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(Edition française)

First successful pregnancy on peritoneal dialysis in reunion island

(Première grossesse avec succès en dialyse péritonéale à La Réunion)

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Summary

We report the first successful pregnancy on peritoneal dialysis (PD), in 2023, in the overseas territories and departments (DOM-TOM) of France, in LA REUNION island, in a 34-year-old woman, a nurse by profession. She had been treated with continuous ambulatory peritoneal dialysis (CAPD) since February 2022. The original nephropathy was Alport syndrome.

Pregnancy began twenty months after the start of dialysis. The patient wished to continue her pregnancy in CAPD in order to carry out exchanges during the day in her office, so as to be more available to her family in the evening.

The first trimester of pregnancy was uneventful. During this period, the patient was informed of the risks of pregnancy, and together we defined our objectives with the means available. Adjuvant drug prescriptions (calcium, aspirin, iron, folic acid, vitamin D, etc.) were adapted during the second trimester, as was the PD protocol, in line with defined objectives. The third trimester required largely hospital-based management.

Infusion volumes were progressively reduced, while the frequency of infusions was increased, thereby increasing the total daily volume of dialysis. Residual renal function remained stable throughout the pregnancy, and plasma urea levels were kept below 20 mmol/L.

She was delivered by Caesarean section under spinal anaesthesia at 33 weeks and 4 days of amenorrhea, with the birth of a 1,800g boy with Apgar coefficients of 5 at 1min, 8 at 3min and 9 at 5min. The baby's development and growth were very satisfactory.

Respect for the patient's choices, her autonomy and her participation in the treatment were decisive factors in the success of the procedure.

Keywords: Pregnancy, peritoneal dialysis, residual renal function, dialysis dose

Résumé

nous rapportons la première grossesse menée avec succès en dialyse péritonéale (DP), en 2023, dans les territoires et départements outre-mer (DOM-TOM) de France, à la REUNION, chez une femme de 34 ans, infirmière de profession. Elle été traitée par dialyse péritonéale continue ambulatoire (DPCA) depuis février 2022. La néphropathie d'origine était un syndrome d'Alport.

La grossesse a débuté 8 mois après le début de la dialyse. La patiente a souhaité poursuivre sa grossesse en DPCA afin d'effectuer les échanges durant la journée à son cabinet pour être plus disponible en famille le soir.

Le premier trimestre de la grossesse a été sans évènement particulier. Durant cette période la patiente a été informée des risques de la grossesse et nous avons défini ensemble nos objectifs avec les moyens disponibles. Les prescriptions médicamenteuses adjuvantes (calcium, aspirine, fer, acide folique, vitamine D..) ont été adaptées au cours du deuxième trimestre ainsi que le protocole de DP en suivant certains objectifs définis. Le troisième trimestre a nécessité une prise en charge en grande partie hospitalière

Les volumes d'infusion ont été progressivement diminués conjointement à une augmentation de leur fréquence qui a permis d'augmenter le volume quotidien total de dialyse. Elle a conservé une fonction rénale résiduelle stable pendant tout la durée de la grossesse et le taux d'urée plasmatique a pu être maintenu inférieur à 20 mmol/L

L'accouchement a été réalisé par césarienne sous rachianesthésie à 33 semaines et 4 jours d'aménorrhée avec naissance d'un garçon de 1800g dont le coefficient d'Apgar était de 5 à 1min, de 8 à 3min et de 9 à 5min. Le développement du bébé, et sa croissance ont été très satisfaisants.

Le respect des choix de la patiente, son autonomie et sa participation au traitement ont été des facteurs déterminants de réussite.

Mots clés : Grossesse, dialyse péritonéale, fonction rénale résiduelle, dose de dialyse

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CASE PRESENTATION

History

The patient, a 34-year-old nurse, was diagnosed with stage 2 renal failure secondary to Alport syndrome (COL4A3) in 2012. She reported no allergies or intolerances and denied any history of smoking or alcohol consumption. Her viral serologies for hepatitis B, C, and HIV were unremarkable.

In 2016, she experienced her first pregnancy, which resulted in a cesarean section delivery at 30 weeks gestational age (GA). During this period, there was a notable decline in her renal function, characterized by the onset of nephrotic syndrome and acute renal failure, with creatinine levels peaking at 650 μmol/L; HD was not initiated. A subsequent renal biopsy illustrated pauci-immune vasculitis accompanied by extracapillary proliferation. Postpartum management included plasma exchange and the administration of the monoclonal antibody rituximab.

