Pregnancy during dialysis: case report and management guidelines

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Introduction

The first successful term pregnancy occurring in a 35-year-old dialysed patient was described in 1971 by Confortini et al. [1]. Since then we have been able to identify 120 published cases of conception occurring in end-stage renal disease (ESRD) patients*. In almost 30 years, the frequency of conception on dialysis has increased, the outcome of such pregnancies has improved, and the overall attitude towards this complex clinical situation has evolved. We report the successful multidisciplinary management of a pregnancy in a haemodialysed patient from our centre. We then propose practical guidelines for the management of such pregnancies based on a careful review of the literature. Our literature search identified 120 cases of pregnancy occurring in dialysed patients, published between 1971 and 1998, allowing us to compare this series to the previously published ones.

Case

A 32-year-old African-American female, gravida four, para two, aborta one, was diagnosed with renal insufficiency in January 1993. She had no significant past medical or surgical history, and she had experienced two previous uneventful term vaginal deliveries. Renal insufficiency was managed expectantly until October 1994, when she was admitted for acute renal failure and massive nephrotic syndrome (proteinuria of 18 g/24 h, serum albumin of 1 g/dl, and serum creatinine of 6.5 mg/dl). A renal biopsy revealed focal segmental glomerulosclerosis and chronic interstitial nephritis. Her renal function continued to deteriorate, and because of anasarca she was started on haemodialysis (HD) in December 1994 (three sessions of 3 h/week). Her dry weight was 55.3 kg.

The patient remained normotensive and had an uneventful dialysis course until presenting in September 1995 with severe abdominal pain. A pelvic ultrasound revealed a single live 7-weeks-old intrauterine gestation. The calculated residual creatinine clearance was 13 ml/min. Following extensive counselling at the Division of Maternal–Fetal Medicine regarding risks of prematurity, pregnancy-induced hypertension, and neonatal morbidity, the patient elected to continue with the pregnancy.

A joint renal/obstetric HD protocol was designed to maintain a predialysis BUN < 50 mg/dl, increasing her HD session time to 4 h, and frequency to 4 times/week. She had been dialysed with a biocompatible high-flux polysulphone membrane (1.8 m²) until the pregnancy was diagnosed. She was then changed to a smaller surface area membrane (1.0 m²), and no reprocessed membranes were used. Standard bicarbonate with glucose, 3.0 mEq/l calcium, and a 3.0 mEq/l potassium dialysate was used. During each dialysis session the blood flow was gradually increased over the first 30 min of HD, from 180 to 300 ml/min, while monitoring the maternal blood pressure. Her Kt/V ranged between 1.02 and 1.66.

Dialysis was performed with the patient in the left lateral decubitus position. The estimated maternal dry weight (EDW) was increased by 500 g every 10 days, corresponding to the usual maternal weight gain in a normal pregnancy. Standard heparin was used for anticoagulation, and daily low-dose aspirin was given to prevent pre-eclampsia. Erythropoietin (Epo) was administered at each HD session, with the dose adjusted to maintain a maternal haematocrit between 32 and 34%. No transfusions were required. She was continued on vitamin D (0.5 μg × 3/week), folic acid (1 mg q.d.), and prenatal vitamins. The patient had evidence of protein–calorie malnutrition during the 8

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*Interested readers can obtain the complete list of corresponding references from the editorial office.
months prior to pregnancy (serum albumin 1.9 g/l). When her pregnancy was diagnosed, a 3000 kcal/day diet was encouraged with more than 100 g of protein a day. Her serum albumin increased to 2.9–3.3 g/l and remained in this range until delivery.

