ORIGINAL ARTICLE

# Pregnancy outcomes in patients with pulmonary arterial hypertension associated with congenital heart disease

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## ABSTRACT

**Objective** There is growing evidence that maternal mortality in pregnant women with pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) is lower than that in available data. In order to evaluate this hypothesis, we collected data of pregnancies in women with PAH-CHD.

**Methods** Women with PAH-CHD followed in seven French referral centres were retrospectively included from 1997 to 2015. All pregnancies were recorded. We collected data on maternal, obstetrical and neonatal outcomes.

**Results** 28 pregnancies in 20 women (26±6 years old) with PAH-CHD were managed during this period. There were 18 complete pregnancies ($\geq$20 weeks' gestation (WG)), 8 abortions and 2 miscarriages. Six (33%, 95% CI (11.9 to 54.3)) patients experienced severe cardiac events. The concerned women had lower resting oxygen saturation (79.6±4.1% vs 89.3±3.8%, p<0.01). The most common cardiac complications during the complete pregnancies were heart failure (n=4) and severe hypoxaemia (n=5). Heart failure was overall severe, requiring inotropic treatment in three patients, mechanical circulatory support in one and led to one maternal death (mortality=5.0% 95% CI (0.1 to 24.9)). Obstetrical complications occurred in 25% of pregnancies. Small for gestational age was diagnosed in 39% (7/18) of fetuses. 12/18 (67%) pregnancies were delivered by caesarean section, of which 10 in emergency for obstetrical reason. Prematurity was frequent (78%), but no neonatal death occurred.

**Conclusions** Outcome of pregnancy in women with PAH-CHD is better than previously reported, with only 5% maternal mortality in our cohort. However, because of the severity of heart failure and the high rate of neonatal complications, patients should still be advised against pregnancy.

## INTRODUCTION

Pregnancy in women with pulmonary arterial hypertension (PAH) is associated with high maternal mortality rates,[1 2] as in pulmonary hypertension associated with congenital heart disease (PAH-CHD). Physiological pregnancy changes that occur during pregnancy and the peripartum phase are poorly tolerated in patients with PAH-CHD. Hence, pregnancy in this condition is still strongly discouraged, and pregnant patients should be counselled to termination of pregnancy.[3] The most recent review covering a period from 1997 to 2007 reported a reduction in maternal mortality in patients with PAH-CHD.[2] Nevertheless, a mortality rate of 28% remains prohibitively high. Moreover, pulmonary hypertension has been recently identified to be an independent risk factor of heart failure in pregnant women with heart disease.[4] Development of new PAH advanced therapies and improvement in high-risk pregnancies management with a multidisciplinary approach[2 5 6] may have been translated into reduced maternal mortality, especially in PAH-CHD. We hypothesised that better management of high-risk pregnancies has improved the outcomes of pregnancy with PAH-CHD. The objective of our study was to describe maternal and fetal outcomes during pregnancy in patients with PAH-CHD identified from our database.

## METHODS

We contacted 22 referral centres of the M3C French network (Centre de reference des Malformations Congénitales Complexes, created in 2006) to retrospectively collect cases of pregnancy in patients with PAH-CHD recorded from institutional PAH registries. Only pregnancies occurring after 1997 were included; as improvement of maternal outcomes in patients with PAH was reported after 1997,[2] this year has been chosen to start the registry. Seven French specialised centres participated in collecting data from 1997 to 2015, the year 2006 being the median year of the inclusions. Data were collected from questionnaires mailed to investigators, and were controlled by reviewing patients' charts in three centres (30% of the total population) by an independent investigator (LB). Patients with other forms of pulmonary hypertension were excluded. Review board of each institution was obtained. All pregnancies including miscarriages, ectopic pregnancies, terminations and completed pregnancies were included.

