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Dialysis in Special Situations

CKJ Review

Pregnancy in end-stage renal disease patients on dialysis: how to achieve a successful delivery

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Abstract

Pregnancy in women with chronic kidney disease has always been considered as a challenging event both for the mother and the fetus. Over the years, several improvements have been achieved in the outcome of pregnant chronic renal patients with increasing rates of successful deliveries. To date, evidence suggests that the stage of renal failure is the main predictive factor of worsening residual kidney function and complications in pregnant women. Moreover, the possibility of success of the pregnancy depends on adequate depurative and pharmacological strategies in patients with end-stage renal disease. In this paper, we propose a review of the current literature about this topic presenting our experience as well.

Keywords: ESRD; delivery; haemodialysis; live birth; pregnancy

Background

The first pregnancy with a successful outcome in patient on haemodialysis (HD) was described in 1971 by Confortini *et al.* [1]. Outcomes of pregnancy in patients with end-stage renal disease (ESRD) have long been considered to be extremely poor, and the literature concerning pregnancy while on dialysis is rather scarce. Pregnancy is a challenging experience for women suffering from chronic kidney disease. The challenge is harder in ESRD patients undergoing maintenance dialysis.

The challenge starts from the diagnosis of pregnancy because β-human chorionic gonadotropin (β-hCG) serum levels may be increased in ESRD patients even in the absence of pregnancy [2]. Thus, ultrasonography becomes mandatory among women with high serum levels of β-hCG to confirm the pregnancy and to obtain the approximate gestational age.

The literature to date offers only surveys, case series or anecdotal reports focussed on the outcomes of pregnancies in ESRD patients undergoing maintenance dialysis. To our knowledge, no clinical trials have been performed in this clinical setting and no guidelines have been published. Some recommendations based on low-grade evidence have been reported by the Italian Society of Nephrology (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#).

Despite the fact that mortality remains high and prematurity and low birth weight are the rule, the number of successful pregnancies in dialysis patients has increased over time with a gain in fetal survival of ∼25% per decade (from 23% in 1980, to ∼50% in the 1998, to over 90% in the recent years). The improvement of outcomes between the nineties and nowadays is due to an acquired expertise in dialysis schedules and technique management, in close monitoring of weight gain of pregnant women and in modelling pharmacological and nutritional approaches to the mothers [3, 4]. In consequence, the analysis of data published in the new millennium is most interesting to focus adequately on this issue.

Frequency of conceptions and live births

In the eighties and nineties, the reported frequency of conception among ESRD patients of childbearing age on dialysis ranged from 1.5 conceptions over 100 patients per year in the USA [2] to ∼11 conceptions per year as reported by EDTA and the main national registries [5–8]. In 1994, Hou [6] reported that over 1281 women of childbearing age undergoing maintenance dialysis, registered

nine conceptions per year that had a successful outcome in ∼52% of cases: a much better result than in earlier years. In 1998, Bagon *et al.* [7] demonstrated a mean conception frequency of four per year in 1472 women of childbearing age.

During the same years, Okundaye *et al.* [9], in a total of 6230 women aged 14–44 years (1699 receiving peritoneal dialysis and 4531 receiving HD) registered 31 conceptions per year (4 and 27 per year in peritoneal dialysis and HD, respectively). The Australian and New Zealand Dialysis and Transplantation Registry from 2001 to 2011 reported seven conceptions per year [10]. These data suggest that frequencies of conceptions reported in the different studies are scattered and do not present a trend toward an increase over time, maybe due to the typical biases of surveys.

Data regarding miscarriage are more polarized with percentages of 70% before 1990 and <40% in the following years [5]. The majority of case series described since 2000 reported ∼70% success rates for pregnancies in HD women [11, 12].

Although fetal wastage remained markedly increased when pregnancy occurs, improvements in management have resulted in an enhanced frequency of live births (40–86% of all pregnancies) [13–15].

Souqiyyeh *et al.* [12] in 1992 reported the higher number of pregnancies with live birth (7%) in Saudi Arabia.

