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Peritoneal Dialysis and Pregnancy

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Abstract

Pregnancy is infrequent and has complicated course in women undergoing renal replacement therapy. According to recent data, rates of conception in women on hemodialysis increased from 1.5% to 15% and 1.1% in women on peritoneal dialysis (PD). Lower rates in patients on peritoneal dialysis are due to mechanical factors on top of functional and physiological irregularities. Due to assumption of almost negligible rates of conception, pregnancy symptoms in patients with chronic kidney disease stage V can be confused with uremic symptoms. Once pregnancy is established, multilevel changes need to be made in this patient population. The coordinated care between a nephrologist, obstetrician, and nutritionist is essential for better outcomes. In this chapter, we review a near-missed but a successful case report and details of pregnancy, outcomes, and complications in women on peritoneal dialysis.

Keywords: peritoneal dialysis, pregnancy, renal failure, maternal complications, fetal complications

1. Introduction

Pregnancy is not only rare but also problematic by maternal and fetal risks and complications in women on dialysis. The first case of female pregnancy while on peritoneal dialysis (PD) was reported in 1980s. The rates of conception in women on peritoneal dialysis are going up but still relatively lower than the rates in women on hemodialysis. Statistically, however, there is no difference in the live birth rate in peritoneal versus hemodialysis women. Due to assumption of almost negligible rates of conception, pregnancy symptoms in patients with chronic kidney disease stage V can be confused with uremic symptoms. In this patient population, basic pregnancy tests are not reliable because most of these markers are cleared

by kidneys and can be falsely elevated. For better outcomes, a multilevel coordinated care is needed for pregnant women on renal replacement therapy.

2. Prevalence

Although conception in end-stage renal disease (ESRD) patients is infrequent, recent data show that the conception rates are improving overtime. According to data from Registry of Pregnancy in Dialysis Patients (RPDP), conception rate in hemodialysis patients over a 4-year period (1992–1995) is 2.4%, whereas it was 1.5% in a 2-year period (1990–1992) in the past [1, 2]. Although most pregnancies in this patient population occur during the first few years on dialysis, there are case reports of pregnancies in women who were on dialysis for as long as 20 years. Repeated pregnancies are also not unknown. Out of 353 pregnant women reported by RPDP, eight became pregnant three times, eight became pregnant twice, and one became pregnant four times [1].

Saudi Arabia dialysis unit questionnaire data reported improved pregnancy rates of 5–7.9% [3, 4]. The Canada reported data with conception rate of 15.9% in women on intensive nocturnal hemodialysis [5]. Pregnancy in peritoneal dialysis patients remains low. According to data collection from 1699, in childbearing-age women on peritoneal dialysis, conception rate is only 1.1% [1].

3. Conception

Menstrual irregularities, infertility, and sexual dysfunction are known to occur in end-stage renal disease (ESRD) patients, and these functional and physiological abnormalities worsen as renal disease progresses. Holley et al. [6] described this parallel relationship where menstrual cycle irregularities begin when estimated glomerular filtration rate (eGFR) fall below 15 ml/min/1.73 m² and progresses to amenorrhea at eGFR below 5 ml/min/1.73 m².

Hormonal abnormality studies in dialysis patients observed an anovulatory cycles even in menstruating women. In 70–90% of the women, progesterone and estradiol hormone levels are low, whereas prolactin levels are high. Luteinizing hormone (LH) levels are elevated and follicular-stimulating hormone (FSH) levels are same or slightly lower to levels in normal women during the follicular phase of menstrual cycle. Although LH levels in women on dialysis are elevated, they fail to have luteal surge of LH, which is directly related to ovulation [7, 8]. Many other fertility-affecting factors in ESRD patients include subclinical hypothyroidism, medications, fatigue, anemia, and depression, which further results in lack of libido [9–11].

Furthermore, lower conception rate in patients on peritoneal dialysis are also due to mechanical factor. Recurrent peritonitis can also lead to fallopian tube obstruction. It is possible that hypertonic dextrose (dextrose dialysate solution) damages the ovum, or the volume to dialysate in the peritoneal space interferes with ovum transfer within the fallopian tube [12].

