uterine artery ligation, 8 B-Lynch suture, and 6 Bakri balloon tamponade. All succeeded and no postpartum hemorrhage occurred. Vaginal delivery was induced in two pregnancies (2/70, 2.86%). A hysterectomy was performed in the remaining one patient (1/70, 1.43%) who underwent severe placenta abruption with intrauterine fetal death, DIC, and uteroplacental apoplexy.

Eleven patients received mechanical ventilation in ICU. Diuretics and Morphine were used to reduce heart load. In patients with low LVEF, positive inotropic agents (e.g. Cedilanid) were used to increase contractility of heart. Despite active treatment, three maternal deaths from HF occurred postpartum in our study; overall mortality was 4.29% (3/70),

while the maternal mortality of normal pregnant women were 21.7/10^5 in China in 2014 [5]. All these three patients had severe heart diseases with cardiac function decompensation (Table 2).

There were 70 pregnancies with 87 fetuses (54 singletons, 15 twins, and 1 triple). Two pregnancies with three fetuses (3/87, 3.45%) (a singleton and a pair of twins) ended in miscarriages at 17 weeks and 18 gestational weeks. Stillbirth occurred in 5.75% of fetuses (5/87). There were 79 live births (79/87, 90.80%) in the study with 79.75% (63/79) premature fetuses and 10.13% (8/79) neonatal deaths. Apgar score of < 7 at one minute was found in 13 neonates (13/79, 16.46%). All the Apgar scores of the newborns who died within 28 days after birth were below 7 within five minutes after birth. Among them, six newborns (6/8, 75.00%) suffered from severe asphyxia with Apgar score ≤ 3. The other two newborns had a relatively small gestational age of 27 weeks. Mean neonatal birth weight was 2174.49 ± 609.57 (817–3430) g. SGA was found in 16 fetuses (16/79, 22.86%). Newborns whose mothers had congenital heart problems received transthoracic cardiograph. No apparent cardiac anomalies were found in the offspring.

We explored primary comorbidities of pregnant women with HF in different subgroups. The incidence of lung infection ($P = 0.031$) or cardiac problems ($P = 0.044$) differs between patients with NYHA classes II and patients with NYHA classes III/IV on admission. The incidence of lung infection ($P = 0.006$) was also different in patients with prenatal HF and patients with postpartum HF (Table 3).

Discussion

Both cardiac output and blood volume increase by 30–50% during late pregnancy, and further fluctuations in cardiac output occurred at the time of labor and after delivery. Pregnant women are prone to cardiac accidents during third trimester, delivery, and immediate postpartum period [3, 6]. In the present study, 77% (54/70) women developed HF at 28–37 gestational weeks, which suggested that a

Table 2 Maternal deaths among patients with HF

Patients	Age (years)	Gestational age at delivery (gestational weeks)	Primary comorbidities
1	17	32	Congenital heart disease (ventricular septal defect), Eisenmenger syndrome, severe preeclampsia, lung infection, multiple organ failure
2	26	35^{+2}	Congenital heart disease (ventricular septal defect and aortic coarctation), Eisenmenger syndrome, severe preeclampsia, lung infection, multiple organ failure
3	25	17	Congenital heart disease (aneurysm of membranous ventricular septum), dilated cardiomyopathy, atrioventricular block, Eisenmenger syndrome, lung infection, multiple organ failure

Table 3 Primary comorbidities of pregnant women with HF in different subgroups

Subgroups		Pregnancy-specific conditions		Nonpregnancy-specific conditions		
		Severe preeclampsia	Multiple pregnancies	Lung infection	Cardiac problems	Moderate/severe anemia
NYHA class on admission (class II vs class III/IV)	χ^2	0.037	1.252	4.629	4.064	1.160
	P	0.847	0.263	0.031*	0.044*	0.281
Onset of HF (during pregnancy vs after delivery)	χ^2	0.193	0.000	7.467	0.000	0.408
	P	0.6601	1.000	0.006*	1.000	0.296
Time of delivery (before 32 vs at or after 32 gestational weeks)	χ^2	0.165	0.160	0.000	0.106	1.105
	P	0.684	0.689	1.000	0.744	0.293
Maternal outcomes (survival vs death)	χ^2	0.000	–	0.000	3.096	–
	P	1.000	1.000	1.000	0.079	0.547
Fetal outcomes (live birth vs miscarriage or stillbirth)	χ^2	2.802	0.000	0.635	0.691	1.089
	P	0.094	1.000	0.426	0.406	0.297
Apgar score in live birth at 1 min (< 7 vs ≥ 7)	χ^2	1.609	0.000	0.402	0.000	0.000
	P	0.205	1.000	0.526	1.000	1.000