In 2014, Piccoli *et al.* [16] published a nationwide Italian survey aimed to compare the incidence of live births from mothers on dialysis in the new millennium (2000–12), with the overall Italian population and the patients with a functioning kidney graft in the same period. They retrieved data for about 23 pregnancies and 24 live-born babies (one twin pregnancy). The live-birth rate resulted in 0.7–1.1 per 1000 women on dialysis aged 20–45 years (72.5 per 1000 women in the normal population and 5.5–8.3 per 1000 women with functioning kidney graft).

Also, live birth percentage in ESRD patients showed an increasing trend from 20–23% in the eighties to the actual 75% [13, 14].

Outcomes for mother and child

Increased risk for severe hypertension of the mother and prematurity in most of the cases were already known for pregnant dialysis patients in the last century. In 1998, hypertension was reported in 79% of pregnant HD patients [9]. In a review of 120 pregnant dialysis patients published in the same period, the mean gestational age at delivery was only 30.5 weeks [17]. Data reported in the new millennium, describe a median gestational age of 33.8 weeks with a median birth weight of 1750 g. More than 40% of pregnancies last >34 weeks; prematurity at <28 weeks is 11.4% and 28-day neonatal survival rate 98% [10].

In another recent nationwide survey 20 mothers on HD and 3 on peritoneal dialysis [16] were analysed. The gross mortality of mothers was not different from that expected in young dialysis populations (1.5 per 100 years of observation). Three infants died in the first month of life. Preterm delivery was the rule (19/21 live infants) with three 'early pre-terms'. All the newborns survived without long-term clinical problems. No major malformations were reported.

To date, the most important reported maternal complication include miscarriage, placental detachment, anaemia, infections, premature rupture of membranes, polyhydramnios, pre-term birth, uncontrolled arterial hypertension, preeclampsia/eclampsia, haemorrhage, need for a caesarean section and maternal death [18, 19]. Preeclampsia and severe hypertension are the greatest risk factors for prematurity and other adverse outcomes. Eighty percent of pregnancies occurred in dialysis women are complicated by hypertension which was responsible for 1% of mortality of mothers in the past. To date, mother mortality is absent [2]. Uncontrolled hypertension must be adequately treated, maintaining diastolic blood pressure <80–90 mmHg [20–22]. As in any other dialysis patient, the initial treatment consists of adjusting volumes using ultrafiltration, but if the cause of hypertension is preeclampsia, fluid extraction could exacerbate hypoperfusion to the various organs [23]. In a single-center series of 52 patients, preeclampsia was associated with lower successful delivery rate (60 versus 92.9%), extremely premature delivery rate (77.8 versus 3.3) and lower gestational age and birth weight compared with those without preeclampsia [24].

The incidence of polyhydramnios—caused mostly by urea-induced fetal osmotic diuresis—has been estimated at 30–70%. Recently published studies have suggested that treatment for this complication consists of increasing dialysis doses [24, 25].

In patients undergoing peritoneal dialysis, mechanical influence of the catheter with the uterus must be considered. For this reason, it is mandatory to check frequently for haemoglobin levels in the peritoneal fluid that would be a sign of abortion or amniorexis (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#).

The most common fetal complications are restricted intrauterine growth, acute and chronic fetal suffering, preterm birth, respiratory difficulty in the newborn, growth in neonatal intensive care units and uterine or neonatal death [26]. Spontaneous abortion before the sixth month has a frequency of 25% of cases while the percentage of live births increased from 20% in the past to the actual 50%. In 1998, an incidence of low birth weight and prematurity of 100% with caesarean sections performed in 66% of successful pregnancies was described [7]. To date, pre-term births occur in 83% of live births (mean gestational age is ∼32 weeks or even less) and the newborn present high mortality (18%) and morbidity (growth retardation in 28–36% and malformations in 10% of cases) [24, 25, 27].