At baseline, we collected the following information: demographic characteristics, prior surgical procedures, New York Heart Association (NYHA) class, cardiac complications preceding pregnancy, saturation, pre-pregnancy body mass index and treatment. Haemodynamic parameters were evaluated by right heart catheterisation whenever possible, or by echocardiography. Biological data were

also collected (haemoglobin, haematocrit). CHD, except isolated atrial septal defect (ASD), ventricular septal defect (VSD) and *patent ductus arteriosus*, were considered as complex anatomy.

Miscarriages (spontaneous fetal loss before 20 weeks' gestation (WG)), first trimester elective abortions and terminations of pregnancy were also collected.

Detailed information concerning each completed (>20 WG) pregnancy was recorded along with antepartum, peripartum and postpartum (up to 6 weeks after delivery) data when applicable. We also recorded information on the maternal vital status at the last follow-up.

Gestational age and modes of delivery, pain management and prophylactic antibiotics were recorded. If labour was induced, indication of induction was analysed (cardiac or obstetrical). Specific long-term treatment was recorded at each step (ie, before, during and after pregnancy). Neonatal outcome was assessed by birth weight and vital status parameters. Corticosteroids use was noted. Documented complications were divided into maternal cardiac, obstetrical and neonatal complications. Cardiac complications were documented as maternal death, arrhythmia, heart failure requiring treatment, systemic thromboembolic complication, worsening of hypoxaemia (decrease in saturation at rest >5% compared with basal saturation) and infective endocarditis. Obstetrical complications such as pregnancy-induced hypertension (systolic pressure >140 mm Hg or diastolic pressure >90 mm Hg, after 20 WG, without proteinuria), pre-eclampsia (pregnancy-induced hypertension with proteinuria ≥0.3 g/24 hours), eclampsia, HELLP syndrome, threatening premature labour (uterine contractions and cervix modification before 37 WG), gestational diabetes mellitus and premature rupture of the membranes (membrane rupture before 37 WG) were recorded. Fetal and neonatal complications included premature delivery (delivery before 37 WG), small for gestational age (SGA) birth weight (<10th percentile), stillbirth (>20 WG), neonatal death (death within the first month after birth) and recurrence of CHD diagnosed by antenatal echocardiography and confirmed at birth by a paediatric cardiologist, or diagnosed by postnatal echocardiography.

## Statistical analysis

Descriptive statistics for nominal data were expressed as absolute numbers and percentages. Continuous variables are presented by mean±SD. Medians and quartiles were computed for continuous variables with non-normal distribution. Association between basal characteristics of women and cardiovascular, neonatal and obstetrical events was assessed using Fisher's test for nominal data and Wilcoxon test for continuous data. Two-tailed probability values ≤0.05 were considered statistically significant. Statistical testing was performed with the use of MedCalc Statistical Software V.12.7.7 (MedCalc Software bvba, Ostend, Belgium; 2013).

## RESULTS
### Study population
During the study period, 28 pregnancies were carried out by 20 patients in seven different French centres. The underlying cardiac congenital malformations are listed in table 1. Seventeen patients had Eisenmenger syndrome (group 1) and three patients had segmental pulmonary hypertension (group 5), according to the last classification of pulmonary hypertension.[7] The three patients with segmental pulmonary hypertension had pulmonary atresia with VSD and aortopulmonary collaterals, and PAH was invasively confirmed with mean pulmonary pressure >25 mm Hg in all cases before pregnancy (pulmonary

