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Case Report

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Pregnancy In Peritoneal Dialysis Using Tidal Automated Peritoneal Dialysis: Largest Case Series. Single - Center Experience

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Abstract

Pregnant women with End Stage Kidney Disease (ESKD) have higher maternal and fetal complications than those with normal renal function. Fetal survival in women who conceive after commencing dialysis is 50%. Renal transplant has been the ideal option for pregnant women with ESKD, but limited organ donation leads to increased cases of pregnant patients in both Hemodialysis (HD) and Peritoneal dialysis (PD). Due to heterogeneity in literature, the lack of a precise control group in most case series, and the lack of unified definitions for relevant outcomes such as preterm, small for gestational age, and preeclampsia, it is challenging to publish standardized guidelines for pregnant PD patients.

In conclusion, we report our unique successful experience of treating eight pregnant PD women who conceived after commencing PD. To the best of our knowledge, this is the largest case series in literature for treating pregnant PD women using Tidal Automated PD.

Keywords: Tidal Peritoneal Dialysis; Pregnancy; Chronic Kidney Disease.

Introduction

End Stage Kidney Disease (ESKD) women of childbearing age are less likely to become pregnant, and pregnancy carries a high risk for maternal and fetal complications. The overall prevalence of conception in the dialysis population is 0.3% to 2.2% per year, but this prevalence has recently increased to 17.8% per 1000-patient-years [1]. This might be attributed to better dialysis adequacy, more frequent and intense dialysis during pregnancy, better correction of anemia by using erythropoiesis-stimulating agents, and improved dialysis-related services [2]. Pregnancy with ESKD on dialysis had an increased risk for maternal and fetal complications, including uncontrolled hypertension, preeclampsia, and HELP syndrome (hemolysis, elevated liver enzyme, and low platelet count), and major fetal complications, which include neonatal death, stillbirth, preterm and small for gestational age. [3]. Hladunewich etal, reported 77 pregnancies in the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) from 2001-2011 with a live birth rate of 73%, while a Canadian cohort of 22 pregnancies using intensified hemodialysis has reported a live birth of 86% [2-3]. Moreover, Jesudason etal, reported that better pregnancy outcomes were observed if conception occurred before commencing dialysis; the live birth rate was 91% compared to 61% who conceived after dialysis initiation. This is probably due to better preservation of residual kidney function [4]. Women of childbearing age on peritoneal dialysis had lower conception rates than those on hemodialysis

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(Hazard Ratio 0.47,95%CL 0.41-0.55) [1]. This might be due to reduced ovulation by hypertonic dialysate [4]. However, fetal survival did not differ significantly from pregnancy in HD. A systematic review by Piccloi etal, showed a higher incidence of small for gestational age in PD compared to HD (66.6%-31%) respectively [5]. PD had myriad advantages during pregnancy, including slow and continuous ultrafiltration, which helps maintain fetal placenta circulation, preservation of residual kidney function, and a steady state in blood urea nitrogen during pregnancy that helps reduce polyhydramnios compared to HD [6]. The ideal PD prescriptions during pregnancy had not yet been identified and depend on multiple factors such as body surface area, residual kidney function, fill volume, and peritoneal equilibration test [7,8,9]. Due to the scarcity of data and lack of guidelines for pregnant PD patients, most clinicians shifted their PD patients to HD after conception during the first trimester [10-13]. Here, we report our experience using Tidal Peritoneal Dialysis for eight pregnant patients who conceived after commencing PD without shifting them to HD with minimal complications. To our knowledge, this is the largest case series in the literature on using Tidal Automated PD (APD) during pregnancy from a single center.