The patient's surgical history is significant for a right breast lumpectomy and radiotherapy in 2017. However, in 2020, she experienced an aggressive tumor recurrence, necessitating chemotherapy, a right breast mastectomy, and targeted trastuzumab therapy. Nephropathy continued to progress after delivery, reaching stage 5 in 2021. Consequently, she commenced PD therapy in February 2022.

Pregnancy follow-up

A subsequent pregnancy was identified in the patient while she was undergoing PD, estimated to have started on October 11, 2022. Prior to the pregnancy, her diuresis was maintained at approximately 1500 mL daily, and she weighed 62 kg with a height of 170 cm. The ultrafiltration facilitated by PD ranged between 500 and 700 mL daily.

Her CAPD treatment regimen included two bags of isotonic glucose solution (GI) (PHYSIONEAL®) and one bag of amino acids (AA) (NUTRINEAL®) during the daytime, coupled with one bag of glucose polymer (ICODEXTRIN®) for extended stasis in the evening. The exchange volume was set at 1.6 L to ensure abdominal comfort. While intraperitoneal pressure was not measured, PD efficiency calculations using the Registre de Dialyse Péritonéale de Langue Française software indicated satisfactory outcomes: the total weekly peritoneal creatinine clearance stood at 27 L, urea Kt/V was at 3.6, and the residual renal clearance oscillated between 4 and 5 mL/min, with the most recent four measurements being 4.93, 4.79, 4.49, and 3.97 mL/min, respectively.

During the first trimester, we augmented our guidance by elucidating the potential pregnancy risks to the patient, encompassing arterial hypertension, eclampsia, preeclampsia, intrauterine growth retardation, prematurity, hypotrophy at birth, and intrauterine demise. This vital information was documented in the medical record. Issues specific to PD were also addressed, with a focus on concerns such as the risk of peritonitis, preterm delivery, and challenges posed by the gravid uterus in maintaining exchange volume. The patient was informed about the potential of elevated maternal urea levels to induce osmotic diuresis in the fetus once its kidneys become functional, possibly leading to hydramnios. Additionally, the importance of understanding the potential for hemodynamic instability and blood pressure variances was highlighted, especially given their ability to adversely impact placental blood flow in the context of conventional HD.

Regarding medication, the administration of drugs considered to be incompatible with pregnancy was ceased. Specifically, the oral calcimimetic (MIMPARA®) was stopped, and the AA bag was substituted with a GI bag (PHYSIONEAL®).

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The patient was informed of the significance of continuing with PD, especially considering the clinical recurrence of vasculitis from a prior pregnancy. This entails potential symptoms such as asthenia, general deterioration, and inflammatory syndrome, among others. The importance of preventing the onset of nephrotic syndrome—with potential complications like severe edema, significant arterial hypertension, and challenging hydro-sodium overload in PD—was emphasized. Additionally, concerns regarding the potential pregnancy outcome while on PD were addressed.

Beyond standard PD monitoring, checks were made for serum folate, vitamin D, and magnesium levels. Deficiencies in these elements could lead to uterine contractions. Screening for anti-SSA and SSB antibodies took place due to their identification as risk factors for atrioventricular block. The patient received advice to undertake a weekly urine dipstick test, with the option to use PD dipsticks. In the event of positive results, a urine cytobacteriological study was suggested, along with a monthly 24-hour proteinuria test.

For the second trimester, nephrological consultations increased to bimonthly intervals. Outpatient prescriptions included folic acid supplementation and native vitamin D, even though existing levels were within the acceptable range (vitamin D at 88 nmol/L, folic acid at 7 μg/L). This adjustment accounted for increased requirements during pregnancy. Magnesium was not prescribed due to concerns surrounding its use in chronic kidney disease patients and the current dosage being deemed sufficient at 0.79 mmol/L. An episode of cystitis due to methicillin-resistant Staphylococcus epidermidis was treated with a 7-day course of pristinamycin. Subsequent urine cytobacteriological evaluations returned negative results 10 days post-treatment.

Within the framework of obstetric-gynecologic monitoring, two ultrasounds were performed: one at 13 weeks GA for prenatal diagnosis and another at 16 weeks for early morphological assessment. Both results were reassuring. In an effort to prevent potential complications, acetylsalicylic acid 100 mg was prescribed for noon intake.