**Table 1** Anatomical defects and baseline characteristics

| Anatomical defect, n (%) | n=20 |
|---|---|
| Ventricular septal defect (VSD) | 5 (25.0%) |
| Pulmonary atresia+VSD and aortopulmonary collaterals* | 3 (15%) |
| Isolated atrial septal defect | 3 (15%) |
| Isolated patent ductus arteriosus | 2 (10%) |
| Double outlet right ventricle+aortic coarctation | 2 (10%) |
| Truncus arteriosus | 2 (10%) |
| Atrioventricular septal defect | 1 (5%) |
| Single ventricle | 1 (5%) |
| ccTGA+VSD | 1 (5%) |
| *Baseline characteristics* | |
|   Age at first pregnancy, years | 26±6 |
|   Simple/complex CHD, n | 10/10 |
|   BMI, mean±SD | 19.2±2.7 |
| NYHA functional class, n (%) | |
|   I | 4 (20%) |
|   II | 13 (65%) |
|   III | 3 (15%) |
|   IV | 0 (0%) |
| Saturation, % | 87±6 |
| Haemoglobin, g/dL | 17.0±1.7 |
| Haematocrit, % | 49.8±6.5 |
| Invasive pulmonary arterial pressure (S/D/M), mm Hg* | 101±16/43±13/62±13 |

*Pulmonary arterial hypertension was confirmed in all cases by catheterisation. Pulmonary pressures were invasively measured in 7/20 patients before pregnancy, including the three patients with segmental pulmonary hypertension. Among patients without invasive measurement of pulmonary pressures, non-invasive pulmonary pressures were available in three patients using echo-Doppler method: in one patient with atrial septal defect, systolic pulmonary pressure was estimated as 90 mm Hg, and in two patients with isolated ventricular septal defect, mean pulmonary pressure was estimated respectively as 45 and 57 mm Hg.
BMI, body mass index; ccTGA, congenitally corrected transposition of the great arteries; CHD, congenital heart disease; NYHA, New York Heart Association.

pressures were respectively measured at 80/45/60, 93/33/54 and 85/50/60 mm Hg).

PAH-CHD was diagnosed in all patients before pregnancy, except for two patients in whom PAH-CHD was diagnosed during the second trimester of pregnancy. Seven women had more than one pregnancy (maximum three pregnancies). Mean maternal age was 26±6 years. Seven (35%) patients had prior history of palliative surgery (four had pulmonary banding, and three had conduits between ventricle and pulmonary artery). Seven (35%) patients experienced cardiovascular complications before pregnancy: atrial arrhythmia in two, heart failure in two, stroke in two, recurrent haemoptysis in two and infective endocarditis in one. Their baseline characteristics are summarised in table 1.

### Maternal outcomes during pregnancy and post partum
Qualifying cardiac events occurred in 6 out of the 18 completed pregnancies (33.3%, 95% CI (13.3 to 59.0)). The most common adverse cardiovascular events after 20 WG were worsening of hypoxaemia (n=5) and heart failure (n=4). Heart failure was particularly severe, requiring inotropic treatment (n=3) and peripheral veno-arterial extracorporeal membrane oxygenation (n=1). All heart failure episodes except one occurred during the early postpartum period. These complications led to the only maternal death that occurred 10 days after delivery (5% mortality rate, 95% CI (1.3 to 24.9)). The deceased patient was the oldest of the cohort (42 years old) and had history of atrial arrhythmia and moderately impaired right

ventricle (RV) function. There were no haemoptysis or infective endocarditis in the whole pregnant population. Table 2 compares basal characteristics and obstetrical management between patients with and without cardiac event during pregnancy (>20 WG) and postpartum period. Resting oxygen saturation was significantly lower, and haemoglobin levels were significantly higher in patients who experienced cardiac complications (p≤0.01). Cases with cardiac events are described in table 3.

Six patients (6/28 pregnancies, 21%) received antiplatelet or anticoagulation therapy during pregnancy; no thromboembolic complication occurred in the cohort. Three patients were treated by oral advanced PAH therapy (sildenafil and tadalafil), and one needed continual oxygen therapy during pregnancy.

### Obstetrical and neonatal events

Among the 28 pregnancies, all singleton, 8 ended in elective abortion at a mean gestational age of 8.5 WG (minimum=5 WG, maximum=15 WG). Two had miscarriages at 8 and 15 WG, with baseline resting oxygen saturation of 84% and 85% in these two patients, respectively. Eighteen (64%) pregnancies were completed (≥20 WG), with a mean gestational age at delivery of 33±3 WG (minimum=28, maximum=38).