Case Presentation

Case 1

A 38-year-old Saudi lady who is a known case of End Stage Kidney Disease (ESKD) secondary to focal segmental glomerulosclerosis was maintained on HD through right AV fistula for six years, and she had an uneventful pregnancy after one year of commencing HD. She was shifted to peritoneal dialysis due to her preference, and she was maintained on 10 liter 1.36% Dianeal over 9 hours, each fill volume of 2 liter and the last fill volume of 2-liter Extraneal. Two years after starting peritoneal dialysis, she was found to be pregnant. Obstetric ultrasound showed a single live product compatible with 16 weeks by measurement of biparietal diameter and cephalic circumference, normal placenta inserted with maturity degree 0, and normal amniotic fluid. Her vitals were as follows: blood pressure 110/70 mmHg, heart rate 88/min, respiratory rate 20/min, afebrile, weight 52 kg and height 155 cm, body surface area 1.4m². Her residual renal function was 1.5 liter per day, and creatinine clearance was 8ml/min. Renal ultrasound showed a right kidney size of 79X30 mm and a left kidney size of 94X55 mm, loss of corticomedullary differentiation but with no hydronephrosis. Peritoneal dialysis prescription was modified to a Tidal of 10 liters Physioneal, each fill volume of 1.5 liter over 9 hours, and Extraneal was discontinued. Lisinopril was stopped and methyldopa 250 mg three times per day was started, and she was maintained on the following medications: calcium carbonate 1.2 gm three times per day, calcitriol 0.5 mg daily, folic acid 5 mg daily, darbepoetin 60 mg weekly, multivitamins, and ferrous sulphate 190 mg daily. Her diet was modified with a total dietary protein of 1.5g/kg body weight and phosphorus 800 mg/day. She had a regular follow-up every week at both the Peritoneal Dialysis Unit and Obstetrics and Gynecology clinic, and through a remote monitoring system. Her average blood pressure readings ranged between 110/70 to 140/80mmHg with an uneventful pregnancy. Delivery was induced at 37 weeks, and she had a normal vaginal delivery, and a baby girl was born with a weight of 1500 gm, a height of 42 cm, and an Apgar score of 7-8. Peritoneal dialysis was held during delivery, and vancomycin and ceftriaxone intraperitoneal were given as prophylaxis.

The baby had a mild ventricle septal defect. PD was started the next day with 10-liter Physioneal over 9 hours, each fill volume of 1.5 liters. The mother was discharged after three days in a stable condition. Table I depicts all the laboratory results in the first, second and third trimesters for all patients, and Table II depicts the maternal and obstetric complications.

Case 2

A 45-year-old Saudi lady with a known case of ESKD secondary to focal segmental glomerulosclerosis, status post-living non-related kidney transplant for 15 years, developed chronic allograft nephropathy requiring renal replacement therapy. She was started on Incremental APD 5 times per week on the following prescription: 10 liters 1.36% over 9 hours, each fill of 1.9 liters with regular follow-up at the PD unit with no complications. Her average urine output was 1600ml per day, her creatine clearance was 8ml/min, and the peritoneal equilibration test showed high average. After 16 months of commencing APD, she was found pregnant when complaining of generalized weakness, nausea, and vomiting in the early morning. Obstetric ultrasound showed a single live product compatible with 14 weeks by measurement of biparietal diameter and cephalic circumference. Therefore, all her anti-hypertension and immunosuppression medications were modified, and the PD prescription was tailored to 10 liters of Tidal APD 70% over 10 hours, each fill of 1.5 liters daily. She was doing fine on weekly regular follow-ups at the PD unit with a nephrologist and an obstetrics gynecologist, as her pregnancy was considered high-risk. The average ultrafiltration was 700-800 ml daily, and the residual renal function was 1000 ml per day. Her blood pressure readings were around 145/80mmHg on the following medications: methyldopa 500 mg Q8 hours, hydralazine 100 mg q8 hours, and labetalol 100 mg q8 hours. On week 25, she developed a very high blood pressure of 200/110mmHg and was admitted to the intensive care unit. Magnesium sulphate and phenytoin infusion were started, and she had a spontaneous vaginal delivery, a baby boy with a weight of 850 gm and an Apgar score of 3-4. The baby was intubated and admitted to intensive neonatal care, and unfortunately, he died two days after delivery. The mother's blood pressure was normalized post-delivery, and PD resumed after two days.

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Table 1: The Laboratory Results in the First, Second and Third Trimesters for the PD Patients

Case No.	1		2		3		4		5		6		7		8	
Gestational age	First Trimester	Third Trimester	First Trimester	Second Trimester	First Trimester	Third Trimester	First Trimester	Third Trimester	First Trimester	Third Trimester	First Trimester	Second Trimester	First Trimester	Third Trimester	First Trimester	Third Trimester
Age	38		45		25		26		22		36		24		19	
Weight	52	63.3	70	74	57	66	71	78	99.5	110	73	73.5	60	68	52	60
Hemoglobin	9.7	10.6	9.5	11	11.6	11	10.5	11.9	12.2	10.3	9.1	9	10.1	11.3	9.8	11
Urea	64	50	71	58	62	39	38	36	58	57	34	37	45	40	38	43
Creatinine	8.47	9.79	11.62	13.56	7.24	7.19	8	9.5	6.2	6.2	4.4	4.95	5.5	5.7	6.7	8
Co2	22	23	20	23	24	24.9	25	28	25	20	23	21	23	27	21	23
Kt/v	1.93	2	2.65	1.77	2.29	2.59	2.1	2.3	2.2	2.5	2.24	2.78	2.7	2.1	2.4	2
Urine volume	1500	1050	1600	1050	2000	1200	2200	1200	1950	1200	1500	1900	2000	2500	1533	1030
Duration Pre-Pregnancy	24 M		16 M		2 m		12 M		2 M		6 M		12 M		8 M	
Duration of Pregnancy	37 W		25 W		37 W		37 1/2 W		37 W + 1D		20 W		38 W		37 W	
Delivery	Normal		Normal		NL		Normal		CS		Normal		Cs		Cs	
Complication			Stillbirth		Hypertension						Aborted					

