A case report of successful pregnancy and delivery after peritoneal dialysis in a patient misdiagnosed with primary infertility

Chi-Young Choi, MD, a Nam-Jun Cho, MD, b Samel Park, MD, a Hyo Wook Gil, MD, PhD, b Yun-Sook Kim, MD, PhD, a Eun Young Lee, MD, PhD a,c,*

Abstract
Rationale: Currently, 15% of women in fertility age are infertile and the frequency is increasing. Among the various causes of infertility, end-stage renal disease (ESRD) has been shown to decrease the frequency of pregnancies compared with normal females. However, dialysis of patients with ESRD increases the likelihood of pregnancy.

Herein, we report successful pregnancy and delivery after peritoneal dialysis in a patient who was misdiagnosed as primary infertility.

Patient concerns: A 37-year-old female who was unaware of her ESRD was misdiagnosed with primary infertility. After undergoing artificial insemination, she was referred to department of internal medicine because of generalized edema, dyspnea, nausea, vomiting, and poor oral intake. After evaluation, she was diagnosed with ESRD and initiated peritoneal dialysis.

Diagnoses: The patients was on peritoneal dialysis for a year and discovered that she was pregnant.

Interventions: During pregnancy, the patient maintained a residual urine output, BUN levels below 50 mg/dL, controlled blood pressure and a targeted hemoglobin range. She obtained adequate calories and protein and was managed by a multidisciplinary team.

Outcomes: The patient delivered a preterm male baby with no anomalies.

Lessons: ESRD should also be considered among the several causes of infertility in fertile women. If ESRD is the cause of infertility, the frequency of pregnancy increases following dialysis. If pregnancy is diagnosed early, intensive renal replacement therapy, adequate nutritional intake and regular fetal monitoring during pregnancy increase the chances of successful delivery while maintaining PD.

Abbreviations: ACEs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CAPD = continuous ambulatory peritoneal dialysis, CGN = chronic glomerulonephritis, CRL = crown rump length, ESRD = end stage renal disease, FHR = fetal heart rate, HD = hemodialysis, IIOC = incompetent internal os of cervix, NICU = neonatal intensive care unit, NST = nonstress test, PD = peritoneal dialysis, RRF = residual renal function.

Keywords: delivery, infertility, peritoneal dialysis, pregnancy

1. Introduction
The frequency of pregnancy is decreasing in fertile women. The major causes of female infertility include ovulatory dysfunction, tubal and peritoneal pathology, uterine pathology, and unexplained factors. End stage renal disease (ESRD) may also induce infertility. It is unusual for women with ESRD to become pregnant. The frequency of pregnancy is 1% to 7% in fertile female patients with dialyzable ESRD.[1] The decline in pregnancy frequency is not precisely understood, but is attributed to anovulation, reduced libido, the absence of follicle stimulation hormone (FSH), and luteinizing hormone (LH) surges.[2] Pregnancy in the presence of ESRD increases the mortality and morbidity of the mother and the fetus compared with pregnancy under normal kidney function due to increased pregnancy-related complications including preeclampsia, hydramnios, hypertension crisis, early uterine contractions, and pre-term delivery.[3]

In 1973, Unzelman et al[4] first reported a case of successful pregnancy and delivery in a patient who had received hemodialysis for 4 years. A recent study reported that pregnancy during intensive renal replacement therapy and multidisciplinary team management may result in significantly better outcomes for both mother and baby.

Herein, we report a case of successful pregnancy and delivery after peritoneal dialysis in a patient who was misdiagnosed as primary infertility.

2. Case report
The patient has provided informed consent for publication of the case. This is a case for a 37-year-old female who was unaware of her ESRD. She was Asian and an office worker. In 2016, she was diagnosed with primary infertility and received artificial


A case report of successful pregnancy and delivery after peritoneal dialysis in a patient misdiagnosed with primary infertility

Chi-Young Choi, MD, a Nam-Jun Cho, MD, b Samel Park, MD, a Hyo Wook Gil, MD, PhD, b Yun-Sook Kim, MD, PhD, a Eun Young Lee, MD, PhD a,c,*

Abstract
Rationale: Currently, 15% of women in fertility age are infertile and the frequency is increasing. Among the various causes of infertility, end-stage renal disease (ESRD) has been shown to decrease the frequency of pregnancies compared with normal females. However, dialysis of patients with ESRD increases the likelihood of pregnancy.

Herein, we report successful pregnancy and delivery after peritoneal dialysis in a patient who was misdiagnosed as primary infertility.