Obstetric surveillance consisted of careful monitoring of maternal blood pressure, uterine and umbilical artery perfusion, and continuous fetal heart rate tracing immediately before, during, and immediately after each HD session from 25 weeks of gestation until delivery. Uterine and umbilical artery perfusion were assessed using systolic/diastolic (S/D) ratios, by Doppler velocimetry. Mean uterine artery S/D ratios (± standard deviations) were 2.32 (0.53) before, 2.23 (0.45) during, and 2.52 (0.40) after HD, while mean umbilical artery S/D ratios were 2.66 (0.34) before, 2.59 (0.45) during, and 2.52 (0.40) after HD. There were no significant changes in uterine or umbilical artery S/D ratios when compared before and during, or before and after HD throughout gestation. There were no significant alterations in maternal mean arterial blood pressure during HD (range 73–106 mmHg). Continuous fetal heart tracings during HD remained reassuring at all times, with no changes in baseline variability or incidence of decelerations.

The patient’s obstetric course was otherwise uncomplicated. The HD protocol was maintained unchanged until 28 weeks gestation, when the patient developed persistent headaches during the last part of each HD session, which prompted a reduction in duration of each HD session to 3.5 h. Maternal hypertension was never documented. Serial obstetric ultrasound examinations confirmed appropriate fetal growth.

The patient was admitted at 31 weeks gestation for preterm labour, which was controlled with i.v. tocolysis using intermittent boluses of magnesium sulphate to maintain a serum magnesium level of 6–8 mg/dl. She also received betamethasone to maximize fetal lung maturity. She remained stable as an inpatient for the next 2 weeks, with no changes required to her HD protocol. She developed premature rupture of membranes at 33 weeks gestation, which was followed soon after by a normal vaginal delivery of a liveborn female infant, weighing 2168 g, with Apgar scores of 8 and 9. The patient had a completely uneventful postpartum course. Her renal disease has remained stable, now 24 months after this successful delivery.

The neonate was admitted to the neonatal intensive care unit immediately after birth, and was noted to have a haematocrit of 38% with a serum creatinine level of 1.9 mg/dl. No polyuria was observed, and the creatinine dropped to 0.5 mg/dl within 6 days. The infant developed mild respiratory distress 6 h after birth, consistent with transient tachypnea of the newborn, and she required supplemental oxygen only for a short period of time. After blood cultures were found to be positive for group B streptococcus, the baby received a 10-day course of i.v. penicillin. All further laboratory parameters remained stable. The infant was subsequently discharged home and is currently thriving at 24 months of age.

**Frequency and outcome of pregnancy in dialysis patients**

Pregnancy appears to be very rare among patients with end-stage renal disease (ESRD). It is difficult, however, to estimate the actual incidence of conception during ESRD. This is because most published case reports only describe successful pregnancy outcomes, and an organized registry of these cases is only available in few countries. In addition, data collection may be incomplete, and many pregnancies are lost before they are clinically confirmed. Three surveys have estimated the incidence of pregnancy in childbearing age women on dialysis to be between 0.75 and 7% [2–4]. In a very recent Belgian survey, the incidence of conception was estimated to be of 0.3 pregnancies for 100 patient-years [5]. In our review, 47% of the reported pregnancies occurred during the first 2 years on dialysis, while women who were on dialysis for more than 10 years appeared less likely to conceive and accounted for only six of the 120 pregnancies.

The chances of a fetus surviving pregnancy on HD are even more difficult to assess. The same three surveys have reported a 19–30% successful pregnancy rate before 1990 although the likelihood of completing a term pregnancy has risen to 52% since then [6]. Okundaye et al. [7] recently reporting the results of the United States Registry, found an overall 40.2% of surviving infants when conception occurred after the beginning of dialysis. Table 1 shows the frequency and outcome of pregnancy during dialysis in the previously published series. In our review, 71% (n = 39) of the 55 cases published after 1990 resulted in a liveborn infant that survived, while only 57% (n = 28) did before 1990. It appears also that both conception and successful outcome are more likely to occur if some residual renal function is present [4]. Interestingly, the two latest surveys both suggest that increasing dialysis time during pregnancy results in longer gestational period, higher birth weight, and higher number of viable pregnancies [5,7].

