CEOG Clinical and Experimental Obstetrics & Gynecology

Clinical characteristics and pregnancy outcomes in parturients with pulmonary hypertension: experience with 39 consecutive cases from China

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Summary

Purpose: The authors aimed to understand the clinical characteristics of pulmonary hypertension (PH) with pregnancy and pregnancy outcomes in Chinese population. *Materials and Methods:* The authors retrospectively analyzed 39 parturients with PH. The patients were divided into mild PH group (n = 20) and severe PH group (n = 19). They compared some clinical characteristics, as well as maternal and fetal outcomes between the mild and severe PH groups. *Results:* The diagnostic rate of PH before pregnancy was 7.7% and the overall maternal mortality was 15.4%. There was no significant difference in age, body mass index, average termination of gestation weeks, and New York Heart Association functional class pre-pregnancy between the mild and severe PH groups. The mortality in the severe PH group (31.6%) was significantly higher than that in the mild PH group (0%) ($p < 0.05$). In addition, the occurrence rate of post-partum haemorrhage (PPH) and natality of low-birth weight neonates (LBWN) were significantly higher in the severe PH group (21.1%; 36.8%) than that in the mild PH group (0%; 10%) ($p < 0.05$), respectively. *Conclusion:* The overall mortality of parturients with PH is high and severe PH increase the risk of death, occurrence rate of PPH, and natality of LBWN.

Key words: Pregnancy; Pulmonary hypertension; Maternal mortality; Post-partum haemorrhage; Low-birth weight neonates.

Introduction

Pulmonary hypertension (PH) is a kind of pathophysiology syndrome characterized by progressively increased pulmonary vascular resistance and pulmonary vascular remodeling, eventually leading to right ventricular failure [1, 2]. The occurrence of PH in pregnancy is rare, which indicates a high-risk pregnancy. A normal pregnancy can induce increased plasma volume and cardiac output because of elevated blood volume, as well as may lead to cardiac failure due to cardiovascular stress [3]. These physiologic changes increase the risks of right ventricular failure and even death for parturients with PH. Parturients with PH has been reported to have an increased maternal mortality with 30-56% [4].

Previous study has suggested that parturients with PH should have a careful management, including the mode of delivery and anesthesia, peripartum monitoring, thromboprophylaxis, and advanced PH therapies, which may improve the quality of life and the outcomes of pregnant women and neonates [5]. Currently, most pregnant patients with PH have received advanced PH therapies, particularly prostacyclin analogues in developed countries [6]. Disappointingly, the maternal and fetal mortalities still remain high.

Although it is known that PH is a contraindication for pregnant woman, the majority of mothers who have suffered from PH before pregnancy still persist in pregnancy [7]. Moreover, one-third of pregnant women who are diagnosed with PH during middle and late pregnancy still choose to proceed with the pregnancy [7]. It is often highly advised for patients with PH to adopt effective contraception or termination of pregnancy when PH exists. Pregnancy outcomes in parturients with PH from Japan [8], Europe, USA and Australia [9], and India [10] have been reported a few years ago. However, few studies have investigated the recent pregnancy outcomes of parturients with PH in Chinese population, and pregnancy outcomes may be have an improvement by effective management for parturients with PH.

Therefore, in the present study, the authors retrospectively recruited 39 pregnant women with PH in Chinese population, aimed to understand the clinical characteristics of PH with pregnancy and pregnancy outcomes, and further investigate whether pregnancy outcomes had been improved.