Patient concerns: A 37-year-old female who was unaware of her ESRD was misdiagnosed with primary infertility. After undergoing artificial insemination, she was referred to department of internal medicine because of generalized edema, dyspnea, nausea, vomiting, and poor oral intake. After evaluation, she was diagnosed with ESRD and initiated peritoneal dialysis.

Diagnoses: The patients was on peritoneal dialysis for a year and discovered that she was pregnant.

Interventions: During pregnancy, the patient maintained a residual urine output, BUN levels below 50 mg/dL, controlled blood pressure and a targeted hemoglobin range. She obtained adequate calories and protein and was managed by a multidisciplinary team.

Outcomes: The patient delivered a preterm male baby with no anomalies.

Lessons: ESRD should also be considered among the several causes of infertility in fertile women. If ESRD is the cause of infertility, the frequency of pregnancy increases following dialysis. If pregnancy is diagnosed early, intensive renal replacement therapy, adequate nutritional intake and regular fetal monitoring during pregnancy increase the chances of successful delivery while maintaining PD.

Abbreviations: ACEs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CAPD = continuous ambulatory peritoneal dialysis, CGN = chronic glomerulonephritis, CRL = crown rump length, ESRD = end stage renal disease, FHR = fetal heart rate, HD = hemodialysis, IIOC = incompetent internal os of cervix, NICU = neonatal intensive care unit, NST = nonstress test, PD = peritoneal dialysis, RRF = residual renal function.

Keywords: delivery, infertility, peritoneal dialysis, pregnancy

1. Introduction
The frequency of pregnancy is decreasing in fertile women. The major causes of female infertility include ovulatory dysfunction, tubal and peritoneal pathology, uterine pathology, and unexplained factors. End stage renal disease (ESRD) may also induce infertility. It is unusual for women with ESRD to become pregnant. The frequency of pregnancy is 1% to 7% in fertile female patients with dialyzable ESRD.[1] The decline in pregnancy frequency is not precisely understood, but is attributed to anovulation, reduced libido, the absence of follicle stimulation hormone (FSH), and luteinizing hormone (LH) surges.[2] Pregnancy in the presence of ESRD increases the mortality and morbidity of the mother and the fetus compared with pregnancy under normal kidney function due to increased pregnancy-related complications including preeclampsia, hydramnios, hypertension crisis, early uterine contractions, and pre-term delivery.[3]

In 1973, Unzelman et al[4] first reported a case of successful pregnancy and delivery in a patient who had received hemodialysis for 4 years. A recent study reported that pregnancy during intensive renal replacement therapy and multidisciplinary team management may result in significantly better outcomes for both mother and baby.

Herein, we report a case of successful pregnancy and delivery after peritoneal dialysis in a patient who was misdiagnosed as primary infertility.

2. Case report
The patient has provided informed consent for publication of the case. This is a case for a 37-year-old female who was unaware of her ESRD. She was Asian and an office worker. In 2016, she was diagnosed with primary infertility and received artificial
The peritoneal dialysis prescription was modified to five 2 L exchanges per day, using 2.5%–1.5%–1.5%–1.5% physiogel (dextrose dialysate solution produced by Baxter Company) and extraneal (icodextrin dialysis solution produced by Baxter Company).

During pregnancy, the protein intake was 1.5 g/kg and the calorie intake was 2000 kcal/day. Daily ultrafiltration was 800 to 1000 mL and blood pressure ranged from 110/70 to 140/90 mm Hg. The hemoglobin level was maintained between 9.5 and 10.5 g/L. The targeted goal of predialysis BUN was <50 mg/dL, which was the cutoff value recommended in previous studies. Although they intermittently exceeded 50 mg/dL occasionally, it was generally maintained below 50 mg/dL. Albumin and electrolyte levels were maintained within the normal range. Urine output was 1000 to 1200 mL/day (Table 1).

The common fetal complications in these patients are abortions in the early stages in pregnancy. And after 20 week, intrauterine growth restriction, premature uterine contraction, and polyhydramnios are common. As a result, it is generally necessary to perform a fetal ultrasound and a fetal heart rate monitoring more frequently than a healthy pregnant woman. Careful uterine and fetal monitoring during dialysis, such as assessment of the fetal heart rate, combined with measures aimed at preventing dialysis-induced hypotension should be performed. Maternal haemodynamic instability may compromise the uteroplacental circulation and may be associated with the induction of uterine contractions. It is recommended to perform a fetal ultrasound frequently to determine its size, amount of amniotic fluid, and length of cervix to find out preterm labor quickly. If the fetus is smaller than 2 weeks, it should be performed once or twice a week.