The third trimester presented the most challenges, resulting in hospitalization. At 27 weeks GA, clinical indicators were positive: blood pressure was stable, and weight was satisfactory at 69 kg (a gain of +7 kg). Yet, severe hypoalbuminemia at approximately 20 g/L prompted the prescription of low-molecular-weight heparin (CALCIPARINE®) to prevent thrombosis. At 28 GA, the patient experienced an isolated, painless hemoperitoneum, which subsided fully within 2 days after several peritoneal lavages. An ultrasound revealed hydramnios while maintaining a well-closed cervix. It was advised that the patient rest and receive visits from midwives at home. At 29 weeks and 3 days GA, the patient entered the gynecological ward due to escalating hydramnios. A 2-day regimen of corticosteroids was administered to mature the fetal lungs, followed by an amniotic drainage that removed 1700 mL of fluid. This procedure was coupled with an infusion of atosiban (TRACTOCILE®) to inhibit uterine contractions. Subsequent to this intervention, the patient was discharged with guidance to abstain from PD for 24 hours to prevent fluid leakage from the drainage site.

The patient was readmitted to the maternity ward at 31 weeks and 2 days GA, confronted with impending preterm labor and a recurrence of hydramnios. A tocolytic infusion (TRACTOCILE®) was maintained for 4 days, after which a second amniotic drainage removed another 1700 cc of fluid.

Regarding the delivery and subsequent maternal and neonatal health, a cesarean section was executed on May 17, 2023, at 33 weeks and 4 days GA. Using spinal anesthesia, a male infant weighing 1800 g was delivered. The neonate had an Apgar score of 5 at 1 min, 8 at 3 min, and 9 at 5 min, indicative of a healthy condition.

The neonate's growth trajectory was positive. By 2 weeks and 3 days postnatal age, he weighed

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2400 g. At the present moment, being 3 months of age (approximately 2 months corrected), the child exhibits healthy development, weighing in at 4 kg and with a height of 60 cm. Reports from the mother convey a socially engaged infant: he displays a keen awareness of his surroundings, enjoys auditory interactions, and has even begun to vocalize in response.

Two weeks following the cesarean section, sutures from the surgical incision were removed. However, the recommencement of PD was postponed for an additional month to ensure the peritoneum healed adequately and prevent any potential leakage of PD fluid through the surgical site.

During this period, the patient underwent renal replacement therapy via conventional HD, facilitated through a central venous catheter. These sessions progressed without complications, with ultrafiltration consistently remaining below 1000 cc.

The patient took responsibility for maintaining the PD catheter, tending to it every alternate day. Additionally, she flushed the catheter using 100 mL of isotonic glucose dialysate every 3 days.

While the nephrologist advised against breastfeeding due to concerns about potential uremic toxins contaminating the breast milk, the infant did receive the mother's colostrum during the stay in the maternity ward—a practice strongly endorsed by the gynecologists. The infant's transition to oxygen independence was swift, paralleled by a smooth adaptation to bottle feeding.

Following corticosteroid therapy, there was a noticeable increase in the mother's blood glucose levels. This necessitated a brief 48-hour period of insulin therapy, though there was no definitive diagnosis of gestational diabetes. The administration of CALCIPARINE® ceased less than a month postpartum, coinciding with the rapid stabilization of albumin levels at 35 g/L and proteinuria registering approximately 0.5 g/24 hours.

On June 27, 2023, CAPD was reinitiated in alignment with the protocol followed prior to pregnancy, marking 1 month and 10 days since transitioning to conventional HD.

PERSONALIZED PRESCRIPTIONS FOR CAPD DURING PREGNANCY

Efforts were consistently made to strike a balance between ensuring the patient's abdominal comfort and keeping the urea level optimally below 20 mmol/L, all while preventing hydro-sodium overload and hypertension (with a target systolic blood pressure of less than 140 mmHg and a diastolic blood pressure of less than 90 mmHg).

Adjustments to the CAPD protocol became more frequent starting in the second trimester to meet these objectives. This involved an escalation in the frequency of exchanges and the total volume exchanged. However, the volume per cycle was reduced due to the patient's abdominal discomfort, as delineated in Table 1.

The criteria guiding modifications to the CAPD were prioritized as follows: urea levels exceeding 20 mmol/L, daily ultrafiltration below 500 mL, systolic blood pressure above 120 mmHg, and a weight gain exceeding 500 g within a span of 2 days.

Throughout the pregnancy, intraperitoneal pressure was not assessed, primarily because any abdominal discomfort induced by the dialysate could be promptly alleviated through drainage and subsequent volume decrement.