4. Diagnosis

Menstrual irregularities and amenorrhea challenge and delay the diagnosis of pregnancy in ESRD women. Human chorionic gonadotropin (HCG) is partially cleared by the kidneys and results in false-positive serum pregnancy tests in ESRD women. Beta-hCG and maternal serum pregnancy-associated plasma protein A (PAPP-A) are generally elevated in ESRD patients because these are inversely correlated with creatinine clearance. Hence, careful interpretation of these tests is advised while screening these women in the first trimester [11, 13, 14].

Therefore, among women suspected of pregnancy should be evaluated by ultrasonography to verify presence of viable fetus and to obtain the approximate gestational age. All confirmed pregnant women should be referred to high-risk obstetrician.

5. Case discussion

There have been multiple case reports of pregnancy in women on peritoneal and hemodialysis. Here, I present my published case to illustrate pregnancy diagnosis difficulty and management in women on peritoneal dialysis.

A 25 years old female with past medical history of hypertension, optic neuritis, history of pyelonephritis, left middle cranial fossa arachnoid cyst, asthma, and end-stage renal disease (ESRD) secondary to autosomal dominant polycystic kidney disease (ADPKD) was transferred to renal clinic with concerning uremic symptoms with nausea, anorexia, and loss of weight. Her medications included diovan, oxycodone, Phenergan, calcium with vitamin D. At the time of presentation to renal clinic, her serum creatinine was 2.7 and estimated glomerular filtration rate (eGFR) of 26 ml/min/1.73 m². Given low chances of conception in ESRD patients, false-positive beta human chorionic gonadotropin (β -HCG) test in this patient population, no concern of pregnancy by patient, and previously unremarkable ultrasound other than ADPKD her symptoms were thought to be due to uremia. After discussion, the patient elected to have a peritoneal dialysis. A PD catheter was placed and she was referred to PD clinic for education, training, and initiation of PD.

Two weeks later, she presented to the emergency room with persistent symptoms of nausea, vomiting, and now abdominal cramps. A computerized tomography (CT) scan of abdomen and pelvis revealed ascending colitis probably inflammatory versus infectious, scattered free intra-abdominal fluid, but no documentation of uterus. Given low concerns of pregnancy, β -HCG test was not obtained and she was discharged with the diagnosis of the gastroenteritis. Even after a month of initiation of PD, patient continued to have nausea, vomiting, and anorexia and her dialysis exchanges were increased to 5/day and calcium supplements were discontinued. Her first dialysis adequacy (Kt/V) was 3.2.

Given persistent symptoms of nausea and vomiting, she was referred to her primary care physician (PCP) for further workup. A pregnancy test with β -HCG was positive, which could be falsely positive because β -HCG is partially cleared by kidneys. Due to high suspicious for

pregnancy, her diovan was immediately stopped and started on labetalol for hypertension management. Obstetrics ultrasound revealed 20 weeks of pregnancy and she was referred to the obstetrician for close follow-up. Thereafter, she continued to have coordinated care by her nephrologist, obstetrician, and nutritionist.

Her dialysis adequacy was maintained with Kt/V urea of >3.0 and blood urea nitrogen (BUN) <50 throughout the pregnancy (**Figures 1 and 2**). She was treated with increased doses of Epogen and iron for anemia and calcitriol for secondary hyperparathyroidism. Her pregnancy remained uneventful and she continued her PD until 38 weeks and 5 days of gestation when she presented to the hospital because she was unable to perform her peritoneal dialysis (PD) for 4 days due to abdominal discomfort.