There were no stillbirths in this series. During pregnancy, fetal growth was impaired in 7/18 (38.99%, 95% CI (17.3 to 64.3)) pregnancies. SGA was significantly associated with lower baseline resting oxygen saturation (85% in mothers with SGA vs 90% in mothers without SGA (p=0.04)). Bilateral notches on uterine artery Doppler were observed in 3/7 patients with SGA.

The mean birth weight was 1741±472 g at a mean gestational age of 33 WG, which corresponds to the 10th centile. The most common neonatal complication was prematurity (77.78% of neonates, 95% CI (52.4 to 93.6)). Among premature births, three were induced preventively (without maternal cardiac complication), six were induced because of maternal complications

and three were induced for fetal indication (severe SGA). There was no neonatal death in our series. Among the offsprings, two cardiac anomalies were diagnosed (11%): one VSD and one pulmonary valve stenosis associated with an ASD. All cases were confirmed by postnatal echocardiography. No additional congenital malformations were diagnosed.

Among the 18 completed pregnancies, 12 (67%) were delivered by caesarean section (CS): ten emergency CS (eight for failed induction of labour, one for severe preeclampsia and one for heart failure) and two elective CS (one for SGA and one for scarred uterus and underlying cardiac condition). CS was performed under general anaesthesia in 3/12 cases (25%), two for the same patient (CS for failed induction of labour and subsequently for scarred uterus for the following pregnancy) and one for severe pre-eclampsia. The other CS were performed under epidural (n=2) or spinal (n=6) anaesthesia, and one with missing data. Vaginal delivery was done in four cases under epidural, one with no analgesia and one with missing data. Spinal anaesthesia was administered in half of patients who experienced cardiac complications; however, complications were not concomitant with or related to anaesthesia. They were all attributed to PAH crisis.

Preventive antibiotic for infective endocarditis was given in seven patients; no maternal infectious complication was diagnosed during the 6 weeks following delivery.

Obstetrical complications occurred in seven patients (25% of pregnancies). They were mainly postpartum haemorrhage (n=4), of which two were under anticoagulation (one under unfractioned heparin therapeutic doses, and one under low molecular weight heparin (LMWH) preventive doses), and one patient required uterine embolisation. Other obstetrical complications were premature labour (n=3, at mean gestational age of 29 WG) and *abruptio placentae* (n=2, one occurring in a patient with anti-vitamin K (AVK) overdose). Five patients

**Table 2** Comparison of basal characteristics and obstetrical management between patients with and without cardiac event during pregnancy (>20 WG) and postpartum period

|  | No complication (n=12) | Cardiac complications (n=6) | p Value |
|---|---|---|---|
| Basal characteristics |  |  |  |
| Age, in years | 28±6 | 29±6 | 0.3 |
| BMI, mean±SD, in kg/m$^2$ | 19.6±2.6 | 19.0±3.7 | 0.6 |
| Haemoglobin, mean±SD, in g/dL | 16.1±0.8 | 19.4±0.8 | 0.01 |
| Haematocrit, mean±SD, in % | 47.4±4.3 | 53.6±8.2 | 0.1 |
| Saturation, mean±SD, in % | 89.3±3.8 | 79.6±4.1 | <0.01 |
| NYHA ≥3 | 1 (7.7%) | 1 (16.7%) | – |
| Complex CHD, n (%) | 8 (66%) | 4 (66%) | 0.3 |
| History of cardiovascular events, n (%) | 3 (25%) | 2 (33%) | – |
| Gestity (complete pregnancy) | 5 (42%) | 2 (33%) | – |
| Obstetrical management |  |  |  |
| Obstetrical complications, n (%) | 4 (33%) | 2 (33%) | – |
| Unplanned delivery, n (%) | 2/9* | 2/6 | – |
| Mode of delivery (caesarean/vaginal) | 6/5† | 6/0 | – |
| Anaesthesia (general/epidural/spinal) | 2/4/3‡ | 1/2/3 | – |
| Treatment during pregnancy |  |  |  |
| Anticoagulation or antiplatelet therapy | 5 | 2 | – |
| Advanced PAH therapy | 1 | 4 | – |
| Term at birth, mean±SD | 35. 9±1.6 | 30.2±1.5 | <0.01 |

