Successful triplet pregnancy in a patient on chronic haemodialysis

Jinil Yoo1, Dilip Unnikrishnan1, Lin N. Lwin1, Hugo J. Villanueva1 and Alf. M. Tannenberg2

1Our Lady of Mercy Medical Center, Bronx, NY and 2Metropolitan Hospital, New York, NY, USA

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Introduction

Pregnancy in patients on haemodialysis (HD) is uncommon and carries a high risk of fetal and maternal complications. Multiple pregnancies carry a high risk even in normal individuals; the risk is higher in dialysis patients. We report a patient with end-stage renal disease (ESRD), who conceived while on HD, and had a successful triplet pregnancy. To our knowledge, successful triplet pregnancy in patients on HD has not been reported previously.

Case

A 36-year-old female with a clinical diagnosis of chronic glomerulonephritis was initiated on HD in May 1998 for worsening renal function (serum creatinine 919 μmol/l; 10.4 mg/dl). In the past, she had three spontaneous abortions including one during first trimester in 1996, three live births by Caesarean section and ventral hernia repair.

In November 1998, she informed us that she was pregnant. Ultrasonography showed triplet gestational sacs in the seventh week of gestation. She was not on infertility treatment. In view of poor perinatal outcomes and maternal complications, the patient was counselled extensively on terminating the pregnancy, however, she expressed her intentions to carry on with the triplet pregnancy. A multidisciplinary renal and obstetric team was formed and plans formulated to achieve optimal maternal health, fetal growth and development. Medications were reviewed; lovastatin was discontinued and amlodipine changed to methyl-dopa. Our goals were to avoid hypotensive episodes during HD, maintain pre-dialysis urea <60 mg/dl (21.4 mmol/l), serum albumin >2.8 g/dl, haemoglobin (Hb) 10–12 g/dl and close monitoring of fetal growth.

The patient received HD through a left arm arteriovenous graft, using a polysulfone high flux dialyser (F-80 dialyzer, surface area 1.8 m², Fresenius 2000H machine) and standard dialysate (K 2, Ca 3.5, HCO3 35); reprocessed membranes were not used. Heparin, 2500 U loading and 500 U/h dialysis, was used for anticoagulation. Her blood flow rate was increased up to 400 ml/min, with blood pressure (BP) monitoring every 15 min to ensure systolic BP in the range of 120–140 mmHg. Volumetric ultrafiltration and dialysate sodium modelling (linear variable sodium 142–137 mEq) were employed. Programmed adjustment of ‘dry’ weight was done by revising the estimated dry weight weekly to an expected weight gain during progression of the triplet pregnancy, in discussion with the obstetric team. Duration of HD was initially 12 h/week (4 h × 3 days/week); this was increased to 12.75 h/week from the twelfth week of gestation (4.25 h × 3/week), 13.5 h/week from the sixteenth week (4.5 h × 3/week), 18 h/week from the twenty-sixth week (3 h × 6/week) and 18.75 h/week (3 and 3.25 h on alternate days × 6 days/week) from the thirtieth week of gestation.

Erythropoietin was administered intravenously during HD, the required dose increased from 1000 U/HD session prior to pregnancy to 14 000 U/session to maintain Hb >10 g/dl (Table 1). The patient was on prenatal vitamins, folic acid and iron supplements. Five doses of 50 mg i.v. iron dextran were given during the twenty-eighth and thirty-second week of gestation for transferrin saturation <20%. Serum albumin levels dropped to 3.1 g/dl in the eighteenth week of gestation, and dietary protein intake was liberalized. The patient was hospitalized at 26 weeks of gestation because of worsening ventral hernia and was initiated on daily HD. At this time, the dialysate was adjusted to contain 3.0 mEq/l potassium, 3.0 mEq/l calcium and 27 mEq/l bicarbonate. Intravenous calcitriol was stopped at 26 weeks when the serum PTH level decreased to 28 pg/ml. Since BP remained low after initiation of daily dialysis, methyldopa was discontinued.

Fetal growth was monitored by abdominal sonography, done monthly during first and second trimesters,
and every 2 weeks during the third trimester. Cardiotocography (non-stress test) was performed twice weekly from 24 weeks of gestation to assess fetal well being. Corticosteroids were administered prior to delivery for fetal lung maturation. The patient was dialysed the previous day, preoperative blood chemistries were checked and we requested the presence of general and obstetric surgeons for the surgery considering the presence of a large ventral hernia. At 34 weeks of gestation, the triplets (two boys and one girl) were electively delivered by Caesarean section. Surgery was performed under epidural anaesthesia and no difficulty due to adhesions from previous surgery was noted. The infants weighed 1.75, 1.78 and 1.48 kg, had Apgar scores of 7, 9 and 8 (out of 9), respectively, and were cared for in the neonatal intensive care unit. The patient underwent ventral hernia repair and was transfused with 1 U of packed red blood cells. Table 1 summarizes pertinent clinical data during pregnancy.