Delayed diagnosis (average 16.5 weeks) due to frequency of amenorrhoea in ESRD women, might increase the risk of taking dangerous medications in the early phases of conception.

Very scarce and scattered are the data regarding long-term outcomes of the newborn.

Non-modifiable factors associated with successful pregnancy

Conception and successful pregnancies are much more frequent when the patients have residual renal function [17]. Residual renal function might be the key factor to explaining the improved outcomes of conception that happened before starting dialysis (in women already undergoing dialysis the residual renal function often declines).

Several studies published in the late nineties demonstrated better outcomes of pregnancies diagnosed before HD was started. Bagon *et al.* [7] described a successful

outcome in 50% of pregnancies occurring in HD patients and in 80% of patients who became pregnant before HD. Okundaye *et al.* [9] in his cohort found that the newborn survival rate was 40.2% in the 184 pregnancies started in ESRD women already undergoing dialysis and 73.6% in the 57 pregnancies in women who started dialysis after conception. Eighty-four percent of infants born to women who conceived after starting dialysis were premature.

Pregnancies started early after dialysis initiation are characterized by a 30% higher infant survival in comparison with women with longer HD vintage [6, 28]. In pregnants on maintenance dialysis for >10 years the fetus frequently presents anomalies [28, 29]. Giatras *et al.* [17] reported that 47% of pregnancies evaluated in their clinic started in the first 2 years of maintenance dialysis while only six successful pregnancies were observed in 120 women undergoing dialysis for >10 years.

Surveys published in the nineties reported newborn survival rates of 40.2% in pregnancies started in ESRD women already undergoing dialysis and 73.6% in pregnancies in women who started dialysis after conception [7]. Successful outcomes were also described in 50% of pregnancies occurring in HD patients and in 80% of patients who became pregnant before HD was started [9].

Recently, in the already cited Australian and New Zealand Dialysis and Transplantation Registry from 2001 to 2011 live birth rates were higher for women who conceived before starting dialysis compared with those who conceived after initiation (91 versus 63%, respectively) but infants had similar birth weight and gestational age. Higher rates of early pregnancy loss before 20 weeks in women who conceived while on dialysis was responsible for this difference in live birth rate. Again, in pregnancies exceeding 20 weeks, the conception before dialysis initiation induced the higher live birth rate [10].

There are no significant data about the impact of maternal age or type of nephropathy on the pregnancy outcome or maternal/fetus prognosis in pregnancies occurred in dialysis patients.

The dialysis prescription

The improvement in outcome observed in recent years probably reflects more aggressive management of women with ESRD who become pregnant [25, 30, 31]. The aggressive management for such patients has the following major components (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#) [8, 18, 24]:

(i) more intensive dialysis schedule with blood urea nitrogen (BUN) levels <16–18 mmol/L. This is usually achieved by increasing the frequency of HD, switching to long nightly HD or lowering the volume of dwells to 800 mL raising their frequency as well in patients on peritoneal dialysis (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#). A better uraemic *milieu* can avoid polyhydramnios, help control hypertension, increase birth weight and gestational age and improve maternal nutrition;

(ii) 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.

Since 1998, the usefulness of increasing the dialysis frequency and dose in patients initiating pregnancy while already on dialysis (up to a weekly Kt/V of 6–8) and the relationship between dialysis dose and birth weight/gestational age [7, 9] was already known. Moreover, it was already clear that the dialysis technique did not influence the infant survival rate as reported by Okundaye *et al*. [9] (39.5 versus 37% in HD and peritoneal dialysis, respectively).

Recent evidence show that after 16–20 weeks, HD dose should be increased from 3–4 sessions/week to daily sessions, and better fetal outcomes are obtained with a HD schedule of 24–28 h/week [32].

Ganjii *et al.* [33] reported their experience about the shift from conventional to nocturnal HD of a pregnant patient with uncontrolled hypertension. This approach induced the normalization of blood pressure and a natural delivery at the 38th week.

In 2005, Haase *et al.* [25] achieved good outcomes in pregnant patients treated with 24–36 h/week haemofiltration.