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Table II: The Maternal and Obstetric Complications

Maternal complications	Case
Exit site infection	Nil
Peritonitis	Nil
Preeclampsia	Case 2,6
Catheter Migration	Nil
Malposition	Case 7,8
Cesarean Section	Case 5,7,8
Obstetric Complications	Case
Premature	Case 2,6
Stillbirth	Case 2
Small for Gestational Age	1,4,5
Polyhydramnios	Nil
Ventricular Septal Defect	Case 1

Case 3

A 25-year-old Saudi lady with a known case of ESKD due to unknown etiology started on incremental peritoneal dialysis through a triple cuff Saudi catheter three times per week due to good residual renal function. Her average urine output was 2 liters, and creatinine clearance was 10 ml/min on the following prescription: 10 liters of 1.36% Physioneal over 9 hours, each fill of 1.9 liters. On examination, her blood pressure (BP) was 120/75 mmHg, heart rate 78 / min, and afebrile, with unremarkable systemic examination. Pregnancy was detected at 14 weeks after amenorrhea, nausea, and vomiting, with a positive BHCG test. Obstetric ultrasound showed a single viable product compatible with 13 weeks by measurement of biparietal diameter and cephalic circumference.

The peritoneal prescription was modified to a Tidal PD 70% with 10 liters Physioneal over 9 hours, each fill of 1.5 liters daily, with regular follow-ups at the PD unit every four weeks and through a daily remote monitoring system as well as follow-ups at the obstetrics and gynecology clinic. During the last trimester, the PD prescription was modified to be a Tidal of 70% 10 liters over 12 hours and a last fill of one-liter Extraneal. At week 24, she developed hypertension, which was treated by methyldopa 250mg every 8 hours and increased to 500mg every 8 hours due to uncontrolled hypertension. Throughout her pregnancy, she was maintained on the following medications: calcium carbonate 1.2 gm three times per day, calcitriol 0.5 mg daily, folic acid 5 mg daily, darbepoetin 60 mg weekly, multivitamins, ferrous sulphate 190 mg daily and aspirin 81 mg daily.

Delivery was induced at the gestational age (GA) of 37 weeks+5 days, and she had a normal vaginal delivery. A baby girl was born weighing 2,010 gm, with a height of 40.5 cm and an Apgar score of 9-10. Peritoneal dialysis was held one day before induction, and one dose of vancomycin and ceftriaxone were given as a prophylaxis.

The mother and her baby were discharged after two days without complications, and the Tidal PD was restarted the next day with each fill of 1.5 liters.

Case 4

A 26-year-old Saudi lady with ESKD secondary to focal segmental glomerulosclerosis and hypertension started on incremental Tidal APD similar to the above-mentioned patients with regular follow-ups at our PD unit every month. She became pregnant 12 months after PD initiation. Pregnancy was identified at eight weeks due to amenorrhea. She had a good residual renal function, an average urine output of 2200ml daily, and APD was intensified daily. Her average blood pressure was 120/70mmHg, and she was maintained on labetalol 100 every 12 hours and hydralazine 50 mg three times per day. She completed a full-term pregnancy at 38 weeks, labor was induced, and she delivered a baby boy of 1600 gm and height of 42 cm with an Apgar score of 8-9. APD was held one day prior to induction, and vancomycin and ceftriaxone were given intraperitoneal as prophylaxis. Both the mother and baby were discharged two days after delivery without complications.

Case 5

A 22-year-old Saudi lady with a known case of ESKD secondary to diabetes mellitus started on incremental tidal APD 70 % 10-liter Physeoneal over 9 hours, each fill of1.5 liters with an average ultrafiltration of 600-900 ml and residual renal function of 1950ml. Two months after commencing APD, she conceived, and the pregnancy was identified at 13 weeks, so APD was intensified daily. At 28 weeks, the dialysis duration was increased to 12 hours, and the Extraneal of 1 liter was added to the PD prescription. At 37 weeks, she delivered through a caesarian section due to fetal distress, a baby boy weighing 1800 gm, and an Apgar score of 6-7. The baby was kept in neonatal care for one week and discharged well. The mother received prophylactic antibiotics similar to the above patients.