Revised manuscript accepted for publication September 1, 2016

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLV, n. 2, 2018
doi: 10.12891/ceog3889.2018

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Materials and Methods

This retrospective study was approved by the Ethics Committee of this hospital. The authors enrolled 39 consecutive pregnant women (aged 18 to 43 years, with an average age of 27 ± 5 years) who were diagnosed with PH in this hospital from January 2006 to December 2012. Among these 39 patients, 32 patients were unipara and seven patients were pluripara. PH was diagnosed according to medical history, physical examination, electrocardiogram, and color Doppler ultrasound of heart. Systolic pulmonary arterial blood pressure (SPABP) was indirectly estimated by the differential pressure of tricuspid regurgitation under color Doppler ultrasound, and then SPABP ≥ 40 mmHg was defined as PH [11]. The authors collected the following data, including maternal age, pregnancy time, maternal history, body mass index (BMI), clinical symptoms, New York Heart Association (NYHA) functional class, PH etiology, delivery mode, anesthesia method, post-partum haemorrhage (PPH), and outcomes of pregnant women and neonates. Low-birth weight neonates (LBWN) were defined as weight ≤ 2,500 grams [12]. PPH was defined as postpartum blood loss in excess of 500 mL during the first 24 hours after delivery according to the World Health Organization (WHO) [13]. In this study, patients were classified into two groups: mild PH (40 mmHg ≤ SPABP < 80 mmHg) and severe PH (SPABP ≥ 80 mmHg). The statistical analysis was performed using SPSS software (version 16.0). *P* values of less than 0.05 were considered statistically significant. Continuous variables were represented as mean ± standard deviation (SD) and analyzed by *t*-test. Categorical variables were expressed by percentages and analyzed using Fischer exact test.

Results

Of the 39 patients, there were 20 patients with mild PAH and 19 patients with serve PH. The clinical characteristics of these patients are shown in Table 1. Based on medical history of patients, 36 patients (92.3%) were diagnosed with PH during pregnancy, while three patients (7.7%) were diagnosed with PH before pregnancy and intermittently took drugs. Among three patients, one case performed induced abortion operation in early pregnancy and two cases chose to continue pregnancy. There were some underlying diseases in patients (Table 2), including 28 CHD, four idiopathic PH, three systemic lupus erythematosus, two rheumatic heart disease, one perinatal cardiomyopathy complicating acute left heart failure, and one anomalous pulmonary venous connection. Among 28 patients with CHD, three cases was diagnosed with CHD before pregnancy, nine cases did not know suffering from CHD before pregnancy, and the other 16 cases did not receive specific pregnancy tests to understand the heart function before pregnancy. The clinical features were also found in these patients. Twenty-two cases (56.4%) showed breathing difficulties, such as chest distress and suppress wheezing after the different levels of activity. Five cases (12.8%) had heart failure and/or hemoptysis. The remaining 12 cases (30.7%) did not have obvious discomfort. The patients with heart failure received drug therapy such as alprostadil, dopamine, or morphine.

Of 39 patients, seven patients terminated pregnancy before 28 weeks' gestation: one case received induced abortion operation at seven weeks' gestation, one case was diagnosed with anencephalus, and then underwent induction of labour at 13 weeks' gestation, two cases underwent induction of labour who were diagnosed with PH at 18 and 22 weeks' gestation, respectively, one case performed induction of labour because of SPABP ≥ 95 at 18 weeks' gestation, one case was spontaneous abortion at 20 weeks' gestation, one case was found stillbirth at 25 weeks' gestation, and then died due to multiple organ failure after cesarean delivery for two days. The remaining 32 patients continued pregnancy to 28 weeks' gestation: 12 cases terminated pregnancy before 37 weeks' gestation due to heart failure and then underwent lower segment cesarean section; the other 20 cases were full-term, including one case with transvaginal delivery and 19 cases with cesarean delivery.

There were no statistical significances in age, BMI, blood pressure, average termination of gestation weeks, and NYHA class pre-pregnancy between the mild and severe PH groups. The overall mortality in these patients was 15.4% (6/39) (Table 1). The death was found in six patients with severe PH and in no patient with mild PH ($p < 0.05$) (Table 1). In addition, PPH rate in the severe PH group (21.1%, 4/19) was higher than that in the mild PH group (0%, 0/20) ($p < 0.05$) (Table 1). Postoperative hospitalization days in the ICU had an increased trend in the severe PH group compared with the mild PH group ($p > 0.05$) (Table 1).