*Data were missing in three cases.
†Obstetrical management data were unknown for one patient.
‡One patient delivered without any anaesthesia, and two modes of anaesthesia were missing in the group without cardiac complication. We have not compared data of obstetrical management because of their small number in each category.
BMI, body mass index; CHD, congenital heart disease; NYHA, New York Heart Association; PAH, pulmonary arterial hypertension.

**Table 3** Case report of patients with cardiac complications

| | CHD | Age at pregnancy (years) | Saturation | NYHA | Pulmonary pressures (mm Hg) | Subaortic ventricular function | Subpulmonary ventricular function | Treatment during pregnancy | Pregnancy duration (WG) | Cardiac event/treatment | Term at cardiac event | Period of event |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Isolated VSD | 31 | 85 | 1 | 115/60/85 | Normal | Normal | Sildenafil (30 mg ×3/day) | 30 | Hypoxaemia (64%)/bed rest and oxygen therapy | Third trimester and early PP | 2015 |
| 2 | DORV+aortic coarctation (diagnosed during pregnancy) | 21 | 80 | 2 | Not available | Normal | Normal | No | 31 | Cardiogenic shock following CS indicated for severe pre-eclampsia/inotropic drugs, inhaled NO+sildenafil and ventricular assistance device | Early PP | 2011 |
| 3 | Pulmonary atresia +VSD+collaterals | 30 | 80 | 2 | 80/45/60 | Normal | Normal | None | 31 | Heart failure/diuretics | Third trimester | 2001 |
| 4 | PDA | 32 | 83 | 2 | Not available | UK | UK | Oxygen therapy | 32 | Hypoxaemia, pulmonary hypertensive crisis and cardiogenic shock/inotropic treatment | Early PP | 2002 |
| 5 | Isolated ASD | 42 | 76 | 2 | 90/52/65 | Normal | Moderately impaired | UFH | 28 | Hypoxaemia, pulmonary hypertensive crisis and heart failure, death/inotropic drugs, prostacyclin+NO and UFH | Early PP | 2004 |
| 6 | DORV+aortic coarctation | 22 | 74 | 3 | 70/55/39 | Normal | Normal | Tadalafil, AVK relayed by UFH | 29 | Hypoxaemia (60%)/bed rest and oxygen therapy | Early PP | 2013 |

Invasive and non-invasive pulmonary pressures were not available in two patients.
ASD, atrial septal defect; CHD, congenital heart disease; CS, caesarian section; DORV, double outlet right ventricle; NO, nitric oxide; NYHA, New York Heart Association; PDA, patent ductus arteriosus; PP, postpartum; UFH, unfractioned heparin; UK, unknown; VSD, ventricular septal defect; WG, weeks of gestation.

received corticosteroids before delivery to prevent prematurity complications. This treatment induced no maternal complication.

Obstetrical and neonatal events are summarised in table 4.

### Follow-up

Follow-up was longer than 1 year for all but one patient, with a median duration of 8.8 years (95% CI (3.7 to 12.7)). Two patients died at age 37 and 45, 4 and 16 years after delivery. In seven patients, NYHA functional class worsened, and PAH advanced therapy was initiated or strengthened after a median delay of 4.5 years following pregnancy. However, there were no significant changes in resting oxygen saturation ($87\%\pm6$ before pregnancy vs $89\%\pm7$ at last follow-up). Finally, three patients experienced arrhythmia and two haemoptysis during follow-up.