**Spontaneous abortions (SAB)** (pregnancy loss before 20 weeks of gestation), and stillbirths (pregnancy loss after 20 weeks of gestation) account for nearly all pregnancy losses, with elective pregnancy termination and early neonatal deaths (in the first 7 days of life) constituting the remainder. In our review, 67 (64.5%) pregnancies resulted in a liveborn infant that survived, with only 15 (16%) of all pregnancies completing 36 weeks of gestation. Otherwise, the fetal outcome was remarkable for 12 (11.5%) SAB, eight (7.7%) stillbirths, 14 (13.5%) early neonatal deaths, four reported elective or medical terminations of pregnancy, and one infant demise 45 days after birth, this information being available for 104 pregnancies out of 120 (see Table 2).

One must acknowledge that the number of SAB is probably underestimated because many pregnancies are lost before they have been recognized. Conversely, the incidence of stillbirths and early neonatal births
are probably closer to the reality. In their latest review, Okundaye et al. [7] found 16.8% of SAB in the second trimester and 25% of SAB in the first trimester, 8.1% of stillbirths, and 8.2% of neonatal deaths, among 184 pregnancies (see Table 1). In the latter survey, the data was obtained by a very detailed questionnaire sent to the dialysis units, the resultant information was estimated to cover nearly 50% of women of childbearing age receiving dialysis in the United States. We suspect that the literature cases greatly underestimate the number of SAB, perhaps by eliminating or ignoring the early (first trimester) pregnancy losses.

The great majority of the births in this population are preterm with a mean gestational age at delivery of 32.4 weeks [7]. In our review, the mean gestational age at delivery was 30.5 weeks (Table 3). While previous studies suggested an increased risk of intrauterine growth restriction (IUGR) in pregnant HD patients, our review of the data does not support this conclusion. In the 92 cases for which information was available, birth weight appears appropriate for each gestational age at delivery, suggesting that the overall mean birth weight of 1.6 kg reflects increased incidence of prematurity rather than significant IUGR (Table 4).

Congenital abnormalities do not seem to be more frequent among HD patients than in the general population, whereas the incidence of polyhydramnios appears increased (22 of our 120 published cases). The pathophysiology of this excessive amniotic fluid production is unclear, with one of the suggested mechanisms being the solute diuresis, due to high blood urea concentration, by the normal fetal kidney [8]. The incidence of polyhydramnios may decrease with the use of chronic ambulatory peritoneal dialysis (CAPD) or with the increase of total dialysis time, where blood urea is kept in a low level.

Prescription of dialysis during pregnancy

In the literature the choice of the mode of dialysis is controversial. Peritoneal dialysis (PD) could improve the outcome of pregnancy among patients with ESRD [9]. However, the experience with PD in pregnancy is still limited to a very small number of cases, and most authors agree not to change the mode of dialysis after conception. More data still need to be gathered concerning the outcome of pregnancies in PD patients and the incidence of eventual specific complications (e.g. peritonitis, catheter obstruction, and leak).

Neither have studies been published regarding the choice of dialysis membrane during pregnancy. Teratogenicity was described in animal studies and attributed to the use of formaldehyde and ethylene oxide. Thus, the use of a biocompatible membrane is recommended [10]. Biocompatible membranes also induce a lesser degree of net protein catabolism than bioincompatible membranes [11]. A smaller surface membrane combined with a longer dialysis time is preferred to a larger-surface dialyser with a standard session duration, as this minimizes fluid shifts, and

![Table 1. Frequency and outcome of pregnancies among dialysis patients from previously published reviews](image.png)
Table 2. Fetal outcome of the 120 reviewed cases (1971–1997)

<table>
<thead>
<tr>
<th>Pregnancies (n)</th>
<th>Pregnancies with available information (% (n))</th>
<th>Surviving infants (% (n))†</th>
<th>Spontaneous abortion* (% (n))†</th>
<th>Stillbirth** (% (n))†</th>
<th>Early neonatal death*** (% (n))†</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>86.6% (n = 104)</td>
<td>64.5% (n = 67)</td>
<td>11.5% (n = 12)</td>
<td>7.7% (n = 8)</td>
<td>13.5% (n = 14)</td>
</tr>
</tbody>
</table>

*Spontaneous abortions; defined as pregnancy loss before 20 weeks; **Stillbirths; defined as pregnancy loss after 20 weeks; ***Early neonatal deaths, defined as deaths occurring in the first week of life; †Percentages are based on totals, excluding cases with unknown information.