Analysis of a Canadian cohort of 22 pregnancies treated with intensified HD revealed a live birth rate of 86.4% and a mean duration of pregnancy of 36 weeks [34]. Longer HD (>36 h/week) was associated with increased live birth rates, longer gestation and greater infant birth weight, compared with shorter dialysis (<20 h/week).

Potassium levels in the dialysate must be increased to 3–3.5 mmol/L in order to avoid hypokalaemia. Electrolyte serum levels must be checked weekly [2, 20]. Low bicarbonate concentrations are recommended (25 mEq/L) because frequent HD might result in excessive alkali transfer to the mother, producing alkalaemia [2, 20]. Frequent HD can also lead to hypophosphataemia, and given that added phosphorous in the dialysate can be a complicated issue, oral supplements or increased dietary intake are recommended [34]. A dialysate calcium concentration of 1.5 mmol/L is suggested in order to satisfy both maternal and fetal daily requirements [2]. Target values of the main laboratory parameters suggested for pregnant HD women are similar to those advised in non-pregnant dialysis patients.

Maternal dry weight and weight gain should be regularly evaluated and adjusted according to the estimated weight of the fetus. In the first trimester, the mother should gain a minimum of 1–1.5 kg. Thus, a weight increase of 0.45–1 kg per week should be achieved. In the third trimester, fetal haemodynamics, weight and growth can also be directly evaluated using ultrasound and this monitoring might induce changes in dialysis prescription accordingly [17].

Maternal blood pressure and heart rate must be closely monitored before, during and after each dialysis session [17] Ultrafiltration doses should be administered on an individual basis in order to avoid episodes of arterial hypotension, hypovolaemia and arrhythmia. Maternal blood volume expansion and weight gain should be proportional to the gestation stage. Severe maternal weight loss due to rapid and excessive ultrafiltration can reduce the fetal–placental blood flow, which could be very harmful for the fetus. As such, these factors must be considered in ultrafiltration prescription [26]. These considerations underline the importance of intradialytic fetal monitoring in order to change dialysis prescriptions.

High biocompatibility dialysers are recommended in pregnant patients [26]. It is best to use membranes with a lower surface area combined with increased time on dialysis in order to avoid excessive fluid losses with consequent episodes of hypotension and sudden changes in osmolarity [20].

Data about peritoneal dialysis are very scarce and limited to a low number of patients. The incidence of pregnancies in these patients is even lower than the rates for HD patients probably because the presence of hypertonic solutions in the peritoneum, previous episodes of peritonitis or physical factors that could interfere with fetal implantation.

Most of the authors do not recommend changing the dialysis technique after conception [35, 36]. Data from the register of pregnant patients on dialysis and several reports showed no differences in the maternal and fetal results between HD and peritoneal dialysis [9, 22, 37]. Peritoneal dialysis has the advantage of not inducing sudden metabolic changes, and allows for a gradual control of fluids, thus avoiding episodes of hypotension. The main disadvantage would be difficulty in maintaining proper nutrition [2].

Adjustment of medications and diet

Attention to nutritional considerations is essential for a successful pregnancy because malnutrition is common in pregnancies of ESRD patients [19]. For this reason, it is mandatory to avoid proteins restriction <1.2–1.3 g/kg of body weight/day in HD and 1.4 g/kg of body weight/day in peritoneal dialysis. Moreover, it is important to add 20 g/day of proteins to daily maternal needs for the correct fetal growth [2, 38] (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#). Some authors a suggest protein intake of 1.8 g/kg of body weight/day [17]. The caloric intake in this clinical setting should be of 35 kcal/kg of body weight/day in HD and 25 kcal/kg of body weight/day in peritoneal dialysis and folate supplementation with 1 mg/day should be administered starting from the first trimester (http://www.nephromeet.com/web/procedure/documenti.cfm?p=lg_2edizione#).