### Changes of pregnancy management and outcomes in PAH-CHD women before and after 2006

Changes are shown in online supplementary file table S1.

### DISCUSSION

#### Maternal death and cardiovascular complications

Mortality rate among pregnant women with PAH-CHD is significantly reduced compared with the recent rate reported in literature review (5% in our series vs 28% in the study of Bedard et al).[2] However, cardiac complications remain frequent and severe, justifying the counselling against pregnancy in patients with PAH-CHD.

The reduction of mortality rates may be explained in several ways. First, we observed an improvement of peripartum management with a very low rate of general anaesthesia. Only two patients had general anaesthesia (one patient had two), and was justified for one with severe pre-eclampsia. The use of general anaesthesia was associated with a fourfold increased risk of death in pregnant patients with PAH associated with CHD.[2] Moreover, all PAH-CHD except two were diagnosed before pregnancy and followed by centres with appropriate expertise in pulmonary hypertension, CHD, anaesthesia and intensive care.

**Table 4** Obstetrical and neonatal events

| Obstetrical complications | n |
|---|---|
| Pre-eclampsia | 1 |
| SGA | 7 |
| Premature rupture of membranes | 1 |
| Preterm labour | 3 |
| *Abruptio placentae* | 2 |
| Postpartum haemorrhage | 4 |
| Diabetes mellitus or infection or gravid hypertension | 0 |

| Fetal/neonatal complications | n |
|---|---|
| Live births | 18 (64%) |
| Birth weight (g), mean±SD | 1717±487 |
| Intrauterine fetal death or stillbirth | 0 |
| Neonatal death | 0 |
| Prematurity (birth <37 WG) | 14 (78%) |
| 33–36+6 WG | 8 |
| 28–32+6 WG | 6 |
| 22–27+6 WG | 0 |
| Recurrence of CHD | 2 (11%) |

CHD, congenital heart disease; SGA, small for gestational age; WG, weeks of gestation.

Finally, the maternal mortality rates of the past series,[1][2] were calculated from published case reports. This type of publication method induces more biases than a cohort such as the one presented here.

In our study, lower resting oxygen saturation is associated with maternal and fetal complications. Maternal complications seem related to pulmonary vascular resistance, that is, severity of PAH in CHD, explaining the association with the degree of right to left shunt and therefore oxygen saturation. Furthermore, recent studies observed better maternal and fetal outcomes in patients with mild pulmonary hypertension.[8][9]

As in previous studies, cardiovascular complications occurred mainly in the early postpartum period. The effects of pregnancy on the cardiovascular system persist for several months after delivery.[10] During follow-up, we reported two late deaths, and we observed an impairment of functional class in almost one-third of patients (7/20). Pregnancy itself may have an adverse effect on cardiopulmonary function,[11] leading to PAH disease progression and probably early death, compared with mean survival in PAH-CHD.[12]

### Management of pregnant women with PAH-CHD

We report no complication during the eight terminations of pregnancy, probably because they were performed early. Dranenkiene et al,[13] also reported the termination of 13 pregnancies without complication. Non-cardiac surgery can be performed without substantial morbidity in PAH-CHD. Nevertheless, even with relatively minor surgery, significant complications, including death, have been described.[14] Referral to major centres with expertise in the care of patients with PAH-CHD is advisable.

The optimal mode of delivery in patients with PAH-CHD remains a matter of debate.[2][6] In our study, CS was performed in 67% vs 72% in the study of Bédard et al, and all of them were justified for obstetrical or cardiac reasons. However, the main indication was emergency for failed induction of labour, suggesting that cardiac conditions might have influenced the team on how long to wait when inducing labour. Although CS was the mode of delivery in all patients who experienced cardiovascular complications, only 2/6 were planned. Data from ROPAC registry show that planned CS does not confer any advantage over planned vaginal delivery in terms of maternal outcome, but is associated with adverse fetal outcomes.[15] Moreover, vaginal delivery is associated with smaller shifts in blood volume, fewer clotting or bleeding complications and lower risk of infections.[16] CS should be indicated only in cases of maternal haemodynamic deterioration or for obstetrical indication.