Table 3. Characteristics of the 120 reviewed case reports

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± STDV</th>
<th>Range</th>
<th>Available information cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean maternal age at diagnosis of pregnancy (years)</td>
<td>29.5 ± 7</td>
<td>16–46</td>
<td>110 91.67</td>
</tr>
<tr>
<td>Mean time on dialysis prior to pregnancy (months)</td>
<td>38.5 ± 37</td>
<td>0.5–192</td>
<td>104 86.67</td>
</tr>
<tr>
<td>Mean gestational age at diagnosis of pregnancy (weeks)</td>
<td>14.1 ± 6.4</td>
<td>4–28</td>
<td>60 54.5</td>
</tr>
<tr>
<td>Mean gestational age at delivery (weeks)</td>
<td>29.3 ± 4.7</td>
<td>16–38</td>
<td>93 77.5</td>
</tr>
<tr>
<td>Mean birth weight at delivery (g)</td>
<td>1382 ± 623</td>
<td>350–2700</td>
<td>92 76.67</td>
</tr>
</tbody>
</table>

Table 4. Mean birth weight of the 120 reviewed cases stratified by gestational age

<table>
<thead>
<tr>
<th>Gestational age at birth (weeks)</th>
<th>Infant’s weight at delivery (Mean (g))</th>
<th>Pregnancies* (n)</th>
<th>Infant survival* (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;24</td>
<td>520</td>
<td>6 5</td>
<td>0 0</td>
</tr>
<tr>
<td>24–25</td>
<td>673</td>
<td>6 5</td>
<td>0 0</td>
</tr>
<tr>
<td>26–27</td>
<td>705</td>
<td>4 4.8</td>
<td>1 25</td>
</tr>
<tr>
<td>28–29</td>
<td>883</td>
<td>10 8.3</td>
<td>5 50</td>
</tr>
<tr>
<td>30–31</td>
<td>1273</td>
<td>13 10.8</td>
<td>9 69</td>
</tr>
<tr>
<td>32–33</td>
<td>1660</td>
<td>19 15.8</td>
<td>16 84</td>
</tr>
<tr>
<td>34–35</td>
<td>1920</td>
<td>19 22.9</td>
<td>19 100</td>
</tr>
<tr>
<td>&gt;36</td>
<td>2217</td>
<td>15 18</td>
<td>15 100</td>
</tr>
</tbody>
</table>

*Percentages are based on totals, excluding cases with an unknown value.

It avoids hypotensive episodes and abrupt osmolality changes.

It is an arbitrary practice to keep BUN below 50 mg/dl. This goal may be difficult to obtain in women who have no residual renal function. Usually the frequency of HD is increased to maintain a predialysis BUN under 50 mg/dl. The increase in dialysis time seems to improve the pregnancy outcome and offers several advantages. It ensures a less uraemic environment for the fetus, and allows the mother a more liberal diet (protein and potassium) and fluid intake. It may help control hypertension, and may also reduce the amplitude of blood volume and electrolyte shifts. Frequent dialysis sessions make fluid removal and achievement of estimated dry weight (EDW) easier. It also lowers the risk of hypotension, which may be associated with fetal distress and premature labour.

Maternal dry weight and weight gain need to be regularly re-evaluated according to changes in the estimated fetal weight. In the first trimester a minimal weight gain of 1–1.5 kg occurs. After the first trimester, weight gain seems to be linear and amounts to 0.45 kg or 1 pound per week. During the third trimester it is also useful to follow fetal weight and growth, using serial ultrasound determinations. If weight gain is excessive, episodes of hypotension can be minimized by the use of isolated ultrafiltration. Scrupulous monitoring of maternal blood pressure and heart rate before, during, and after dialysis can also help the clinician estimate more accurately the amount of fluid that has to be removed.