*$P < 0.05$

gradual increase in maternal cardiac workload precipitated the onset of HF during the third trimester, the same as Fu's report [7]. From 1997 to 2010, there was only one case of perinatal HF in every 5719 deliveries in Sweden, increasing from one in 6936 deliveries during 1997–2003 to one in 4994 deliveries during 2004–2010 [8]. The rate of peripartum HF was one in every 789 deliveries in our present study.

Barasa et al. [8] reported HF in pregnancy and after delivery was linked to preeclampsia, obesity, twin deliveries, and mothers born in low- and middle-income countries. Our study identified hypertensive disorders in pregnancy (including preeclampsia), lung infection, and heart diseases to be top three comorbidities or risk factors for HF. Other precipitating factors of HF included multiple pregnancies, anemia, and hyperthyroidism etc.

Preeclampsia is associated with a fourfold increased female-specific risk of asymptomatic cardiac abnormalities, and it precipitated HF in women with preexisting heart disease resulting in a rate as high as 30% of the patients [7, 9]. Peripartum cardiomyopathy was found in one-third of the patients complicated with preeclampsia and HF [10]. Our study found that 51.43% of pregnant women with HF were complicated with severe preeclampsia. These findings indicate that patients with potential heart disease who develop preeclampsia should be monitored carefully to avoid HF.

Lung infection (48.57%) was another major comorbidity of HF in our study, which aggravated the existing heart load, especially when patients were complicated with heart diseases, gestational hypertensive disease, or multiple pregnancies. Decreased heart function, lung congestion, and lung infection promote each other, forming a vicious cycle. This finding gave us an insight with regard to the importance of anti-infection treatment of HF.

Although hemodynamic changes are well tolerated in healthy pregnant women, women with cardiac diseases are prone to develop HF. Baseline NYHA class greater than II, cyanosis, reduced left ventricular systolic function, left heart outflow tract obstruction, signs of HF before pregnancy, cardiomyopathy, and pulmonary hypertension were reported to be predictive risk factors for HF [7, 11, 12]. Fifty-seven patients of HF (57/70, 81.43%) were scored ≥ 1 at admission in our study according to the CARPREG scoring system [7, 11, 12]. There were two peaks of heart failure onset: one peak at the end of the second and beginning of the third trimester, and another peak around delivery. Women complicated with heart disease and preeclampsia had a risk of 30% to develop HF during their pregnancy [11]. HF was reported to account for 35% of female cardiovascular mortality [13]. In our study, 35.71% patients with HF suffered from cardiac diseases. All three deaths in our study occurred in patients with congenital cardiac malformations developing Eisenmenger syndrome. It seems that patients with severe congenital heart malformation complicated by Eisenmenger syndrome tend to be more at risk of death.

In line with literature, we identified multiple pregnancy as an important risk factor of HF [7, 14]. Sixteen cases of HF (16/70, 22.86%) were multiple pregnancy in our study. A multiple pregnancy has a much greater impact on maternal cardiac output and peripheral resistance than a singleton pregnancy does [15]. When a multiple pregnancy is complicated by cardiac disease or other risk factors for HF, cardiac function deteriorates and subsequent HF is likely to occur. Assessment of cardiac function in a multiple pregnancy and avoidance of other risk factors for HF including lung infection and inappropriate transfusion are recommended.

From our research, moderate-to-severe anemia is a risk factor for HF in pregnant women. The primary reasons can be seen in two ways. One is that anemia increases the burden on the heart and thus increases the risk of HF. In this way, transfusion might improve the situation. However, on the other hand, improper transfusion might increase the burden on the heart and increase the incidence of HF. In our study, two patients had HF after improper transfusion for anemia.