Since the requirements for vitamins increase due to the fact that intensive dialysis promotes their elimination, these molecules should be administered throughout the pregnancy [39]. The main vitamins to be supplemented are vitamin C, thiamine, riboflavin, niacin and vitamin B6 [35].

Occurrence of hypocalcaemia should be avoided by giving 1.5–2 g of supplementary calcium daily that are necessary for a normal fetal growth in a woman with a normal dietary calcium intake of 800 mg/day. However, it is important to check weekly for serum calcium because both the calcium provided by the dialysate (1.5 mmol/L daily) and calcium intake of chelating agents might induce maternal hypercalcaemia and secondary fetal hypocalcaemia and hyperphosphataemia with impaired skeletal development [20].

The placenta converts calcidiol into calcitriol, thus 25-OH vitamin D must be measured every trimester, administering supplements if levels are low [2].

Although primary hyperparathyroidism is known to increase the frequency of pre-term births by 10–20%, the effects of hyperparathyroidism on the fetus are unknown. The use of calcitriol is indicated in these cases in order to control both hyperparathyroidism and 1,25-OH-vitamin D deficiency. Calciferol does not appear to be toxic at reasonable doses. Dosage adjustments must be based on weekly calcium and phosphorous measurements [20].

Sevelamer, lanthanum carbonate, aluminium hydroxide, cinacalcet and paricalcitol have not been tested or established for use during pregnancy/lactation [40, 41].

Anaemia during pregnancy is associated with increased incidence of pre-term births, which results in greater infant mortality rates [42].

In a survey published in 1998, only 5.9% of women had a haematocrit >30% throughout pregnancy. Twenty-six percent of women treated with EPO and 77% of women not receiving EPO required transfusions [9].

Asamiya *et al*. analysed 24 pregnant patients on HD and demonstrated a positive correlation between maternal haemoglobin and a successful pregnancy [37].

Since the physiologic changes and demands of pregnancy may result in worsening of anaemia, pregnant women often require an increase of 50–100% of EPO dosages to maintain an adequate red cell mass (haemoglobin of 10–11 g/dL with a haematocrit of 30–35%) [22, 26]. No increases of incidence of hypertension nor teratogenicity have been demonstrated with the use of erythropoietin during pregnancy [26, 43].

Both the mother and the fetus need 10–15 mg of iron per day. Oral supplements would be insufficient. Intravenous administration has proven to be safe and effective in maintaining the desired serum ferritin levels of 200–300 µg/mL [20].

Heparin does not cross the placenta and is not teratogenic. It must be used in order to avoid coagulation of the vascular accesses [2]. Warfarin crosses the placenta and is contraindicated in these patients [26].

Several different types of medications are used to treat hypertension in pregnant women. α-methyldopa is commonly used; no adverse side effects have been observed in infants, and they are relatively few in the mother: fatigue, depression and, in a small percentage of patients, hepatitis [20]. Hydralazine has been used both orally and intravenously without evidence of severe side effects. However, it is not effective as oral monotherapy [2, 44].

Among β-blockers, only labetalol is widely used because it does not produce adverse effects on newborns [2, 45].

The experience with clonidine and prazosin is limited, and these drugs do not appear to provide any serious benefit [2, 46].

Nifedipine, nicardipine and verapamil can be administered safely. These molecules have been used in cases of severe hypertension, and do not appear to be associated with congenital defects when prescribed during the first trimester. Only limited experience has been gained using diltiazem. We must remember that combined therapy with magnesium can lead to severe episodes of hypotension [23, 44].

Diuretics can be used when no other alternative exists, but must be stopped in the case of preeclampsia [2]. The literature reported neonatal thrombocytopenia, haemolytic anaemia, electrolyte imbalances and jaundice with thiazides [47].

Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB) and minoxidil are contraindicated due to their adverse effects on the newborn [20, 48–50].

Summary and conclusions

Outcomes of pregnancies and prognoses of mothers and newborns have improved in the recent years although no guidelines in this field are available in the literature. However, the burden of maternal and fetal complications is still high. Hypertension, preeclampsia, polyhydramnios, pre-term birth, low birth weight and malformations present significant occurrences in this clinical setting.