Dialysate potassium concentration may have to be increased to 3 or 3.5 mmol/l. Serum electrolytes need to be monitored weekly in order to avoid hypokalaemia. The progesterone-induced increase in ventilation in normal pregnancy results in a respiratory alkalosis ($pCO_2$ 25–30 mEq/l). A secondary decrease in renal acidification reduces serum bicarbonate from 24–30 mEq/l to 18–21 mEq/l. In patients with impaired renal function, this compensation cannot appropriately take place. Therefore a low-bicarbonate dialysate (25 mEq/l) has been recommended by Hou [2]. According to her experience, frequent HD may result in the transfer of excessive amounts of alkali to the mother,
thus generating substantial alkalaemia. In our case alkalaemia was not observed, although we used a standard bicarbonate dialysate. A careful monitoring of the maternal respiratory rate, O₂ saturation, and electrolytes during HD is recommended.

During normal pregnancy the digestive absorption of calcium is increased, physiological hypercalcaemia and functional hyperparathyroidism occur, calcitriol levels increase, and parathyroid-hormone-related peptide (PTH-rp) levels increase [12]. In HD patients, calcium metabolism is also greatly altered, even though hypercalcaemia cannot occur. Both the calcium coming from the dialysate and the calcium ingested from calcium carbonate used as a phosphate binding agent also need to be taken into account. A 3.5-mmol/l dialysate ensures a 1-g influx of calcium at each session, and this amount exceeds the cumulative amount of 25–30 g calcium required for calcification of the fetal skeleton. Daily HD with such a dialysate, however, can induce hypercalcaemia. A 2.5 mmol/l dialysate needs to be supplemented with 1–2 g of oral calcium carbonate, to avoid overall calcium loss. A calcium-rich dialysate also appears to help control hyperphosphataemia and secondary hyperparathyroidism. These patients’ calcium, phosphate levels should be monitored weekly, before and after HD. Hyperphosphataemia can affect fetal skeletal development and frequent monitoring is mandatory if calcium binders are used. Vitamin D should be monitored monthly and supplemented only if low. Some studies have suggested that the human placenta is a source of 1,25(OH)₂-vitamin D₃. This placental contribution could be of major significance in pregnant women in whom endogenous renal 1,25(OH)₂-vitamin D₃ production is deficient [13]. However, it is not clear whether this placental production has any significant clinical impact during pregnancy.

Fetal monitoring during haemodialysis

The few recommendations concerning fetal monitoring that have been published do not address the issue of fetal assessment or fetal wellbeing during HD. Fetal surveillance during HD once fetal viability has been reached is of critical importance, given the acute fluid shifts that can occur and the resulting potential for acute hypotensive episodes. Significant changes in amniotic fluid have also been documented during HD, which further emphasizes the need for close fetal surveillance [14]. The objective should be to minimize uteroplacental and fetal perfusion disturbances. In one study describing the Doppler assessment of uterine and umbilical perfusion during HD, it was found that both pulsatility index of the umbilical artery and the fetal heart rate increased significantly after HD, and it was postulated that this might reflect fetal hypovolaemia due to acute fluid withdrawal [15].

Obstetric surveillance should consist in careful monitoring of maternal blood pressure before, during, and immediately after each HD session. Fetal heart rate monitoring should begin at the time of fetal viability (25 weeks), until delivery. The frequent Doppler velocimetry measurements during our patient’s pregnancy proved to be remarkably stable, unlike the results obtained by Oosterhof [15]. This may be the result of the precautions taken to ensure maternal haemodynamic stability during each HD sessions. Hypotensive episodes are known to be more frequent during the last 30 min of the dialysis treatment. Therefore we recommend continuous fetal heart monitoring towards the end and shortly after each HD session. In addition serial obstetric ultrasound examinations should confirm appropriate fetal growth and estimate the amniotic fluid volume every 2–4 weeks.