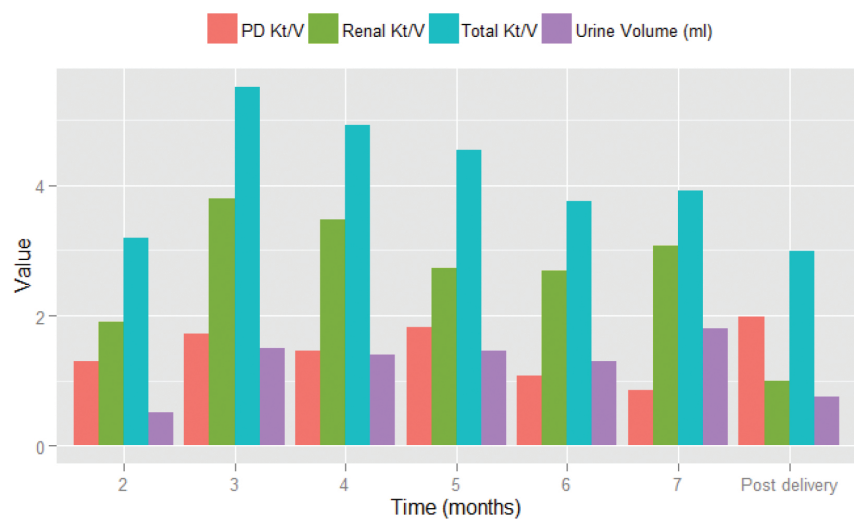


Figure 1. Kt/V and urine volume measurement in a woman on peritoneal dialysis during pregnancy.

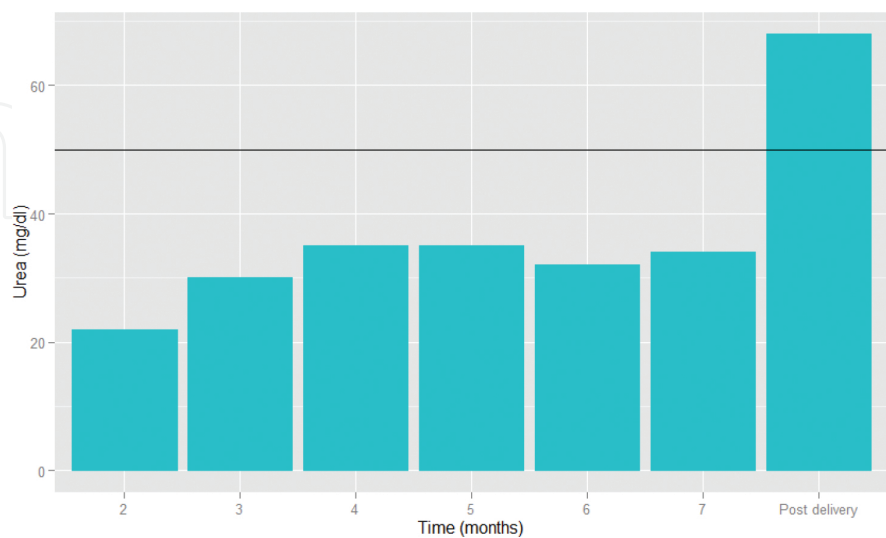


Figure 2. BUN measurement in a woman on peritoneal dialysis during pregnancy.

Since patient was not able to continue PD, an option of hemodialysis was discussed with the patient. She declined to start on the hemodialysis, rather chose an induction of labor for delivery. PD was continued with small frequent exchanges during labor. A healthy baby was delivered with uneventful postpartum period. Regular PD prescription was resumed 12 h after delivery. She was discharged to home 3 days after delivery [11].

6. Drug therapy

The physicians need to be very careful of medications used to treat kidney disease in pregnant women. It is also important to evaluate medication risk on fetus. Since most common antihypertensive medicines such as angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are associated with neonatal morbidity and mortality, these should be discontinued. Alternative antihypertensives such as β -blockers and hydralazine are relatively safe during pregnancy.

7. General obstetrical management

As mentioned earlier, all women with diagnosis of pregnancy while on dialysis should be referred to high-risk obstetrician. Some of the general guidelines that high-risk obstetrician follows include increased frequency of prenatal visits, early detection and treatment of asymptomatic bacteriuria, detect early signs of preeclampsia, frequent fetal surveillance, and preterm intervention or induction of labor.

8. General nephrology management

All nephrologists needs to be aware that although low risk but women on dialysis can become pregnant. The differentiation of uremic and pregnancy symptoms is the key. Early detected pregnant dialysis women should receive a multilevel coordinated care.

Some of the general guidelines include increased frequency of dialysis, BUN goal <50 mg/dl, target Kt/V goal of 2.2–2.4, increased doses of potassium supplements, Epogen, and iron, and maintain adequate volume and weight.

9. Maternal risks and complications

The maternal complications include premature birth, uncontrolled hypertension, miscarriage, placental detachment, anemia, and infection, premature rupture of membranes, polyhydramnios, preeclampsia, eclampsia, hemorrhage, C-section, and even maternal death.