### Discussion

#### Diagnosis of pregnancy

Early diagnosis of pregnancy in ESRD requires careful attention. Irregular menses, amenorrhea and nausea are common in this group and a mildly elevated beta-subunit of human chorionic gonadotropin observed in some patients with renal failure may give a false-positive pregnancy test [1–3]. Late diagnosis delays intensive antenatal care, reducing successful outcome. As recommended, we used abdominal sonography to confirm pregnancy and assess gestational age as soon as we were informed about the pregnancy.

#### Rate of conception and outcome in dialysis patients

Fertility of patients on dialysis is low. The US Registry reported that 2.2% of the female patients of childbearing age became pregnant over a 4-year period (0.5/100 patient years), while the Belgian National Survey noted 0.3/100 patient years [4,5]. However, the number of successful pregnancies in dialysis patients has improved over the years [6]. In a report of 344 pregnancies in 1998, 42% had surviving infants, 42.5% resulted in abortion and 13.5% had perinatal mortality [4]. The outcome was better in patients who conceived before starting dialysis compared with those who became pregnant while on dialysis [4,5]. Fetal risk of prematurity and growth retardation is high in pregnant dialysis patients [3,5]. An increase in congenital anomalies is also documented in pregnancies on dialysis [4]. Maternal mortality is uncommon although serious complications have been reported [3,5].

#### Control of BP

We switched our patient from amlodipine to methyl-dopa for BP control. Calcium channel blockers are increasingly used for hypertension in pregnancy. However, they may potentiate the neuromuscular blockade and hypotensive effect of magnesium used in the treatment of eclampsia [1,2]. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are contraindicated in pregnancy because they may cause oligohydramnios, renal dysplasia, neonatal anuria and pulmonary hypoplasia, especially when used in the third trimester [1–3]. After initiation of daily HD, the patient remained normotensive without any antihypertensive medications. Throughout pregnancy, the focus was on preventing intradialytic hypotension.

#### Management of anaemia

In our patient, the weekly dose of erythropoietin required to maintain acceptable Hb levels increased from 3000 U prior to pregnancy to 42 000 U during the third trimester. We used i.v. erythropoietin, as is the routine in our HD unit, without any complications. Erythropoietin therapy was not associated with uncontrolled hypertension in these studies [1,2,5]. Our patient was given parenteral iron to maintain transferrin saturations over 30%. It is recommended that

### Table 1. Clinical data during course of the triplet pregnancy

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</thead>
<tbody>
<tr>
<td>Pre HD BP (mmHg)</td>
<td>134/75</td>
<td>124/70</td>
<td>132/75</td>
<td>132/72</td>
<td>141/78</td>
<td>131/74</td>
<td>128/74</td>
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<td>Pre HD weight (kg)</td>
<td>85.6</td>
<td>86.7</td>
<td>89.3</td>
<td>92.6</td>
<td>96</td>
<td>96.9</td>
<td>97.9</td>
</tr>
<tr>
<td>Post HD weight (kg)</td>
<td>84.5</td>
<td>85.5</td>
<td>87.5</td>
<td>91.9</td>
<td>95</td>
<td>96.3</td>
<td>97.7</td>
</tr>
<tr>
<td>Pre HD BUN (mmol/l)</td>
<td>19.9</td>
<td>12.8</td>
<td>17.5</td>
<td>9.9</td>
<td>7.1</td>
<td>10.4</td>
<td>5.7</td>
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<tr>
<td>Hb (g/dl)</td>
<td>12.5</td>
<td>11.2</td>
<td>8.9</td>
<td>10</td>
<td>9.9</td>
<td>11.2</td>
<td>10.2</td>
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<tr>
<td>Hct (%)</td>
<td>38.6</td>
<td>34.2</td>
<td>27.8</td>
<td>31.8</td>
<td>31.3</td>
<td>34</td>
<td>30.8</td>
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<tr>
<td>Epogen (U/week)</td>
<td>3000</td>
<td>15000</td>
<td>33000</td>
<td>33000</td>
<td>42000</td>
<td>42000</td>
<td>24000</td>
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<tr>
<td>Serum albumin (g/dl)</td>
<td>3.6</td>
<td>3.8</td>
<td>4.2</td>
<td>3.1</td>
<td>3.0</td>
<td>2.9</td>
<td>2.8</td>
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<td>Serum creatinine (µmol/l)</td>
<td>698</td>
<td>530</td>
<td>548</td>
<td>468</td>
<td>486</td>
<td>495</td>
<td>282</td>
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<tr>
<td>Serum sodium (mEq/l)</td>
<td>133</td>
<td>137</td>
<td>136</td>
<td>139</td>
<td>136</td>
<td>137</td>
<td>135</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/l)</td>
<td>15</td>
<td>17</td>
<td>13</td>
<td>16</td>
<td>20</td>
<td>28</td>
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parenteral iron, when required, be given in small doses (100 mg/dose or less) to avoid acute iron toxicity in the fetus [1,3,6].