At 21 weeks of gestation, the McDonald operation was performed due to incompetent internal os of cervix (IIOC) findings. Since then, the patient remained bedridden. Starting with the 24th week of gestation, the patient was administered tractocile (atosiban, Ferring, Saint-Prix, Swiss) in an effort to suppress uterine contractions. At 27 weeks and 2 days, the variability of fetal heart rate decreased. Therefore, we inserted a tunneled cuffed catheter to prepare for cesarean section. At 27 weeks 4 days, an urgent cesarean section was performed because fetal heart rate variability disappeared and late deceleration occurred in a nonstress test (NST). Hemodialysis (HD) was started from the day of surgery. Cesarean section was uneventful and delivered a preterm male baby with no anomalies, weighing 1060 mg, and 36 cm tall with an Apgar score of 3 and 7 at 1 and 5 minutes, respectively. The baby was transferred to the neonatal intensive care unit (NICU), intubated for 17 days and administered 3 doses of surfactant therapy. In the first blood test of the baby, creatinine was 4.94 mg/dL, which decreased later to 0.86 mg/dL after 10 days. Neonatal jaundice was detected.

**Table 1**

| Laboratory parameters in the pregnant. | Pre pregnancy | At 10 weeks | At 20 weeks | At 27 weeks | Reference ranges |
|---------------------------------------|--------------|-------------|-------------|-------------|-----------------|
| **Gestational Age**                   |              |             |             |             |                 |
| Weight, kg                           | 62           | 67          | 72          | 78          | 12–16 g/dL      |
| Urine volume, ml/day                 | 1200         | 1000        | 1000        | 1200        | 3.5–5 g/dL      |
| Hemoglobin, g/dL                     | 9.6          | 10.3        | 9.5         | 10.2        | 0.5–1.2 mg/dL   |
| Albumin, g/dL                        | 4            | 3.9         | 3.6         | 3.3         | 0.5–1.2 mg/dL   |
| Creatinine, mg/dL                    | 5.8          | 7.1         | 6.5         | 5.9         | 0.5–1.2 mg/dL   |
| Blood urea nitrogen, mg/dL           | 47.5         | 47.7        | 39.1        | 38.6        | 3–7 mg/dL       |
| Phosphorus, mg/dL                    | 4.2          | 4.7         | 3.7         | 5.2         | 2.5–4.5 mg/dL   |
| Uric acid, mg/dL                     | 5.7          | 8.6         | 8.5         | 7.2         | 3.5–6.1 mmol/L  |
| Potassium, mmol/L                    | 3.9          | 3.6         | 4.6         | 4.1         | 3.5–6.1 mmol/L  |
Phototherapy was performed to treat the newborn. The baby’s initial total bilirubin was 2.6 mg/dL, 6.5 mg/dL on the third day and normalized after 1 month. Initial hemoglobin level was 13.7 g/dL. However, since premature infants develop anemia, erythropoietin was administered to prevent blood transfusion, and is a standard therapy for premature infants. Body weight decreased from 1250 to 1110 g on day 9 of birth, increased to 2560 g on discharge and increased to 8000 g after 7 months. A month after the operation the caesarian section scar was completely healed and PD was resumed.

3. Discussion

Among the many causes of infertility, ESRD interferes with pregnancy in women due to anovulation, loss of libido, and endocrine changes. Additionally, even if pregnancy ensues in women with ESRD, it increases the risk of maternal and fetal mortality and morbidity.[1] Therefore, a tendency to discourage pregnancy in women with ESRD has been reported. However, successful delivery by women with ESRD has also been reported.[7,8] We also reported successful pregnancy and delivery in a 29-year-old patient with diabetic ESRD undergoing hemodialysis.[5] Studies reported increased rates of pregnancy and successful delivery in women undergoing dialysis.[6,9] Despite multiple challenges faced by women on dialysis, prolonged dialysis, appropriate hemodynamic stability, effective management of obstetric complications, and adequate correction of anemia and malnutrition are needed for successful deliveries.[10]