Anaemia and iron management in pregnant dialysis patients

The first reported successful use of Epo during pregnancy in a HD patient was published in 1990 [16]. In our review 24 of 120 patients were treated with Epo, representing only 65% of the pregnancies reported after 1990. After 1992 Epo was used in 90% of the pregnancies. However, a drop in the haematocrit has been observed even during human recombinant Epo-treated pregnancies, and blood transfusions may still be required. The Epo dose in such pregnancies is a matter of controversy. Low doses, such as 2000–4000 IU twice weekly, are sufficient for some [17]. High doses (40–60 IU/kg six times a week) are required for others, in combination with intensive HD treatment [18]. An intermediate dose of 100 IU/kg/week in divided doses seems a reasonable starting-point, with further increments depending on the haematocrit and the clinical tolerance. A target haematocrit between 30 and 35% is recommended (the haematocrit in normal pregnancy is 32–34%).

Another controversial issue is whether or not Epo crosses the human placenta. Early concerns were based on animal studies using massive doses of Epo with deleterious effects on the murine fetus [19]. In humans, strong indirect evidence argues against placental permeability to Epo. The absence of correlation between Epo levels in the mother and the fetus is an indirect indication that Epo levels are not in equilibrium across the placenta [20]. The high molecular weight of Epo makes a passive diffusion through the placenta very unlikely and there was no transfer observed in vitro with perfused human placenta [21]. Finally there seems to be no Epo receptors in human placenta [22]. Therapeutic use of Epo in the mother is thus unlikely to have any haematological consequence in the fetus.

The occurrence of hypertension with Epo treatment is thought to be secondary to the increase of red blood cell mass but the mechanism of hypertension in this setting is probably multifactorial [23]. It is often difficult to know if hypertension is secondary to Epo use, to pregnancy itself, or to the underlying renal disease. When the haematocrit is not corrected by Epo, or when hypertension disappears after delivery, the
role of Epo in the pathogenesis of hypertension seems unlikely.

Interestingly, Epo has been shown to improve sexual function and to induce regular menstruation in some studies [24]. This effect could be mediated by a decrease in prolactin levels under Epo treatment [25] even though hormonal changes associated with Epo seem only transitory [26]. The mechanism by which prolactin is decreased by Epo treatment is not known. The improved sexual function reported with Epo treatment may be related to improvement in the general health status. Therefore Epo treatment may have other advantages than haemotocrit increments.

Daily iron losses are increased during HD and are estimated to be 780 mg per year. Therefore, Grossman et al. [27] recommend an i.v. 500-mg dose of iron, administered as soon as pregnancy is diagnosed if transferrin saturation is lower than 30%. Oral iron absorption is poor in HD patients and many authors have proposed i.v. iron supplementation during dialysis sessions. Depending on the iron preparation used, i.v. iron should be given in low doses (10–40 mg) at each dialysis session, or in higher doses (100–1000 mg) less frequently [28]. This substitution should be monitored with transferrin saturation measurements (maintained over 30%) rather than with ferritin levels (which may reflect stores that are not available for haemoglobin production) [27]. Folic-acid deficiency in the first trimester of pregnancy has been associated with neural-tube defects. Dietary potassium restrictions, frequent in ESRD patients, are often associated with folate deficiency. The normal recommendations during pregnancy are 0.4 mg daily supplements; recent data indicate that this dose should be increased to 0.8 mg in HD patients (making a total daily dose of 0.8–1 mg/day).

**Nutrition during pregnancy and dialysis**

Malnutrition is common among HD patients. The nutritional problems of patients with ESRD have been well described [29], and are complicated by the nutritional requirements of pregnancy. It has been estimated that the minimal daily dietary protein intake (DPI) in healthy individuals is approximately of 0.6 g/kg. For HD patients, a protein intake of 1.4 g/kg/day is needed to maintain a positive or neutral nitrogen balance during non-dialysis days. Thus a minimum of 1.2 g/kg/day is suggested as the safe level of DPI [30]. The recommended DPI for a pregnant woman is 1.2–1.3 g/kg. Adding the DPI for HD patients, and the additional daily protein requirements for pregnancy, a pregnant HD patient should be ingesting 1.8 g/kg/day of protein.