**Adequacy of HD**

We decided to admit the patient at the twenty-sixth week of gestation primarily because of worsening ventral hernia and initiated daily HD. Daily dialysis helped maintain low pre-dialysis BUN, minimize BP fluctuations, prevent intradialytic hypotension by decreasing interdialytic weight gain, and improve maternal protein and calorie intake. We used potassium 3 mEq/l, bicarbonate 27 mEq/l dialysate and aimed for a pre-dialysis BUN < 60 mg/dl (21.4 mmol/l), to maintain a less azotaemic environment for the fetus [7]. Attaining a low pre-dialysis BUN minimizes solute diuresis by the normal fetal kidney, thus decreasing the incidence of polyhydramnios [3]. In pregnancy, progesterone causes physiologic respiratory alkalosis by respiratory centre stimulation. A lower bicarbonate in dialysate is hence recommended to prevent alkalaemia, especially with daily HD [1,3]. Upon initiation of daily HD, the potassium content of dialysate should be increased and calcium content decreased to prevent hypokalaemia and hypercalcaemia, respectively [1]. Available data suggest that outcome is better if pregnant dialysis patients receive 20 h or more of dialysis per week [1–3,6].

**Calcium and phosphorus**

A 3.5 mEq/l calcium dialysate can cause 1 g influx of calcium at each dialysis session; therefore, the concentration of calcium in the dialysate should be decreased when patients are switched to daily dialysis to prevent hypokalaemia [2]. Pregnant dialysis patients on a 2.5 mEq/l calcium dialysate usually require oral calcium supplements of 2 g/day [1,2].

**Nutrition**

A protein intake of 1.8 g/kg/day is generally recommended in pregnant HD patients. Initiation of daily HD allowed us to liberalize the diet with a higher protein content. The usefulness of biochemical parameters (e.g. serum albumin) is complicated by co-morbid illnesses in the dialysis patient and haemodilution of pregnancy. Water-soluble vitamins are lost during dialysis and require supplementation. Pregnant patients on dialysis require up to 0.8 mg/day of folate; folate deficiency can cause neural tube defects [1].

**Fetal monitoring**

There are no standard recommendations for fetal monitoring in dialysis patients. We used the following protocol: (i) sonography performed monthly in the first and second trimester and then every 2 weeks to evaluate fetal growth and development, and (ii) cardiotocography (non-stress test) done twice weekly from the twenty-fourth week of gestation to assess fetal well being. Contraction stress testing using oxytocin should not be undertaken due to risk of precipitating premature labour [1,2]. Elective delivery by 34–36 weeks is preferred once fetal lung maturity is shown, although premature labour or other complications result in early delivery in most instances [1]. The infant with normal kidneys has a BUN and creatinine similar to the ESRD mother’s, and will experience solute diuresis after delivery. This requires intensive care monitoring of fluid and electrolyte status [1,2].

**Premature labour**

Premature delivery is an important problem in patients on HD, with a high incidence of neonatal death. Polyhydramnios contributes to pre-term labour; polyhydramnios probably results from solute diuresis by the normal fetal kidney increasing amniotic fluid production [5]. Frequent dialysis may reduce the incidence of polyhydramnios [6].

**Triplet pregnancy**

Consequent to advances in treatment of infertility, the incidence of multiple pregnancies has increased from approximately 1 in 8000 pregnancies in 1978 to a more recent estimation of 1 in 849 to 1 in 2083 pregnancies [9]. Outcomes of triplet gestation have also improved over the years, from a perinatal mortality of 232 per 1000 births during 1946–1976 to a perinatal mortality of 41 per 1000 reported in 1995 [9]. The mean gestational age in a series of 57 triplet pregnancies was 33 weeks, with a range of 24–37 weeks [9]. Another study noted that when triplet pregnancy patients were electively hospitalized in the third trimester, they had a lower incidence of pre-eclampsia and increased fetal weight compared with those followed as outpatients [10].

**Conclusion**

The incidence of pregnancy and successful outcome in patients on dialysis has increased in recent years. However, fetal and maternal morbidity and mortality remain significant, and appropriate counselling should be offered to dialysis patients who are pregnant and to those of childbearing age [6]. The success rate for multiple pregnancy is much lower; reduction in the number of fetuses by selective termination may be an option depending on acceptability of the patient. All aspects of dialysis including duration, adequacy, nutrition, anaemia, calcium and phosphate metabolism and BP control need to be closely followed throughout the course of pregnancy. With careful monitoring and intensive HD, a successful outcome is possible even in a high-risk triplet pregnancy in patients on HD.

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References


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