Case 6

A 36-year-old Yamani lady with a case of ESKD secondary to diabetes mellitus started incremental APD similar to the above patients. Six months after Tidal APD commencement, she became pregnant, and the pregnancy was detected at a gestational age of 12 weeks due to amenorrhea. APD was intensified, similar to the other patients, and she was following in the PD unit weekly with average blood pressure readings of 135/80 mmHg and urine output of 1600 ml per day. At 20 weeks, she developed abdominal pain and then aborted a baby boy weighing 830gm, who was dead upon delivery. APD was continued two days after the delivery without further complications.

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Case 7

A 24-year-old Saudi lady with ESKD of unknown etiology started on Tidal incremental APD similar to the above patients. She got pregnant one year after commencing APD. The pregnancy was detected at eight weeks due to amenorrhea. She was regularly followed up at our PD unit and through remote monitoring, at the beginning monthly, then on the second and third trimesters weekly. Her average urine output was around 1700-2000ml, and her blood pressure reading was 130/75 mmHg. She had a full-term pregnancy, and at 38 weeks, labor was induced, but due to breech position, a caesarian section was done, and she delivered a baby girl weighing 2200 gm and with a height of 39 cm and an Apgar score of 9-10. The patient received antibiotic prophylaxis, and PD was held one day before labor induction until four weeks after the caesarian section, during which she was shifted to HD.

Case 8

A 19-year-old Saudi lady with a known case of polycystic kidney disease started on a Tidal APD with 80% due to good residual renal function, with an average urine output of 2500 ml. Eight months after APD commencement, she got pregnant, so APD was intensified, similar to the other patients. She completed 37 weeks without complications, and a caesarian section was done due to fetal distress; a baby boy was born uneventfully with an Apgar score of 8-9. APD was held for four weeks and then resumed, similar to the previous patients.

Discussion

Renal transplant has been the ideal option for pregnant women with ESKD, but the limited number of organ donations leads to increased cases of pregnancy in both HD and PD [14]. The first successful pregnancy in HD was reported in 1971 [15]; a decade later, a successful pregnancy was reported in CAPD [16]. There has been a substantial increase in reported cases of pregnant dialysis patients during the last few years. This number increased from 90 cases in 2000 to 574 in 2014 [17]. This increase in the number of pregnancies was mainly attributed to improved dialysis adequacy, more intensified dialysis regimen, and general improvement in dialysis services [18-20]. Maternal perinatal mortality is very low, 2 out of 543 pregnancies, and the prevalence of fetal malformation is only 2%; this risk is similar to the general population [21-22]. Recently, there has been a remarkable improvement in pregnancy outcomes during dialysis, ranging from a 21% survival rate reported by the European Dialysis and Transplant Association to 70% in recent case series [23-25]. The conception rate for dialysis women during a childbearing age is low, ranging from 0.3 to 4.1% [26-27]. This is due to multiple factors such as decreased libido, low progesterone levels, anovulation, amenorrhea, and losing both luteinizing and follicular stimulation hormone surge [28]. Due to menstruation irregularities during dialysis, precise pregnancy identification in women with ESKD on dialysis is challenging because of the mildly persistence elevation of beta-human chorionic gonadotropin in dialysis populations. It takes an average of 16.5 weeks to confirm pregnancy in dialysis patients, and simultaneous pelvic ultrasound is highly recommended once pregnancy is suspected in order to verify the presence of a viable fetus and estimate the gestational age [29-30]. Pregnancy during PD has potential adverse maternal outcomes, including gestational hypertension, preeclampsia, eclampsia, and increased maternal mortality. Therefore, regular fetal ultrasound assessment after 20 weeks of pregnancy is crucial in identifying placenta artery abnormalities that might help early detect high-risk patients who develop preeclampsia [14]. Two of our patients developed preeclampsia, leading to abruptio placenta and intrauterine fetal death. Pregnancy in ESKD patients is more common in HD than in PD (2.4% -1.11%) respectively [8]. Once pregnancy occurs, the fetal outcomes are preferable in the PD population due to the myriad advantages of peritoneal dialysis, including good residual renal function, a more stable metabolic environment, and, most importantly, the absence of intradialytic hypotension that could have potentially deleterious effects on fetal growth and survival [8]. Nakabayashi reported 15 pregnancies conceived on dialysis, and he found that fetal survival is correlated with duration of dialysis, residual renal function, gestational age of more than 33 weeks, and birth weight of more than 1782 gm [31]. Fetal survival in women who conceive after commencing dialysis is 50%, and the risk is further compounded for women aged 35 years and older. Joly et al. reported the risk associated with pregnancy aged 35 years and above in a large retrospective study of 385,120 pregnant women aged 35-40 years old who were at higher risk of placenta previa, breech presentation, emergency cesarean section, small for gestational age, stillbirth, and gestational diabetes Mellitus. Women aged 40 and above had a higher odds ratio for the same risks [32]. Three of our patients were older than 35 years; one of them developed preeclampsia, the other developed intrauterine fetal death, and the third completed her pregnancy successfully. The total number of successful pregnancies during PD until 2017 was 47 from 54 pregnant women [8]. Multiple case reports and a case series have reported better pregnancy outcomes in women who conceived before commencing PD and in women who used hybrid HD [8-14]. This is contrary to our case series, in which none of our patients used HD, and all of the patients conceived after PD initiation. The most common fetal complications include prematurity, polyhydramnios, intrauterine fetal death, stillbirth, small for gestational age, and fetal distress [32]. One of our babies developed respiratory distress post-delivery that necessitated

