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## Peritoneal Dialysis and Hemodialysis in Pregnancy

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*Management of women who require dialysis during pregnancy is an unusual and challenging clinical problem for both the nephrologist and the obstetrician. More than 200 pregnancies have been reported in women requiring hemodialysis, and more than 50 pregnancies in women on peritoneal dialysis. Surveys from several countries of pregnancy in dialysis patients provide data regarding management and outcomes. Conception rates are significantly lower in women on dialysis, and when these women do become pregnant, the spontaneous abortion rate usually exceeds 40%. However, in the pregnancies that continue, as many as 71% result in surviving infants.*

*Pregnant women require longer, more intense hemodialysis, and enough experience has been reported to support the use of peritoneal dialysis as well as hemodialysis during pregnancy. The patients typically experience anemia, hypertension, and premature delivery. Most infants are small for gestational age, and the stillbirth rate is as high as 12%. While the potential problems are many, sufficient data has been accumulated to provide clinicians with guidelines to help them manage pregnant women on dialysis and to achieve successful outcomes.*

*(Hemodial Int., Vol. 5, 97–101, 2001)*

### Key words

Pregnancy, peritoneal dialysis

### Introduction

Management of women requiring dialysis during pregnancy is a challenging clinical problem that necessitates close cooperation between the obstetrician and the nephrologist. A patient may require dialysis during a pregnancy for several reasons. First, the women may have an underlying renal disease that progresses during pregnancy. In other cases, acute renal failure develops *de novo*, requiring dialysis during pregnancy. Finally, there are women who have end-stage renal disease and who subsequently become pregnant. In conditions where fetal wastage has already occurred, dialysis management proceeds in a manner and with indications no different than those for patients in the non pregnant condition. This discussion reviews experience with dialysis in preg-

nant patients who require either peritoneal dialysis or hemodialysis.

### Dialysis and pregnancy

Hemodialysis was first used in pregnancy in 1961 for managing acute renal failure in a woman with acute phenytoin poisoning [1]. Other cases of acute renal failure requiring dialysis during pregnancy have subsequently been reported [2]. In such cases, dialysis is mandatory to prevent maternal morbidity or mortality. The goal of dialysis therapy in these patients is not only to prevent maternal complications, but also to allow gestation to proceed long enough for successful delivery. Fetal well-being is, therefore, an essential consideration when dialysis is necessary during pregnancy.

Pregnancy in dialysis patients is unusual. The first successful pregnancy of a woman with end-stage renal disease was reported in 1971 by Confortini *et al.* [3]. Since that time, several hundred cases have been reported of successful deliveries in pregnancies complicated by development of renal failure requiring dialysis, or in pregnancies in which the woman conceived while on dialysis [2,4].

### Conception in end-stage renal disease patients

The incidence of conception in end-stage renal disease patients is difficult to determine; however, several large series have reported results in unsuccessful and successful pregnancies [5–14]. In a large review reported from the Registry of the European Dialysis and Transplant Association (EDTA), the conception rate was 0.9%, significantly below that of women in the general population [5]. In dialysis units in Saudi Arabia, the conception rate was 7% [8]. A survey by Hou [9] of 206 American dialysis units in 1990 and 1991 identified 60 pregnancies before and during the survey period in a population that included 1281 women between the ages of 18 years and 44 years. Among these women of childbearing age, 1.5% became pregnant on dialysis during the time period of the survey. Similarly, a survey by Bagon *et al.* [10] from Belgium reported on pregnancies occurring in 1% of the childbearing dialysis-patient population. In the United States, the registry of pregnancy in dialysis patients reported that, of 6230 women of childbearing age, 2.4% of hemodialysis patients and 1.1% of peritoneal dialysis patients became pregnant [12].

Conception rates are, therefore, very low in women on dialysis. Reductions in fertility are related to hormonal factors that result in either amenorrhea or anovulatory menstrual cycles and diminished libido, possibly related to elevated prolactin levels and inadequate erythropoietin production

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[14–16]. Despite significant reductions in fertility, women of childbearing age on dialysis must be told that conception may still occur, and that contraception, preferably using a barrier method, should be employed to prevent unwanted pregnancy.

Once pregnancy occurs in a woman with chronic renal disease or end-stage renal disease, it must be decided whether continuation of the pregnancy may jeopardize maternal survival or cause irreversible renal impairment. This decision may be out of the question for women who would consider a therapeutic abortion objectionable. Although no absolute prediction of outcome is possible, advice can be offered based on an understanding of the general outcomes of pregnancy in women requiring dialysis.