Table 1. Recommended interventions and target values in pregnant women on dialysis

Blood pressure control
Medications to avoid: diuretics, ACE inhibitors and ARB
Preferred treatments: α-methyldopa, labetalol, nifedipine nicardipine, verapamil
Maintain diastolic blood pressure between 80 and 90 mmHg
Prevent hypotension and volume decrease
Prevent metabolic acidosis
Intensify dialysis treatment
Increase the frequency of dialysis sessions (5–7 per week)
Maintain a predialysis BUN <16–18 mmol/L
Increase in maternal weight of 1–1.5 kg in the first trimester; thus 0.45–1 kg per week in the last trimester
Use the minimum possible dose of heparin
Use biocompatible membranes
Calcium/phosphorous metabolism
Avoid hypocalcaemia and hyperphosphataemia
Provide calcium supplementation of 1.5–2 g daily, dietary calcium of 800 mg daily and dialysate calcium of 1.5 mmol/L
If necessary, use calcium chelating agents and vitamin D. Avoid post-dialysis hypercalcaemia
Anaemia
Provide iron (10–15 mg/day) and folic acid (1 mg/day) supplementations
Increase of 50–100% EPO dosage
Maintain haemoglobin at 10–11 g/dL, haematocrit at 30–35% and serum ferritin of 200–300 μg/mL
Nutrition
Provide protein intake of 1.2–1.4 g/kg pre-pregnancy weight/day + 20 g/day
Provide calories intake of 25–35 kcal/kg/pregnant weight/day
Provide water-soluble vitamins supplementation

The literature identifies some key points for the management of pregnancies occurring in ESRD patients (Table 1). First of all it seems assumed that, thanks to the presence of residual renal function, pregnancies started before initiating dialysis are characterized by better outcomes in comparison with pregnancies occurring in women already undergoing maintenance dialysis. Moreover, the rate of successful pregnancies is inversely correlated to dialysis vintage. This relationship might be explained by the fact that renal function declines gradually over time. Due to the lack of significant data about the impact of maternal age or comorbidities on the pregnancy outcome, in ESRD patients it is assumed as valid what it is known in the general population.

The dialysis dose—but not the technique—influences pregnancy outcomes. Both in HD patients and in peritoneal dialysis patients the increase of dialysis dose—higher number of HD sessions and >24–28 h of HD per week, low-volume/highly frequent dwells, BUN levels <16 mmol/L—has been associated with higher gestational age, live birth rates, birth weight and lower rates of maternal hypertension, polyhydramnios and prematurity.

The tight control of maternal weight gain and ultrafiltration rate during the pregnancy is mandatory in order to keep constant the maternal/fetal haemodynamics avoiding growth retardation or unsuccessfully outcomes. The intra-dialytic fetal monitoring might be an important tool in this field.

Fetal growth needs adequate iron and calcium storages and supplementations of vitamins and folates lost during the treatment. There is consensus in keeping serum ferritin levels of 200–300 μg/mL by administering 10–15 mg of iron intravenously per day. Oral calcium intakes of 1.5–2 g daily should be prescribed and phosphorus supplementations should be administered in the case of dialysate-induced hypophosphoraemia.

In ESRD patients undergoing maintenance dialysis, EPO dose should be increased of 50–100% during the pregnancy in order to achieve haemoglobin levels of 10–11 g/dL. Moreover, folate administration is advised. This approach has rather cancelled the need of blood transfusions in recent years.

The right nutrition is mandatory in pregnant women undergoing dialysis. Avoiding protein restriction <1.2–1.3 g/kg of body weight/day in HD and 1.4 g/kg of body weight/day in peritoneal dialysis is advised in order to preserve fetal growth. The latter could be favoured also by introducing 20 g/day of proteins to daily maternal needs. The caloric intake in this clinical setting should be 35 kcal/kg of body weight/day in HD and 25 kcal/kg of body weight/day in peritoneal dialysis.