Initially, total, urinary, and peritoneal clearances were evaluated and deemed satisfactory. However, these initial results did not necessitate repetitive measurements. The weekly creatinine clearance stood at 27 L per week, with a Kt/V for urea at 3.6 and a residual renal clearance ranging from 4 to 5 mL/min.

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Table I. Trends in PD prescriptions throughout pregnancy

GESTATIONAL AGE	CAPD REQUIREMENTS	VOLUME PER EXCHANGE	NUMBER OF EXCHANGES	TOTAL VOLUME	UREA (mmol/L)
2 weeks	3 isotonic GI bags + 1 icodextrin bag	1.6 L	4	6.4 L	22.5
4 weeks + 3 days	4 isotonic GI bags + 1 icodextrin bag	1.6 L	4	6.4 L	19.9
9 weeks + 4 days	6 isotonic GI bags + 1 icodextrin bag	1.6 L	7	11.4 L	20.3
13 weeks + 3 days	6 isotonic GI bags + 1 icodextrin bag	1.6 L	7	11.4 L	18.6
15 weeks + 1 day	6 isotonic GI bags + 1 icodextrin bag	1.6 L	7	11.4 L	23
17 weeks + 3 days	7 isotonic GI bags + 1 icodextrin bag	1.6 L	8	12.8 L	19.8
19 weeks + 3 days	7 isotonic GI bags + 1 icodextrin bag	1.6 L	8	12.8 L	18.8
24 weeks + 1 day	7 isotonic GI bags + 1 icodextrin bag	1.6 L	8	12.8 L	14.7
25 weeks + 4 days	8 isotonic GI bags + 1 icodextrin bag	1.6 L	9	6.4 L	14.7
26 weeks	9 isotonic GI bags + 1 icodextrin bag	1.5 L	10	14.4 L	16.3
27 weeks	9 isotonic GI bags + 1 icodextrin bag	1.5 L	10	15 L	15.1
28 weeks	9 isotonic GI bags + 1 icodextrin bag	1.4 L	10	15 L	14.8
29 weeks + 1 day	10 isotonic GI bags + 1 icodextrin bag	1.4 L	11	14 L	15.1
30 weeks	10 isotonic GI bags + 1 icodextrin bag	1.4 L	11	15.4 L	22.8
31 weeks + 3 days	11 isotonic GI bags + 1 icodextrin bag	1.3 L	12	15.4 L	18.7

** Gl = glucose solution*

The target for urea, set at less than 20 mmol/L, was achieved in most tests (Figure 1).

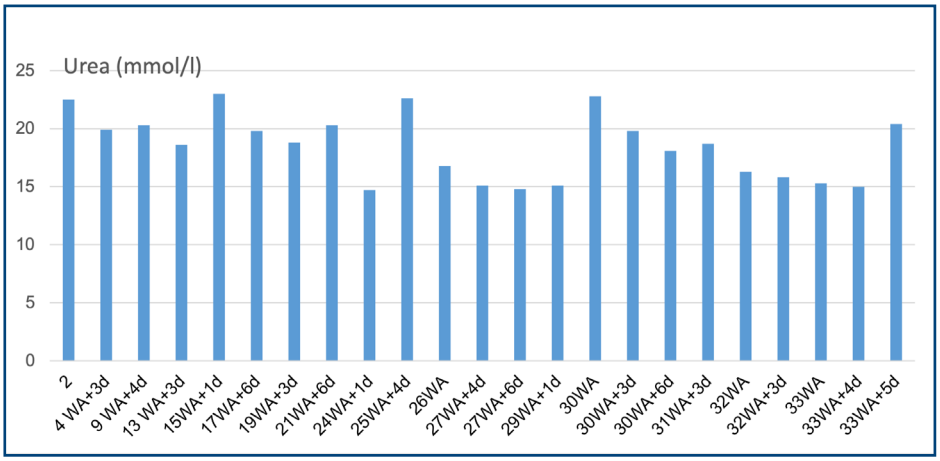

Figure 1: Evolution of maternal plasma urea levels throughout pregnancy. GA denotes gestational age

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Ultrafiltration consistently averaged approximately 600 mL per day, while residual diuresis was sustained at about 1500 mL per day (Figure 2). The monthly weight gain was consistently around 1 kg.