We found 57.14% HF patients came from rural community and 40.00% did not receive proper prenatal examination and antenatal visits. Those patients developed HF or other severe complications when they were sent to the hospital. Thus, preconception assessments and intensive antenatal visits are important for high-risk pregnancies to reduce severe maternal and fetal morbidities and mortalities.

The treatment of HF in pregnant women is more difficult than in nonpregnant women. Management of HF requires a multidisciplinary team including obstetricians, cardiologists, anesthetists, and neonatologists. Treatment during pregnancy is conducted substantially in accordance with current guidelines for nonpregnant patients [16]. Patients with decreased cardiac ejection function were given positive inotropic agents (e.g., Cedilanid) to increase contractility of the heart. Other drugs should be used to reduce cardiac load. Commonly used cardiac drugs that are relatively safe in pregnancy include beta blockers, digoxin, Cedilanid, and diuretics [17]. Drugs for hypertension include methyldopa, labetalol, and hydralazine. Magnesium sulfates are used in severe preeclampsia and eclampsia.

Pregnancies with HF have higher rates of adverse maternal and fetal outcomes. It's difficult to balance between timely termination of pregnancy to reduce maternal complications and prolongation of pregnancy to reduce perinatal complications caused by prematurity. Premature delivery may shorten the period of volume load and develop a more active treatment plan for HF. Timing and mode of delivery should be carefully planned by a multidisciplinary team. Although vaginal delivery with epidural anesthesia is the preferred mode of delivery, CS is usually performed when there is a need for prompt delivery.

The rate of CS was 95.71% in this study, which was much higher than the average CS rate (34.9%) in China in 2014 [18]. After delivery, careful monitoring of hemodynamic status should be done for at least for 72 h. We found 14.29% patients developed HF after delivery, and 90% of postpartum HF occurred within 3 days of postpartum. It was reported that hemodynamics might be abnormal up to 10 days after delivery in patients with a severe cardiac lesion [3].

Reports found that maternal mortality was less than 1% for women in NYHA class I or II, and for class III or IV maternal mortality increases to 7% [3]. Patients included in our study were mainly NYHA class III or IV (81.43%) on admission, and the maternal mortality was 4.29%, which was almost two hundred times as much as reported in normal pregnant patients in China [5]. The most common neonatal complications were prematurity (79.75% in live birth).

This study had several strengths. All cases performed transthoracic echocardiography to identify whether there was a preexisting or underlying heart disease. The management was performed by a multidisciplinary team, consisting of obstetricians, cardiologists, neonatologists, and ICU physicians. This study also had some limitations. This study was a retrospective one. The single-center limiting sample size of the study might not fully reflect the clinical characteristics. Ideally, the authors would like to suggest a regional or even a national study in order to better elucidate these events.

HF is strongly linked to severe preeclampsia, lung infection, cardiac problems, and multiple pregnancies. Peripartum HF is associated with high maternal and neonatal morbidity and mortality, high CS rate, and long hospital lengths of stay. Hypertensive disorders in pregnancy, lung infections, and cardiac problems are most common precipitating factors of HF in pregnancy. It seems that patients with severe congenital heart malformation complicated by Eisenmenger syndrome tend to be more at risk of death. High-risk patients require multidiscipline close follow-up during pregnancy, labor, and postpartum, which is necessary for a good prognosis.

Acknowledgements We thank Eranga Harshika Abeysundera for polishing the language.

Authors' contribution HC was involved in project development, data collection, data analysis, and manuscript writing. HY was involved in data collection, data analysis, and manuscript editing. XW was involved in manuscript editing.

Funding This study was supported by the Academic and Technical Leader's Foundation of Sichuan Province (No. 2016-183-31).

Compliance with ethical standards

Conflict of interest The authors declared no potential conflicts of interest.

Ethical approval This retrospective study was approved by the Institutional Review Board of West China Second University Hospital.

Research involving human participants and/or animals For this type of study, formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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