

*Case Report***Pregnancy in End-stage Renal Disease Patients on Long-term Hemodialysis: Two Case Reports**

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Abstract

Although still uncommon, pregnancy in haemodialysis (HD) patients does occur and frequency has been increased in the past 20 years. But unfortunately, the rates for premature delivery, neonatal death, maternal hypertension, and preeclampsia in the pregnant HD patient are much higher than in the general population. Infants are often born both prematurely and small for gestational age. We report here two cases of pregnancy in women on long-term HD, one successfully and the other unsuccessfully managed, despite the same treatment strategy. Case 1 was a 43-year-old female patient, 10th gravida, after six years of maintenance HD whose pregnancy was successfully managed up to the 33rd week of gestation with a delivery of a healthy boy weighing 2,100 g. Case 2 was a 32-year-old female patient, 2nd gravida, after five years of maintenance HD, whose pregnancy ended in spontaneous abortion with intrauterine death at week 19 of gestation. Maternal hypertension and anaemia contributed partly to the unsuccessful outcome.

A successful pregnancy in HD patients requires multidisciplinary management, but considering the previous nephrological/prenatal/gynaecological/obstetric recommendations, many open questions remain when it comes to the best treatment and management of pregnancy in these women.

Key words: haemodialysis, pregnancy, anaemia, hypertension

Introduction

In 1971 Confortini *et al.* [1] reported the first successful pregnancy in a 35-year-old woman on chronic HD. Over time, the outcome of pregnancies in patients on HD has markedly improved, from only 23% live births during the 1980s based on a report from the European Dialysis and Transplant Association [2], to 50–100% (overall 76.25%) surviving infants from the systematic reviews in the recent

literature (2000 through 2008) [3]. The results of 90 pregnancies reported in the new millennium confirm that pregnancy is still a challenge but also a possibility [3,4]. Nevertheless, fetal mortality in pregnant women on HD is still much higher than in the general population [4]. Polyhydramnios-possibly due to fetal solute diuresis caused by high placental blood urea nitrogen (BUN) concentration, maternal hypertension and premature rupture of the fetal membranes are suspected of causing premature delivery [5]. Shifts in acute fluid volume, electrolyte imbalance, and hypotension could also contribute to the major dialysis-related complications resulting in impairment of the uteroplacental circulation [6]. There are some recommendations for HD management of pregnant patients to improve outcomes, but systematic nephrological and prenatal/ gynaecological/obstetric treatment approach cannot be found in the literature. We report here two cases of pregnancy in women on long-term HD, one successfully and the other unsuccessfully managed.

Case presentation**Case report 1**

A 43-year-old female patient, 10th gravida with three living offsprings (1988, 1990, 1993 year) and a history of five abortions before 1988. During the first trimester of her 9th pregnancy (may1996), she developed placental abruption with peripartur haemorrhage, complicated with fetal death and acute renal failure. Bilateral renal cortical necrosis was documented in a contrast-enhanced CT scan in this patient who presented with anuria and remained dependent on dialysis. Renal biopsy was not done due to patient's refusal and she was diagnosed as a case of ESRD in July 1996. She remained on maintenance HD three times a week, with no significant problems.

After six years on maintenance HD (in 2002), she presented with abdominal distension and amenorrhea and was found to be 16 weeks pregnant, diagnosed by serum HCG testing and pelvic ultrasound, but amniocentesis was not