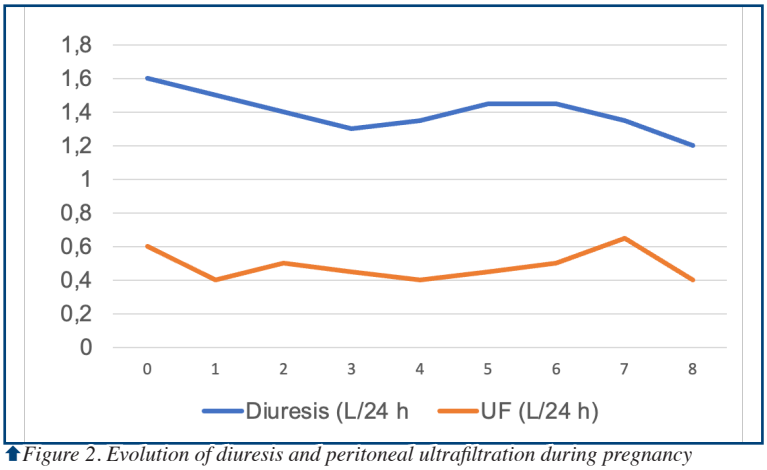

Figure 2. Evolution of diuresis and peritoneal ultrafiltration during pregnancy

Throughout the pregnancy, the patient's blood pressure experienced a mild elevation, though it remained stable without the requirement for antihypertensive medication. The mean arterial pressures recorded during the first, second, and third trimesters were 110/70, 120/75, and 135/85 mmHg, respectively. The heart rate remained consistent, ranging between 73 and 83 beats per minute.

Albuminemia and proteinuria

As the pregnancy progressed, laboratory findings indicated the presence of nephrotic syndrome. It was notable that there were no clinical indications of vasculitis, such as a decline in general health, general symptoms, fever, or inflammatory syndrome. The only discernible changes were a gradual reduction in albumin levels coupled with an increase in proteinuria, as illustrated in Table 2.

Table II . Evolution of albuminemia and albuminuria during pregnancy

DATE (MONTH)	START	1st	2nd	3rd	4th	5th	6th	7th
Albumin (g/L)	32	32	24	22	21	20	20	21
Albuminuria (g/L)	0.98	1.2		5.6		8.2		13

There were no other discernible causes of protein leakage that could account for the hypoalbuminemia at the dialysate level. Two 24-hour collections of drained dialysate, one in November 2022 and the other in March 2023, showed consistent daily protein losses of 4 g and 4.6 g, respectively.

Hemoglobin

The target hemoglobin level of 10 to 12 g/dL was met in the majority of measurements. However, achieving this required increasingly larger doses of an erythropoiesis-stimulating agent (ARANESP®) as the pregnancy advanced (Figure 3).

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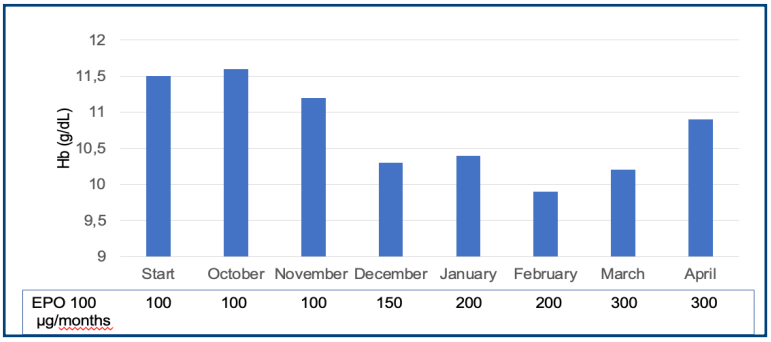

Figure 3. Evolution of the Hb (hemoglobin) level (g/dL) and the monthly EPO (darbepoetin alfa (ARANESP®)). dose month by month during pregnancy

Iron reserve

The patient's iron reserve was satisfactorily maintained through the administration of oral iron supplementation (TARDYFERON® at doses of 80 mg in the morning and evening), as depicted.

Uric acid

Given the frequent association of hyperuricemia with vascular complications during pregnancy, particularly preeclampsia [11], careful monitoring throughout the pregnancy was deemed necessary. Blood uric acid levels remained consistently within the accepted range, starting at 429 μmol/L and stabilizing between 315 and 407 μmol/L during the pregnancy.

Parathyroid hormone

Prior to her pregnancy, the patient's hyperparathyroidism had been managed with calcimimetics (MIMPARA®). With the cessation of this medication due to potential unknown fetal effects, there was concern that her condition could deteriorate. Nevertheless, monthly assessments of her serum parathyroid hormone levels revealed fluctuations between 400 and 600 μmol/L until the pregnancy's conclusion.