Both PD and HD are possible modes of renal replacement therapy in pregnant ESRD women. The superiority of either mode is debatable in the absence of comparative studies investigating the effectiveness of either method.[11] A few studies showed no significant differences in maternal and fetal outcomes among pregnant women on hemodialysis and peritoneal dialysis.[11,12] The guideline presented by the Italian Study Group on Kidney and Pregnancy in 2015 suggests maintenance of a pre pregnancy dialysis mode.[11] Maternal predialysis blood urea nitrogen (BUN) levels should be maintained below 50 mg/dL.[3] BUN levels below 50 mg/dL have been associated with maternal and fetal mortality and morbidity. Hypertension should be controlled to avoid proteinuria and preeclampsia. Alpha-methyldopa, beta-blockers, and hydralazine are safe drugs.[5] Angiotensin-converting enzyme inhibitors (ACEs) and angiotensin receptor blockers (ARBs) are contraindicated in pregnancy. Anemia can be managed by erythropoietin safely to achieve a target hemoglobin level above 10 to 11 g/dL and transferrin saturation above 30%.[14,15] It is recommended to maintain caloric intake of 30 to 35 kcal/day and protein intake of 1.8 g/kg/day.[14] Oral iron, folic acid and vitamin B12 also should be supplemented.[5,15] The frequency of visits should be personalized and fetal monitoring should be intensified.[15]

In our patient, the diagnosis of pregnancy was made in the 7th week, which was earlier than the mean time of diagnosis of 16.5 weeks. During pregnancy, the patient maintained a residual urine output, BUN levels below 50 mg/dL, controlled blood pressure and a targeted hemoglobin range. She obtained adequate calories and protein and was managed by a multidisciplinary team. She underwent urgent caesarean section due to reduced fetal heart rate. However, the cesarean section was uneventful and the patient delivered a preterm male baby with no anomalies.

ESRD should also be considered among the several causes of infertility in fertile women. If ESRD is the cause of infertility, the frequency of pregnancy increases following dialysis. However, the risk of pregnancy-related complications is increased in women becoming pregnant while undergoing peritoneal dialysis. However, if pregnancy is diagnosed early, intensive renal replacement therapy, adequate nutritional intake and regular fetal monitoring during pregnancy increase the chances of successful delivery while maintaining PD.

Acknowledgments

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2017R1D1A3B03027898) and Soonchunhyang University Research Fund.

Author contributions

Writing – original draft: Chi-Young Choi.
Writing – review & editing: Nam-Jun Cho, Samel Park, Hyo Wook Gil, Yun-Sook Kim, Eun Young Lee.

References

[1] Holley JL, Reddy SS. Pregnancy in dialysis patients: a review of outcomes, complications, and management. Semin Dial 2003;16:384–8.
[2] Levy DP, Giarras I, Jungers P. Pregnancy and end-stage renal disease—past experience and new insights. Nephrol Dial Transplant 1998;13:3005–7.
[3] Hou S. Pregnancy in chronic renal insufficiency and end-stage renal disease. Am J Kidney Dis 1999;33:23–52.
[4] Robinson CE, Unzelman RF, Chojnacki RE. Survival of an infant of a mother dependent upon hemodialysis. J Pediatr 1973;82:537–8.
[5] Kim YI, Jung HJ, Kim JH, et al. Successful pregnancy and childbirth in a patient with diabetic kidney disease receiving hemodialysis. Soon-chungyang Med Sci 2012;18:138–40.
[6] Barua M, Hladunewich M, Keumen J, et al. Successful pregnancies on nocturnal home hemodialysis. Clin J Am Soc Nephrol 2008;3:392–6.
[7] Abdallah A. Pregnancy in peritoneal dialysis and an infant with a ventricular septal defect. Saudi J Kidney Dis Transpl 2015;26:111–4.
[8] Lim TS, Shammuganathan M, Wong I, et al. Successful multigravid pregnancy in a 42-year-old patient on continuous ambulatory peritoneal dialysis and a review of the literature. BMC Nephrology 2017;18:1–5.
[9] Piccoli GB, Conin A, Consiglio V, et al. Pregnancy in dialysis patients: is the evidence strong enough to lead us to change our counseling policy? Clin J Am Soc Nephrol 2010;5:62–71.
[10] Bahadi A, El-Kabbaj D, Guelzim K, et al. Pregnancy during hemodialysis: a single center experience. Saudi J Kidney Dis Transpl 2010;21:646–51.
[11] Shenim D. Dialysis in pregnant women with chronic renal disease. Semin Dial 2003;16:379–83.
[12] Asamiya Y, Onubou S, Matsuda Y, et al. The importance of low blood urea nitrogen levels in pregnant patients undergoing hemodialysis to optimize birth weight and gestational age. Kidney Int 2009;75:1217–22.
[13] Cabudul G, Castellino S, Gernone G, et al. Best practices on pregnancy on dialysis. J Nephrol 2015;28:279–88.
[14] Walsh AM. Management of a pregnant woman dependent on haemodialysis. EDTNA-ERCA J 2002;28:91–4.
[15] Vázquez-Rodríguez JG. Hemodialysis and pregnancy: technical aspects. Cir Cir 2010;78:99–102.