General anaesthesia is associated with a high risk of death in pregnant patients with PAH-CHD,[2] and spinal anaesthesia could be associated with severe hypoxia caused by systemic hypotension. Therefore, we advise using titrated epidural anaesthesia which allows a good pain control, without the potentially deleterious hypotensive effect of a standard-dose spinal anaesthetic.

There is no standard thromboprophylaxis for pregnant women with PAH-CHD and right to left shunt, with both thrombotic and bleeding risks.[17] In our study, six patients were treated by different anticoagulation regimens, and we reported no thromboembolic event. In parallel, half of haemorrhagic complications occurred, mainly postpartum haemorrhages, in patients who were treated by anticoagulant. Unlike in the review of Bédard et al,[2] haemorrhage was not associated with maternal cardiac event in our series. However, in this latter study, pulmonary embolism was reported as a cause of death in pregnant patients with PAH-CHD during postpartum.[2] Our study cannot specify the type and the extent of thromboprophylaxis required for pregnancy and PAH-CHD.

Only three patients were treated by oral advanced PAH therapy (sildenafil and tadalafil) during pregnancy, of which two had postpartum deep hypoxaemia, but no heart failure. This constitutes only one-third of complete pregnancies recorded during the recent period (after 2006). As other studies,[18] we reported no side effects of sildenafil on mothers or offsprings, while animal studies have shown that bosentan may have teratogenic effects,[19] and is thus contraindicated during pregnancy. To our knowledge, there are no other reports of pregnancy under tadalafil; the one we describe was complicated by SGA and prematurity, probably in relation with the maternal cardiac condition. Other PAH therapies, such as nitric oxide and prostacyclin analogues, were administered as a last resort when patients were haemodynamically unstable. Early use of targeted PAH therapy, from the first trimester of pregnancy onwards, and before cardiac decompensation, combined with an early planned delivery, may improve outcome of pregnancies in women with PAH.[9][20]

Finally, no infective endocarditis occurred during postpartum period, whether the patients received antibiotic prophylaxis or not. This supports recent recommendations of the European Society of Cardiology.[21]

### Fetal and neonatal outcome

SGA and prematurity were the main neonatal complications, prematurity being clearly related to maternal complications. These two complications are common in case of maternal cyanotic CHD.[22][23] As in the present study, haemoglobin and arterial oxygen saturation before pregnancy were the most important predictors of fetal outcome.[22–24]

### Study limitations

Because it is a retrospective study, some data are lacking. Although this was a national cohort during a relative long period, the number of pregnant patients with PAH-CHD was relatively small. This could be at least partially explained by the counselling against pregnancy in patients with PAH-CHD. We recognise a recruitment bias from specialised centres. Some pregnant women with PAH-CHD may have been managed in non-specialised centres. However, the French M3C network is established since 2006, and the rate of pregnant women addressed to these centres did not change after this date. Larger, multicentre, prospective studies are required to determine the exact pregnancy-related risk in PAH-CHD, specifically to determine the role of advanced PAH therapy in this setting.

### CONCLUSION

Outcome of pregnancy in women with PAH-CHD has improved in this national network collaborative series with a lower rate of maternal mortality than other publications; however, the severity of maternal complications and the high rate of prematurity and SGA remain of concern. In line with current guidelines, women with PAH-CHD should be counselled against pregnancy, or for early termination if pregnant. If they decide to continue with the pregnancy, antenatal and postpartum care should be provided by a multidisciplinary experienced team.

## Congenital heart disease

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# Pregnancy outcomes in patients with pulmonary arterial hypertension associated with congenital heart disease

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**Notes**