#### Outcomes of pregnancy during dialysis

Initial reports of experience with dialysis during pregnancy came from either case reports or small series of patients. More recent reviews have focused on surveys of existing populations and have included women on both hemodialysis and peritoneal dialysis [5–14]. Table I presents some of these data. Most of the surveys included all patients who required dialysis during pregnancy. Distinguishing between women who conceived before starting dialysis, and those who conceived while on either hemodialysis or peritoneal dialysis is therefore important. Also, several of the series report data only from pregnancies that continued after the first trimester; others were true surveys and provide data regarding both spontaneous and therapeutic abortion rates.

In 1980, the Registry of the EDTA reported on 115 pregnancies in women on dialysis from 1986 to 1978 [5]. The registry recorded 45 therapeutic and 54 spontaneous abortions, and 16 live births; 12 women conceived while on dialysis. Roxe and Parker [6] in 1984 reported the results of their survey of 43 pregnancies in 35 women, all of whom conceived on dialysis. Eleven women underwent therapeutic abortions, and 4 spontaneous abortions occurred. Of the

26 pregnancies that continued, only 6 resulted in live births, including one set of twins, for a birth rate of 14%.

In 1988, Redrow *et al.* [7] reported outcomes of 14 pregnancies in 13 women; 9 of these women had conceived while on dialysis—6 on peritoneal dialysis and 3 on hemodialysis. In this group of patients, there were 4 spontaneous abortions and no therapeutic abortions. Ten live births resulted, including one set of twins.

In a survey of dialysis units in Saudi Arabia, Souqiyeh *et al.* [8] identified 27 pregnancies, all of which were conceived on dialysis. There were 11 spontaneous abortions and no therapeutic abortions. Although 50% of the women delivered live infants, only 30% of the infants survived.

Bagon [10] reported 5 pregnancies and surveyed experience with pregnancy in dialysis units in Belgium from 1976 to 1996. In 1472 women of childbearing age, 15 cases of pregnancy lasting beyond the first trimester (1%) were seen. Pregnancy was successful in 50% of cases on hemodialysis and 80% of cases on peritoneal dialysis. Of the 10 pregnancies conceived on dialysis, 5 proceeded to live births.

Romao *et al.* [11] reviewed the experience of 17 pregnancies in women dialyzed at one hospital in Brazil. Of these pregnancies, 12 were conceived on dialysis: 1 on peritoneal dialysis, and 11 on hemodialysis. Two patients experienced spontaneous abortions, and one fetus died 3 days after delivery. All the other infants (75%) survived.

In 1998, Okundaye *et al.* [12] reported the results of a 1992 survey of U.S. dialysis units collecting data from 48% of the women of childbearing age on dialysis. In this registry, 344 pregnancies in 318 women were reported; outcomes were available for 320 pregnancies. Of the 344 reported pregnancies, 209 occurred after initiation of dialysis and 58 before initiation, with the conception time unknown in 77 women. Between 1992 and 1995, 135 pregnancies occurred in women on hemodialysis and 18 in women on peritoneal dialysis. Fetal survival was 39.5% for women on hemodialysis and 37% for

TABLE I Reports of pregnancy in existing dialysis populations (hemodialysis and peritoneal dialysis).

Reference	Pregnancies reported on dialysis (n)	Conceptions		Therapeutic abortions (% of conceptions on dialysis)	Spontaneous abortions (% of conceptions on dialysis)	Infant survival	
		Before dialysis (n)	On dialysis [n (%)]			(% of conceptions before dialysis)	(% of conceptions on dialysis)
EDTA, 1980 [5]	115	4 <sup>a</sup>	12 <sup>a</sup>	39% <sup>b</sup>	47% <sup>b</sup>	Unable to calculate	Unable to calculate
Roxe and Parker, 1984 [6]	43	0	43 (100%)	26%	9%		14%
Redrow <i>et al.</i> , 1988 [7]	14	5	9 (64%)	0	21%	100%	56%
Souqiyeh <i>et al.</i> , 1992 [8]	27	0	27 (100%)	0	41%		30%
Bagon <i>et al.</i> , 1998 [10]	15	5	10 (67%)	Not reported	Not reported	80%	50%
Romao <i>et al.</i> , 1998 [11]	17	5	12 (71%)	0	17%	60%	75%
Okundaye <i>et al.</i> , 1998 [12]	344	58 <sup>c</sup>	209 <sup>c</sup>	2.1%	25% 1st trimester 16.5% 2nd trimester (Unknown in 77 women)	74%	40%
Toma <i>et al.</i> , 1999 [13]	74	0	74 (100%)	19%	12%		49%

<sup>a</sup> Only successful pregnancies reported.