9.1. Premature birth

According to RPDP reported birth in women on dialysis, 84% of infants were born prematurely, 44% weighed less than 1500 g, and 28% were small for gestational age. Gestational age of survived infants f women on peritoneal dialysis ranged from 31 to 38 weeks [1].

9.2. Hypertension

Hypertension in pregnant dialysis patients is very common. Approximately, 80% of pregnant dialysis women have a blood pressure (BP) higher than 140/90 and even more than 50% have BP greater than 170/110. Given continuous therapy in PD to achieve euvolemic status, it is thought that PD patient should have lower risk of hypertension, but small studies have shown no difference [11, 12]. Since hypertension in dialysis patients is mostly related to their volume status, it poses another challenge to determine dry weight in pregnant dialysis women (see below for details).

9.3. Preeclampsia/eclampsia/HELLP syndrome

Preeclampsia is when pregnant women develop high blood pressure and a significant amount of protein in the urine after the 20th week (i.e., late second or third trimester) of pregnancy. If left untreated, it can lead to an acute and life-threatening condition with tonic-clonic seizures, called eclampsia. HELLP syndrome is identified with a group of hematological alterations including hemolysis, elevated liver enzymes, and low platelet count. In 10–20% of the cases, HELLP can occur as a complication in women with severe preeclampsia or eclampsia [15].

Preeclampsia is difficult to diagnose in dialysis patients due to anuria that makes unable to determine proteinuria. In these patients, preeclampsia diagnosis relies on the assessment of worsening blood pressure, fetal growth retardation, alterations in placental Doppler blood flow and hematological abnormalities in case of HELLP syndrome [11, 15].

9.4. Urea clearance, dialysis adequacy, and polyhydramnios

In pregnant women on dialysis, blood urea nitrogen (BUN) level is an important marker of overall fetal outcome. Many isolated clinical cases and retrospective studies have reported improved fetal survival in women with BUN <50 mg/dl. Increased frequency of dialysis to four to six sessions per week to achieve at least 20 h of dialysis per week helps to keep BUN goal <50 mg/dl [16, 17]. It also helps better control of hypertension, improves maternal nutrition, and prevents polyhydramnios [11].

There is no commonly accepted target Kt/V for pregnant PD patients. However, Okundaye and Hou [18] has reported target Kt/V goal of 2.2–2.4 for better outcomes. Higher Kt/V is achieved by increasing fill volume that might be difficult in pregnant patients due to discomfort. Intensive PD is very important in the third trimester when fetal urea production is increased to 540 mg/day. This can be achieved by increasing small volume exchanges as we did in our reported patient.

Approximately, 30–70% pregnant dialysis women have incidence of polyhydramnios. Due to urea-induced osmotic diuresis there is increased production in fetal urine that further leads to excess amniotic fluid. Increased dialysis dose in this patient population can help reduce these complications [19, 20].

9.5. Electrolytes, vitamins, minerals, and acid-base abnormalities

Most of the electrolytes abnormalities occur due to increased dialysis dose in these patients. Hypokalemia gets worse in dialyzed pregnant PD patient that requires increased doses of potassium supplementation. Usually, phosphate binders are discontinued in hemodialysis patients. Phosphate replacement might be needed in pregnant PD patients [11, 18].

Minerals and water soluble vitamins are often removed by intensive dialysis and usually require double the dose of daily multivitamins, particularly folic acid. The pregnant PD women do not have metabolic alkalosis that is usually seen in hemodialysis patients and requires lower bicarbonate bath to maintain normal physiological bicarbonate goal of 25 meq/L [12].

9.6. Anemia

The etiology of anemia in pregnant dialysis women is multifactorial including erythropoietin resistance probably from pregnancy induced cytokines, high demand of red blood cell production for fetal growth, and the iron and red blood cell loss from intense frequent dialysis. Therefore, iron requirement increases to 30 mg/day and erythropoietin requirement increases by 50% [5].

9.7. Nutrition and weight gain

Nutritional assessment and counseling is very important to ensure adequate protein and caloric intake. Adequate protein intake might be difficult in this patient population due to nausea, anorexia, and protein loss due to intensive dialysis. The pregnant dialysis women should take in 1 g/kg/day protein, adding 20 g/day for fetal growth [21]. For development of fetal skeleton, maternal diet should include an additional 30 g of calcium supplementation [12].