There was one patient with spontaneous abortion and six patients with iatrogenic abortion before 28 weeks' gestation. However, there was one patient with stillbirth and nine cases with LBWN after 28 weeks' gestation. Neonatal survival rate was 96.7% (30/31). The natality of LBWN was higher in the severe PH group (36.8%, 7/19) than that in the mild PH group (10%, 2/20) ($p < 0.05$) (Table 3). Compared with the mild PH group, the number of term delivery was low and preterm delivery rate was high in the severe PH group, but without significant differences ($p > 0.05$) (Table 3).

Discussion

Pregnancy in women with PH is intolerable and these patients will face a serious risk [4]. In the present study, the authors found that the diagnostic rate of PH before pregnancy was 7.7% and the overall maternal mortality was 15.4%. The mortality in the severe PH group was significantly higher than that in the mild PH group. In addition, the occurrence rate of PPH and natality of LBWN were significantly higher in the severe PH group than that in the mild PH group.

The present study found that three (7.7%) patients suffered from PH before pregnancy, and 36 patients were diagnosed with PH during middle and late pregnancies.

Table 1. — *Clinical characteristics, management, and outcomes of parturients with pulmonary hypertension (PH).*

Maternal characteristics	Mild PH (n=20)	Serve PH (n=19)	*p*
Age (years)	27.7 ± 5.5	26.8 ± 5.2	NS
BMI (kg/m^2)	22.5 ± 8.2	24.1 ± 4.7	NS
Systolic pressure (mmHg)	126.45 ± 18.2	114.9 ± 17.7	NS
Diastolic pressure (mmHg)	80.6 ± 14.5	77.8 ± 13.7	NS
Termination of gestation weeks (weeks)	33.75 ± 7.9	31.8 ± 8.5	NS
NYHA class pre-pregnancy (%)			—
I-II	10 (50%)	6 (31.6%)	
III-IV	10 (50%)	13 (68.4%)	
ICU hospitalization days after cesarean section (days)	3.4 ± 4.3	6.4 ± 5	NS
Mode of delivery (%)			—
Caesarean section	16 (80%)	15 (78.9%)	
Vagina delivery	1 (5%)	0 (0%)	
Anesthetic technique (%)			—
Neuraxialanesthesia	9 (45%)	4 (21.1%)	
Generalanesthesia	7 (35%)	11 (57.9%)	
PPH (%)	0(0%)	4 (21.1%)	< 0.05
Maternal death (%)	0(0%)	6 (31.6%)	< 0.05

BMI: body mass index, NYHA: New York Heart Association, ICU: Intensive Care Unit, PPH:post-partum haemorrhage

Table 2. — *Underlying diseases in parturients with pulmonary hypertension (PH).*

Type of lesion	Mild PH (n = 20)	Serve PH (n = 19)
IPAH	1	3
Congenital heart disease	14	14
Rheumatic heart disease	2	0
Other etiology*	3	2

* When PH was secondary to connective tissue disease, peripartum cardiomyopathy, anomalous pulmonary venous connection
IPAH: idiopathic pulmonary artery hypertension

Table 3. — *Fetal and neonatal outcomes of parturients with pulmonary hypertension (PH).*

Outcome	Mild PH (n = 20)	Serve PH (n = 19)	*p*
Abortion	3	4	NS
Preterm delivery	4	9	NS
Term delivery	13	6	NS
LBWN	2	7	< 0.05

