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Pregnancy in pulmonary arterial hypertension: midterm maternal and fetal outcomes

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Objective

To test the hypothesis, that pregnancies with pulmonary arterial hypertension (PAH) may be feasible with acceptable maternal and fetal risks. Before the turn of the century, pregnancy in women with pulmonary arterial hypertension (PAH) was associated with maternal mortality rates of 30% and neonatal mortality rates of 11%. In more recent series, despite improved management of PAH, pregnancy-associated maternal mortality remained high, ranging from 11% to 25%. As of today, there is no cure for PAH, and case reports have suggested that pregnancy may accelerate disease progression. Hence, current pulmonary hypertension guidelines continue to recommend that all patients with PAH avoid pregnancy. However, with recent therapeutic advances, an increasing number of young women with PAH have well-controlled disease and are able to lead a near-normal life. This is particularly true for women who are responders to calcium channel blockers but also for women who respond well to other PAH treatments. Despite the known risks of becoming pregnant with PAH, some women are willing to accept these risks and actively plan pregnancy.

Methods

At our institution, since 2007, we have been offering individualized advice to women with PAH who consider becoming pregnant. As a basic rule, we never encourage patients to become pregnant. However, in patients with well-controlled disease indicated by a low-risk profile and a pulmonary vascular resistance < 500 dyn x s x cm−5 on therapy, we take a neutral position, share our experience together with published data, and indicate that we support any decision made by the patient and their families. In patients with less well-controlled disease, we strongly advise against pregnancy but still signal our full support in case the patient decides to become pregnant. In addition, in 2007, we initiated prospective documentation of pregnancies in patients with PAH and formed a multidisciplinary team consisting of pulmonary hypertension specialists, obstetricians, anesthesiologists, and cardiothoracic surgeons for standardized management of these patients. Our strategy includes planned delivery by cesarean section under peridural or spinal anesthesia during the 38th gestational week with post-partum intensive care monitoring. Extracorporeal membrane oxygenation (ECMO) standby is ascertained in patients considered at high risk of developing post-partum right heart failure. PAH medications are maintained during pregnancy except for endothelin receptor antagonists, which are discontinued when pregnancy is detected and reintroduced after delivery (all patients are discouraged from breastfeeding).

Results

In this report, we present the outcomes of all women with PAH whom we attended to during pregnancy between January 2007 and November 2019. Follow-up ended in October 2020. There were 25 pregnancies in 16 patients. A total of 5 patients had a total of 5 spontaneous abortions and 3 terminations of pregnancies. This included 1 patient who became pregnant during an accelerated phase of PAH progression. On gestational Week 10, she developed hyperemesis and subsequent right heart failure. She required awake ECMO support during which pregnancy was terminated. After 17 days on ECMO, bilateral lung transplantation was performed. She did well for some time after transplantation but died 2.5 years later from chronic lung allograft dysfunction. A total of 13 patients had a total of 17 successful pregnancies—1 with twins—and delivered 18 newborns who all were healthy at the time of birth. During pregnancy, all patients remained stable except 1. This patient initially had an uneventful course of her pregnancy. However, at gestational Week 36, she developed a febrile respiratory tract infection followed by rapidly progressive right heart failure. She underwent an emergency cesarean section but required ECMO support within a few hours after delivery. No recovery was seen despite maximized medical therapy, including IV Treprostinil, and she underwent lung transplantation 31 days after delivery. Both mother and offspring were alive and well at the last follow-up, which was 2 years after transplantation. The post-partum follow-up of the remaining patients ranged from 1 to 12 years (median, 6 years). A total of 6 patients (Numbers 4, 5, 6, 7, 12, and 13 in the tables) showed signs of clinical worsening within 9 to 22 months after delivery. All of these patients responded favorably to treatment escalation and were alive at the end of the observation period. At the last follow-up, all but 1 patient presented in the World Health Organization Functional Class I or II, and 6-minute walking distances ranging from 442 m to 716 m. The offspring of our patients (age ranging from 1 to 12 years) were invariably doing well at the end of the observation period. All of them had normal findings at the legally required infant checks, and all children aged ≥18 months had normal results on the Child Behavior Checklist tests.

Conclusion

Taken together, our data reinforce the notion that pregnancy in patients with PAH is a risky and complex undertaking. Still, our data suggest that good midterm outcomes are achievable, especially in patients with well-controlled disease when treated by a multiprofessional team experienced in the management of PAH and pregnancy. In this series, all mothers who delivered a baby were alive at the end of the observation period, and their infants were healthy and normally developed. During follow-up, several patients showed signs of clinical worsening, but the relatively long intervals between delivery and clinical worsening did not suggest that pregnancy was a triggering factor. Although our data are limited by the small number of patients, we believe that today, an individualized risk-based approach with shared decision making may be a more appropriate approach to pregnancy in PAH than the current guideline recommendation to avoid pregnancy in all of these patients.