Finally, the pharmacological approach to hypertension in pregnant dialysed mothers is very challenging due both to the teratogenic properties of the widely used medications in the general population and the contraindications of certain drugs in ESRD. Taking into account what literature offers to date, nifedipine, nicardipine, verapamil, alpha-methyldopa and labetalol are the molecules of choice in this clinical setting.

Despite the fact that mortality remains high and prematurity and low birth weight are the rule, the number of successful pregnancies in dialysis patients has increased over time with a gain in fetal survival of from 23% in 1980 to over 90% in the recent years. This improvement has happened even if no guidelines are available to date in the literature about pregnancy management in ESRD patients nor guidelines about chronic kidney diseases focus sufficiently on the issue of pregnancy.

However, in our opinion, due to the human and psychological impacts of the event 'pregnancy' for ESRD women it would be desirable to edit at least consensus statements of experts to advise nephrologists that will face this 'event'.

How did we face the challenge of pregnancy in dialysis?

A 29-year-old woman suffering from ESRD due to chronic pyelonephritis had been on bicarbonate HD for 1 year. She had no comorbidities and some residual renal function persistence. Blood pressure (120/80 mmHg) and body weight (BMI 23 kg/m^2) were normal. She was on omeprazole (20 mg/day) and allopurinol (150 mg/day).

In 2006, she was diagnosed with pregnancy at the eighth week. Thus, HD schedules and intra-HD therapies were changed as reported in Table 2. Dialyser (low-flux polysulphone, 1.5 m^2 Diacap® BBraun Melsungen) and patient positioning during dialysis (supine) were not changed. Dialysate composition was constant during the pregnancy with sodium 140 mmol/L, potassium 3 mmol/L and calcium 1.5 mmol/L without any phosphate. Unfractionated heparin was used until the seventh month then low-molecular weight heparin (LMWH) was introduced. Blood gas analysis was performed at the start/end of each HD session and every 2 h during the sessions. Blood pressure was monitored continuously during each session.

Taking into account what usually happens to pregnant women, we postulated a dry-weight increase of 800–1000 g per month. No antihypertensives were administered during pregnancy and there was no oedema.

In order to control the anaemia we administered iron gluconate and darbepoetin oral calcium (2 g/day), folate (5 mg/day) and calcitriol (0.25 μg/day) were prescribed. We suggested oral protein supplementation to attain daily

Table 2. HD schedules and intra-HD therapies during the pregnancy.

Month	HD per week	Type of HD	Duration of HD (min)	Dry weight (kg)	Heparin (IU/h)	QB (mL/min)	QD (mL/min)	Iron gluconate (mg/w)	Darbepoetin (mcg/week)
1	3	BD	195	47	1500	250	500	0	10
2	3	BD	195	47.5	1500	250	500	62.5	10
3	6	BD	300	47.7	1500	150	500	0	10
4	6	BD	300	49.8	1000	130	500	0	10
5	6	BD	300	51.8	1000	130	500	0	30
6	6	BD	300	53.5	1000	130	500	187.5	30
7	6	BD	300	56.5	1000	130	500	187.5	30
8	6	BD	300	57.8	1500[a]	130	500	0	30
9	6	BD	240	57.8	1500[a]	250	500	0	30

[a]LMWH.

protein and caloric intakes of 1.5 g/kg and 35 kcal/kg of body weight, respectively.

Caesarean birth at the 36th week was performed. The newborn (male) had a body weight of 2.230 g, length of 450 mm and skull circumference of 310 mm without significant anomalies. The apgar score was 8 (1 min) and 10 (5 min). After 2 days, bronchiolitis required 24-h ventilatory support with oxygen (concentrations >40%) followed by a 24-h course of CPAP. Moreover, the newborn presented sepsis successfully treated with ampicillin and gentamicin. After 10 days the newborn was discharged in stable condition.

The infant grew up between the 5th and the 10th percentile both for weight and height in the first 36 months of life and his clinical history was unremarkable.

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