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intubation. Early pregnancy identification during peritoneal dialysis is paramount to nephrologists and obstetricians. Medications with deleterious adverse effects on the fetus should be avoided once pregnancy is planned or detected, particularly angiotensin-converting enzyme inhibitors and angiotensin receptor blockers [8]. Other essential medications during dialysis, such as sevelamer carbonate, lanthanum, aluminum hydro-oxide, cinacalcet, and paricalcitol, have not been examined yet during pregnancy, and their safety is uncertain. There have been eight reported cases of peritonitis and five exit site infections in pregnant PD patients; two of the eight cases occurred postpartum and were associated with premature rupture of the membrane in two cases and neonatal death in one case [8]. None of our patients developed peritonitis. Other specific complications related to PD therapy include hemoperitoneum [33], catheter displacement [34], catheter-related pain, and outflow dysfunction [8]. The uterus usually enlarges during pregnancy, which could lead to catheter displacement, inevitably affecting dialysis adequacy, causing fluid overload, and poor pregnancy outcomes. All our patients were on triple cuff PD catheters, known for zero catheter migration rate and better dialysis adequacy [35]. None of our patients developed catheter displacement. Malnutrition is common in pregnant PD women due to decreased appetite induced by uremia, metabolic acidosis, large uterus, and high glucose load associated with PD fluid. Thus, protein restriction is not usually advised during pregnancy with ESKD, and a minimal daily protein intake of 1.4-2.1 g/kg/day is recommended [36]. In addition, regular monitoring of calcium and Vitamin D3 levels and administering low-dose aspirin are essential to prevent preeclampsia and eclampsia. Providing water-soluble vitamins and minerals during pregnancy is crucial for any successful pregnancy, as folic acid in high doses prevents neural tube defects in the early stage of pregnancy. Other vitamins such as vitamin c, thiamine, riboflavin, and Vitamin B6 are also important [8-14]. Delivery is usually induced at 37 weeks of gestation if there are no maternal or fetal complications. This will give the clinician enough time to drain the PD fluid and to give intraperitoneal prophylactic antibiotics. A vaginal delivery is usually preferred [14,36]. All our patients received intraperitoneal antibiotics (vancomycin and ceftriaxone), and the PD fluid was drained. Six of our patients had spontaneous vaginal delivery, and none developed peritonitis postpartum. Peritoneal dialysis is resumed 48 hours after delivery, and if the patient requires cesarean section, it is preferred to wait 4-6 weeks postpartum and then resume PD gradually. Given the heterogeneity in literature and lack of a control group in most case series like our series, as well as the lack of clear definitions for relevant outcomes such as preterm, small for gestational age, and preeclampsia, it is challenging to publish standardized guidelines for pregnant PD patients. For these reasons, individualization of dialysis prescriptions and meticulous follow-ups are paramount for any successful pregnancy during dialysis. The favorable outcomes of our series are mainly attributed to our patients' good residual renal function, meticulous follow-ups with expert PD nephrologists and obstetricians, remote monitoring of our patients, and the use of triple cuff PD catheters that aided in improving dialysis adequacy with zero catheter migration. These findings need to be confirmed by further studies.

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Dr. Amani Alhwiesh, Hatem H. Althubain ,Kareemah Alquraish 1,Nour Alnas1i ,, Suzan Al-Audah, and Badran AlHwiesh were responsible for collecting the cases and drafting the case presentation. Dr. Amani, Dr. Ibraheem, and Dr. Nadia performed the literature review and drafted the discussion. Prof. Alhwiesh, Mohamed A. Nasreldin, and Dr. Khadija contributed to writing and reviewing the manuscript.

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