done due to patient's refusal. The patient was dialyzed with bicarbonate dialysate and low-flux polysulfone F6HPS membrane with 1.3m² effective surface dialyzers that were not reutilized. The HD schedule was increased during pregnancy to 4 hours 4 times weekly between the 16th to the 23rd week of gestation, 4 hours 5 times weekly between the 24th to the 28th week of gestation and 4 hours 6 times weekly after the 28th week of gestation. As a consequence, her pre-dialysis blood urea levels decreased from 22.1 mmol/l (20th week), 17.7 mmol/l (24th week), 15.6 mmol/l (28th week) to 14.4 mmol/l at the end of pregnancy, and serum creatinine dropped from 622 µmol/l to 455 µmol/l. As part of her medication, the required dose of erythropoietin (Epo) was increased from a mean weekly dose of 6000 units to 10000 units during pregnancy, but her haemoglobin level ranged between 90 and 72g/l. Iron was also increased from 50mg/weekly to 100 mg/weekly, but transferrin saturation was 22.8% (24th week) and 15.9% (28th week). Blood pressure was controlled by minimal dose of alpha methyl dopa of 125mg two times a day, and blood pressure using the ambulatory blood pressure monitoring was 119/76 mmHg (20th week) and 114/72 mmHg (28th week). She also received calcium carbonate, 1500 mg/day as a phosphate binder, multivitamins and folic acid. On the 33rd week of gestation, the patient had a caesarean section delivery of a live boy weighing 2,100 g. After delivery, the mother returned to the schedule of three dialyses per week. The patient and her boy have remained healthy eight years after.

Case report 2

A 32-year-old female patient, 2nd gravida without living offsprings. ESRD was a result of focal segmental glomerulosclerosis proven by renal biopsy in 1996. Her first pregnancy (1997) was complicated by pre-eclampsia with abortion in the 28th week and as her renal function continued to deteriorate, maintenance HD was initiated in April 1997 (three sessions a week). In the first two years of HD she was with poor volume control and hypertensive, depressive, and developed pulmonary tuberculosis that resolved successfully within 6 months. After the first two years of maintenance HD, she remained normotensive and had a regular dialysis course.

Five years after the onset of maintenance HD (2002), the patient informed the nephrologist that she might be pregnant. Gynecological and ultrasound examination confirmed the presence of a live fetus at 13 weeks of gestation. From then onwards, HD prescription was changed to 4 days a week and 5 days a week after 16 weeks of pregnancy, with duration of 4 hours per session. The patient was dialyzed by using bicarbonate dialysate (with Enoxaparin sodium as anti-coagulant) with low-flux polysulfone F6HPS membrane (1.3m² effective surface). As expected, Epo and iron requirements were increased during her pregnancy (Epo, from a weekly dose of 6000 units, to a mean of 10.000 units and iron, from 50mg to 100 mg iv once every week), but her haemoglobin level ranged between 81 g/l (14th week) and 65 g/l (16th week), and transferrin saturation between 15.2% and 13.6%, thus requiring

additional treatment of two units of red blood cells in the 17th week. Hypertension remained of concern during the pregnancy, and she was treated with alpha methyl dopa, 250 mg three times a day, between the 13-14th week of gestation with a dose increase over the next week up to 1500 mg/day. Blood pressure using the ambulatory blood pressure monitoring was 135/91 mmHg (14th week) and 156 /103mmHg (17th week). Interdialytic weight gain reached no more than 2.0 kg. She, also, received calcium carbonate 1500 mg/day as a phosphate binder, multivitamins and folic acid. She was intensively followed by the nephrologist and obstetrician, but nevertheless, the pregnancy ended in spontaneous abortion with intrauterine death at week 19 of gestation. After the delivery, the mother returned to the previous treatment strategy of three dialyses per week and within the following eight years she had no significant problems.

Discussion

It has been shown that the prognosis for successful conclusion of pregnancy is better for patients who started HD after initiation of pregnancy as compared to those who conceived after starting HD (73.6% and 40.2%), respectively [4]. Our article reports cases representing patients who conceived long after starting HD (case 1-after six years, case 2-after five years).

Most published papers report that increasing HD hours improves pregnancy outcomes, specifically with respect to gestational age, birth weight, and infant survival [4,7]. In the largest study to date, the Registry for Pregnancy in Dialysis Patients reported the better infant survival in women who received dialysis ≥20 hours per week [4]. By 2002, there were enough data available to say that 75% of infants would survive if dialysis was increased to 20 or more hours per week, but that smaller increases in dialysis time were not beneficial [8]. Increasing dialysis dosage reduces predialysis BUN levels and intensified ultrafiltration may reduce the occurrence of polyhydramnios, thus lower the risk of premature labour and rupture of membranes in the later stages of pregnancy. Recommendations regarding the dialysis prescription for the pregnant woman on HD suggest maintaining predialysis BUN concentration of ≤50 mg/dl (17.85 mmol/l) is an appropriate goal [5]. Asamiya *et al.* showed that a birth weight equal to or greater than 1500g, or a gestational age equal to or exceeding 32 weeks corresponded to BUN levels of 48-49mg/dl (17.14-17.49mmol/l) or less [9]. In our case 1, we gradually increased the number of the weekly dialysis sessions and the mean pre-dialysis BUN was maintained at 22.1 mmol/l, 17.7 mmol/l, 15.6 mmol/l and 14.4 mmol/l respectively during pregnancy, which may have contributed in part to the successful outcome