LBWN: low-birth weight neonate

However, Bédard *et al.* [5] showed that the diagnostic rate of PH before pregnancy was approximately 64.3% (47/73), which was higher than the present study. PH during pregnancy might be undiagnosed or asymptomatic PH, and then presented due to the pregnancy stress, as well as may be caused by dramatically increased SPAP because of pregnancy. The present study showed that there were 25 patients with CHD, in which nine cases did not know suffering from CHD before pregnancy, and the remaining 16 cases did not have specific pregnancy tests before pregnancy. These results indicated that the low diagnostic rate of PH might be associated with the present current insufficient preconception care. Therefore, it is necessary to strengthen preconception care and perform early cardiac ultrasound screening more than once. In the present study, the most common clinical manifestations for pregnancy with PH were breathing difficulties after the different levels of activity (56.4%), heart failure (12.8%), and hemoptysis (10.2%), while 30.7% patients did not have obvious discomfort. Because the symptoms such as chest distress and wheezing after activity also appeared in healthy pregnant women, the diagnosis of PH was often delayed, even some patients were misdiagnosed with upper respiratory tract infection. Thus, echocardiography also should be considered for pregnant women accompanied by breathing difficulties.

The overall maternal mortality of patients with PH was 15.4% (6/39) in the present study, which was consistent with the study of Ma *et al.* [14] with the 17% (5/30) mortality and the study of Bédard *et al.* [5] with a mortality of 24.7% (18/73). However, a previous study showed that the mortality of parturients with PH was 30-56% [4]. These differences may be related to data collection, research design, and regional difference. In addition, in recent years, advances in the treatment of patients with PH such as the usage of drugs like sildenafil might be an important factor [15, 16]. The present study also showed a higher mortality in severe PH patients than that in mild PH patients, which indicated that the higher SPABP might result in increased maternal mortality. Furthermore, PPH was one of the significant causes of maternal mortality, which could aggra-

vate the hemodynamic instability in patients with PH [17]. The authors found that the occurrence rate of PPH was higher in the severe PH group than in the mild PH group, indicating that higher mortality of patients with PH may be associated with the occurrence of PPH.

Though it is recommended for patients with PH to adopt contraception and pregnancy termination early, many of them still persisted in pregnancy. In the present study, in addition to the patients with abortion, all but one of patients chose the caesarean section. It is still controversial for the mode of delivery in patients with PH. In several studies, caesarean section was recommended to be performed in patients with PH because of its low risk of hemodynamic instability [18, 19]. However, vaginal delivery also had some advantages such as fewer bleeding and complications [20, 21]. Perniciously, vagina delivery might induce high risk of right ventricular pressure due to pushing, so it should be avoided in these patients. For anesthetic method of cesarean section, it should be chosen according to the NYHA class of patients as following: neuraxial anesthesia for NYHA class I–II and general anesthesia for NYHA class III–IV, since anesthetic agents could induce less vasodilation and cardiac depression [22-24]. Therefore, the present authors also followed this principle in this study in order to maintain the normal vasodilation.

PH in pregnancy had been proved to have a high risk of fetal and neonatal complications, such as preterm delivery, fetal intrauterine growth retardation, stillbirth, and neonatal death [5]. The present study also found these complications. There were one stillbirth, one neonatal death, and nine LBWN, which was similar to the report of Bédard *et al.* [5]. Subbaiah *et al.* [10] suggested that patients with severe PH had a higher incidence of preterm delivery and intrauterine growth retardation compared with patients with mild PH. This may be related to adverse fetal growth environment caused by severe hypoxemia when pregnant women suffering from severe heart disease, poor cardiac function or severe heart failure. Similarly, the present authors also found a higher natality of LBWN and preterm delivery rate, as well as a lower term delivery rate in the severe PH group than in the mild PH group; however, the differences in term and preterm delivery rates had no statistical significance.

Limitation of the current study is that the sample size is not sufficient and data bias may be present due to retrospective data. A large sample data is necessary to further understand the effect of PH on patients with pregnancy in Chinese population.

Conclusion

The present study demonstrated that the overall mortality of parturients with PH is high and severe PH increases the risk of maternal death, occurrence rate of PPH and natality of LBWN. Thus, maternal and neonatal outcomes in parturients with PH should have comprehensive management based on multidisciplinary team, including physicians, obstetricians, anesthesiologists, and pediatricians.

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