Serum albumin and transferrin are normally used to evaluate the adequacy of protein status. Serum albumin is probably the most extensively examined index of nutritional status, because of its easy availability and strong association with outcome (e.g. mortality) in ESRD patients [31]. However, albumin may reflect the degree of underlying illness rather than the overall nutritional status. Plasma volume increases by 50% over the course of pregnancy, and this increase begins during the first trimester of pregnancy. The alterations in different plasma parameters should be taken into account when interpreting laboratory data in a pregnant woman. It should be noted that in the dialysis population, most pregnancies are not diagnosed until the second trimester, by which time these alterations in laboratory parameters would be expected to be manifest.

In HD patients losses of essential nutrients such as, amino acids, and water soluble vitamins into the dialysate contribute to the impaired nutritional status. Grossman et al. propose the doubling of the usual dose of water-soluble vitamins for these patients [28]. Vitamin A being fat-soluble, is not dialysable, and its supplementation is not indicated unless deficiency is determined by measurement. Supplementation of other divalent cations and trace elements are rarely necessary. The only exceptions are iron and calcium, as already discussed above.

**Infertility and contraception in ESRD patients**

It is well known that HD patients conceive rarely, making the clinical finding of pregnancy in ESRD unusual and often unexpected. The subfertility of these patients is thought to be multifactorial. Their libido and sexual function are usually considerably altered. Amenorrhoea and anovulation are present in more than 50% of cases [32]. Prolactin and LH levels are usually increased and GnRH pulsatility altered. Other factors such as malnutrition (vitamins, trace elements), uraemic toxins, uraemic neuropathy, and pharmacological agents (antihypertensive drugs, anti-emetics, digoxin) are probably also involved in the infertility associated with haemodialysis [33].

Birth control is advisable for women who do not wish to conceive, especially if regular periods are still present or if residual renal function is maintained. Although a recent study reports the almost complete absence of counselling of HD women by their primary care physicians, these issues should be addressed and discussed with women of childbearing age [32]. The choice of a contraceptive method is often difficult. Barrier methods (diaphragms and condoms) can be used safely, while intrauterine devices might be associated with increased infection episodes and bleeding during HD. Oral contraceptives are safe in the absence of hypertension, diabetes, or active lupus erythematosus. Dialysis patients are usually hypoestrogenic and the use of combined oral contraceptive pills might protect their bone tissue already at risk from renal osteodystrophy.

Holley et al. [32] report an early age for menopause in HD patients (47 years old). No previous studies are available to confirm this finding. It could be integrated in the accelerated aging attributed to uraemia (the uraemic milieu may affect follicular development or...
accelerate follicular atresia). One must acknowledge that HD women are often amenorrheic or have irregular menses, making the determination of the exact age of menopause very uncertain. On the other hand, a recent study showed they often underwent early hysterectomy for dysfunctional bleeding [34]. This data reinforces the concern about unrecognized hypo-oestrogenic states in women who already have multiple cardiovascular and osteoporosis risk factors. Therefore we recommend that hormonal contraception be used when not contraindicated in women who do not wish to conceive.

Although pregnancy occurring in end-stage renal disease remains rare, the frequency of conception during dialysis appears to have increased. The outcome of such pregnancies also seems to be improving with the advances in obstetrics, neonatal medicine and treatment of dialysed patients. It should, however, be emphasized that the beneficial outcome of a pregnancy occurring after the beginning of dialysis treatment relies primarily on its multidisciplinary management. It remains difficult to encourage pregnancy or fertility treatment in a dialysed patient, but this review of the literature has led us to a more optimistic view of such high-risk pregnancies. It is important that the patient and her spouse be clearly and precisely informed of the risks involved for the fetus and herself in order to allow their decision in the best conditions possible.

References