Anaemia and hypertension (HTA) are the most frequent maternal complications observed in the HD population during pregnancy and require intensive management. Recommendations for anaemia management of the pregnant HD patients suggest that Epo doses need to be increased by approximately 50% in order to maintain target haemoglobin levels of 10–11 g/dl. The reason for the higher Epo

doses is unknown, but increased vascular volume with subsequent hemodilution and possibly erythropoietin resistance (due to enhanced cytokine production) during pregnancy may contribute to it [5]. New implications regarding the link between anaemia and pregnancy come from studies in rats, which suggest a possible suppressive effect of endogenous estradiol on erythropoietin induction through iron restoration [10]. This is not consistent with our observation, because, despite the increase of Epo doses for approximately 60% in both cases, the haemoglobin levels were below 90 mg/l, especially in case 2, which may have resulted partly to the unsuccessful outcome.

Common maternal complications observed in HD population during pregnancy include HTA, occurring in 42-80% of these women and polyhydramnios [11]. The pathogenesis of maternal HTA in HD patients is complex, but hypervolemia and inappropriate elevated total peripheral resistance are likely central to the refractory nature of this comorbid condition. Common to both HTA in ESRD and preeclampsia is the impairment in vascular responsiveness [12]. Antihypertensive medications are often required to maintain maternal diastolic blood pressure in the 80-90 mmHg range. The mainstays of treatment are methyl-dopa, B-blockers, and hydralazine [5]. The patient in case 1 with successful delivery remained normotensive on minimal dose of antihypertensive medications and intensified dialysis throughout pregnancy. However, in the other case 2, HTA was difficult to control during pregnancy despite the maximum dose of methyl-dopa and increased dialysis frequency, which most probably, at least partly contributed to the unsuccessful outcome. Haemoglobin level in case 2 was not achieved to the levels recently recommended for pregnant HD patients because of the risk to further increase her high blood pressure with higher doses of Epo [6]. The occurrence of HTA with Epo treatment is thought to be secondary to the increase in red blood cell mass, but the mechanism of HTA in this setting is probably multifactorial. However, studies on HTA among pregnant HD patients are lacking.

Several large surveys confirmed that infants born to women on HD are usually premature, with an average gestation of 32 week [3-5]. According to the article by Hou, 82% of babies born to HD patients reported to the registry were born before term and 18% were born before 28 week of gestation with the mean gestational age of 29.5 weeks for women dialyzed less than 20 h/wk and 34 weeks for women dialyzed more than 20 h/wk. [8]. In contrast, Baua *et al.* show that the mean gestational age in nocturnal home hemodialysis (NHD) cohort was 36weeks, but what potential advantages may NHD offer to improve pregnancy outcomes is unknown [12]. Our finding in case 1 is in agreement with earlier reports regarding gestational age since we failed to prolong gestational age beyond 32 weeks.

We reported on two cases of pregnancy in women on long-term HD who had different outcomes despite the same management: successful in a 43-year-old female patient in her 10th pregnancy and unsuccessful in a 32-year-old female patient in her 2nd pregnancy. Maternal hypertension and anaemia contributed in part to the unsuccessful outcome in case 2.

Conclusions

In conclusion, our case reports illustrate that following the recommendations for dialysis management in pregnant women may result in successful outcome, but only an international registry of pregnancies in HD patients will help answer the many open questions on the best management of pregnancy in HD women.

Conflict of interest statement. None declared.

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