DISCUSSION

The patient, a practicing nurse, was provided with an overview of various renal replacement therapies. She opted for CAPD, which facilitated her to continue her professional activities during the early stages of pregnancy while minimizing disruptions to her family life.

Interestingly, during the latter phase, at the 31st week of amenorrhea, she managed to perform 12 exchanges daily. Upon consultation, she indicated that the stasis duration at times was as short as an hour, attributed to abdominal discomfort.

To provide relief, APD was recommended. Although she attempted this approach, she discontinued it within 24 hours due to the aforementioned abdominal discomfort.

Research by Hladunewich et al. highlighted that an increased regimen of HD, 36 hours compared to 20 hours weekly, led to better pregnancy outcomes among HD patients, which was evident in the elevated live birth rates (48% versus 85%), increased GAs (27 weeks in comparison to 36 weeks), and a rise in the infant birth weights (from 1748 g to 2118 g) [12, 13].

In a study involving 33 pregnancies undergoing HD, Asamia et al. found that urea concentrations less than 20 mmol/L corresponded with improved birth weights and GAs [14].

The majority of nephrologists advocate for daily HD during pregnancies that involve dialysis. A

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comprehensive retrospective study, which incorporated 41 dialysis centers in France from 1985 to 2015, documented 100 pregnancies, with 90% of these women receiving daily HD commencing in the third trimester [15, 16].

In the domain of PD, documented pregnancies are rare [17, 18]. The treatments prescribed exhibit marked variability, and predominantly, these cases transition to conventional HD [19, 20]. A particularly unique scenario involves the initiation of PD in women with end-stage renal disease who have not commenced dialysis. In the Bulletin de la Dialyse à Domicile, Jacobs discussed the cases of two women, both several months pregnant, without any prior dialysis experience; one case was from 2007 and the other from 2021 [21]. The primary objective of this publication was to underscore the feasibility of initiating PD in patients already pregnant without prior dialysis experience and to illustrate that PD treatment can be initiated early in pregnancy and successfully carried through to term.

On the island of La Réunion, a French territory situated in the Indian Ocean southeast of Africa, the demographic is younger than on mainland France. Notably, while there have been reported cases of pregnancies in individuals on HD, no such reports exist for those on PD. Nephrologists on the island commonly believe, in line with existing literature, that patients should transition to HD upon pregnancy. Consequently, we proposed a shift to HD for our patient in her second trimester. However, she was adamant about continuing her pregnancy on PD.

After ensuring her comprehensive understanding of the associated risks and respecting her informed choice—a sentiment we emphasized on multiple occasions—we consented to support her throughout her PD pregnancy. The patient's autonomy was evident even during her hospitalization. This facilitated seamless therapeutic adjustments in CAPD, particularly as the progression of her pregnancy necessitated more frequent changes. She executed the exchanges meticulously, adhering strictly to aseptic techniques, and thus avoided complications like catheter infections or peritonitis.

Owing to the challenges and often the infeasibility of conducting randomized studies, combined with the absence of standardized management protocols, PD's efficacy can be comparable to daily HD, provided certain conditions conducive to success are met [22]. These conditions include the patient's young age and a robust multidisciplinary collaboration involving nephrologists, gynecologists, nursing staff, and the patient to ensure optimal therapeutic adherence. The advantage of patient autonomy is also a significant consideration.

CONCLUSION

Recent observations and updated literature evidence suggest enhanced chances of pregnancy in patients undergoing dialysis. Continuous modalities of renal replacement therapy, whether HD or PD, ensure hemodynamic and biological stability. When combined with the preservation of residual renal function, this gives patients the liberty to select the dialysis modality that aligns best with their psycho-professional needs. Our proficient handling of the PD technique empowered us to propose this treatment option to the participant during her pregnancy after ensuring she was thoroughly counseled about the procedure and its implications.

Ethical considerations

Throughout her pregnancy and subsequent PD follow-up, we maintained uninterrupted communication with the patient. She granted her consent for the publication of her case.

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Contributions of authors

Dr. Asma Omarjee, provided outpatient obstetrical follow-up, then organized maternity admission and management through to delivery, and reviewed the article; Dr. Delphine Hebmann, nephrologist at the CHU de la réunion, contributed to the nephrological follow-up, and inpatient management of the patient's pregnancy, and reviewed the article. Dr Ali Aizel, the patient's referring nephrologist, provided outpatient follow-up of CAPD, and of the patient's pregnancy, and wrote the article.

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