Weight gain determination in pregnant dialysis patient is very difficult. About 9 L of total body water increases in pregnancy that leads to intravascular expansion due to vasodilatation, making fluid removal difficult. The pregnant mother should gain a minimum of 1–1.5 kg in the first trimester and 0.45–1 kg/week afterward [17]. Estimated dry weight (EDW) should be increased to 400 g/week after first trimester to account for fetal weight of about 500 mg/week in the second and third trimester [20]. A pregnant woman with a normal body mass index should gain maternal weight of 11–15 kg [11].

9.8. Peritonitis and bloody effluent

There is limited information on peritonitis in pregnant CAPD patients. In three reported cases of peritonitis in pregnant PD patients, labor occurred in two women. One resulted in still birth

and other in premature baby who survived [18]. RPDP reported that five out of six pregnancies which were complicated by peritonitis, resulted in surviving infants. One woman had second trimester spontaneous abortion. There is always risk of peritonitis from any pregnancy-associated infections due to connection between peritoneum and fallopian tubes. Cephalosporins and penicillins are safe antibiotics to use in pregnancy associated peritonitis [18].

In nonpregnant PD patients, bloody effluent is rarely a sign of a serious problem. However, it is concerning in pregnant PD patients and can indicate impending abortion or placental abruption [22]. These patients should be hospitalized for observation and placental separation should be ruled out with fetal ultrasound [11].

9.9. Anticoagulation

Heparin does not cross the placenta and is not teratogenic. Low molecular weight heparin (LMWH) appears to be as safe as unfractionated heparin (UH) in pregnant women. LMWH has a favorable dosing route and interval and requires less monitoring than UH. Therefore, it can be safely used in pregnant women to prevent access clotting in HD and to maintain fibrin free dialysis in PD. Coumadin is contraindicated in these patients [11, 23].

9.10. Labor and delivery

At the time of labor and delivery especially in cases of preeclampsia magnesium is given in high doses. In this patient population, magnesium must be administered with caution and maintain magnesium levels below 5–7 mg/dl to prevent toxicity [23].

Dialysis status by itself does not warrant for C-section. However, if required for obstetric reasons, C-section can be performed successfully in PD patients. The abdomen should be drained before surgery and if it is possible surgery should be done extraperitoneally. In 24 h after the surgery, peritoneal dialysis can be resumed with small volume exchanges. In cases of PD fluid leakage, patients should be switched to hemodialysis for 2 weeks [11, 12].

10. Fetal risks and complications

All infants born to women on dialysis should be observed in high-risk setting. Major complications in the newborn are due to growth retardation and prematurity.

Neonates born with BUN and serum Cr same as of their mother's serum BUN and Cr which leads to osmotic diuresis and can cause significant volume contraction and electrolytes imbalance if losses are not replaced. Several retrospective studies and clinical cases have reported increased fetal survival in women with BUN <50 mg/dl. Breast milk will have high concentration of urea and in cases of breast-feeding it can lead to osmotic diuresis in these infants [11, 18].

Infants who are exposed to hypercalcemia during pregnancy are at increased risk of hypocalcemia and tetany after birth [12].

11. Overall outcomes

In a series, Redrow et al. [22] concluded that peritoneal dialysis is superior to hemodialysis. However, data reported by them did not support this conclusion. According to an early report by RPDP, there is no statistical difference in the live birth rate in peritoneal (47.6%) versus hemodialysis (46.4%) patients [1]. In a single center study, Chow et al. reported worse outcomes in peritoneal dialysis patients [24]. Theoretically, peritoneal dialysis is considered superior to hemodialysis for pregnancy given more stable biochemical parameters, higher mean hemoglobin, gentle daily ultrafiltration, and no required systemic anticoagulation [25].

12. Conclusion

The rates of pregnancy in ESRD women are increasing overtime. Besides the challenges of functional and physiological irregularities seen in hemodialysis patients, PD women also face mechanical challenges. Most of the patients who get pregnant while on PD are transitioned to daily HD during pregnancy with the goals of keeping their BUN <50 mg/dl and spKt/V > 2.2–2.4. However, the live birth rate not different between PD (47.6%) and HD (46.4%) receiving women. A highly coordinate care between patient, her nephrologist obstetrician, neonatologist, dialysis nurse, and her nutritionist is essential for better outcome.

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