<sup>b</sup> Relationship of conception to dialysis not reported.

<sup>c</sup> Unknown in 77 women.

women on peritoneal dialysis. The first-trimester spontaneous abortion rate was 22.8% in both groups of patients, with second-trimester spontaneous abortion rates of 13.4% and 22.8% for women on hemodialysis and peritoneal dialysis respectively. Only 54% of pregnancies that reached the second trimester had a successful outcome.

In Toma's 1999 survey of Japanese dialysis units [13], enough data was reported in 74 pregnancies, all conceived on dialysis, to determine that 48.6% resulted in a surviving infant, 12.2% ended in spontaneous abortion, and 18.9% ended in elective abortion. The neonatal death rate was 12.2%. In one of the centers included in Toma's series, 15 of the dialysis patients who became pregnant reported fetal survival of 73.3% [14]. At this center, fetal survival was associated with pregnancy within the first 6 years of renal failure, with urine production, with a gestational age of at least 33 weeks, and with a birth weight greater than 1780 g. In most reports, fetal survival appears to be higher for women who conceive before starting dialysis, suggesting that residual renal function may be one important factor in predicting a successful outcome for women requiring dialysis during pregnancy.

#### *Managing pregnant patients on dialysis*

The cumulative experience of these reported pregnancies in women on dialysis serves as a guide to physicians involved in managing such cases. The greatest risk is clearly to the fetus, though Okundaye [12] reported two deaths attributed to pregnancy in women on dialysis. Management of pregnancy in dialysis patients is, therefore, aimed at providing a milieu that will support fetal well-being until delivery.

In acute renal failure or rapidly progressive chronic renal failure, the major therapeutic decision is when to initiate dialysis. Fetal survival and gestational age may be improved with lower serum creatinine and blood urea nitrogen (BUN) [4]; therefore, to maintain fetal well-being, it has been recommended that dialysis therapy in pregnant women be initiated earlier than in non pregnant women [17]. Absolute values have not been established, but the range of serum creatinine levels at which dialysis should be considered in pregnancy is 3.5 – 5.0 mg/dL or at glomerular filtration rates below 20 mL/min [4,17]. In women already on dialysis, treatment regimens should be intensified to minimize interdialytic weight gain and to limit fetal exposure to high levels of BUN or other waste products. Several of the surveys reported better outcomes in terms of survival or gestational age, or both, with longer dialysis [4,8,10–12]. Okundaye's data [12] showed a trend toward better survival and decreased prematurity when dialysis was increased to 20 hours per week. Most nephrologists who manage pregnant women on dialysis will therefore increase dialysis time, but the ideal quantity of dialysis that should be delivered is unknown. Bagon reported weekly  $Kt/V_{\text{urea}}$  values of between 6 and 8 in 3 patients in whom that parameter was measured [10].

It has been suggested that potassium, calcium and bicarbonate may require adjustments in the dialysis bath and that

heparin can be used at low doses. Values for these parameters should be monitored closely in pregnant patients so that treatment can be individualized. In making the adjustments, it is important to remember that serum bicarbonate will fall by 4 – 6 mmol/L because of respiratory acidosis. Acetate and bicarbonate baths have both been used; sodium and glucose should be maintained in the bath at levels sufficient to prevent rapid changes in the fetal environment. No differences have been reported between biocompatible and standard cuprophane hemodialysis membranes.

It has been recognized that women on peritoneal dialysis may successfully conceive and be managed with this dialysis modality. The first sustained pregnancy in peritoneal dialysis was reported in 1983, when Cattran and Benzie [18] described a pregnancy in a woman who conceived after 2.5 years on continuous ambulatory peritoneal dialysis. At 30 weeks, the patient experienced spontaneous labor with delivery of a still-born infant. Since that time, more than 50 successful pregnancies have been described in women who were initiated on peritoneal dialysis when advanced azotemia developed or who were already on maintenance peritoneal dialysis when they conceived [2,4,7,9,10–12]. In these patients, fetal survival has been reported to be 63% – 80%, suggesting that peritoneal dialysis is another appropriate treatment modality for women who require dialysis during pregnancy.

In patients who develop advanced renal failure during pregnancy, the placement of a peritoneal dialysis catheter is technically feasible, although catheter leakage and complete non function have been reported. Most patients are able to tolerate exchanges of at least 1500 mL. As pregnancy proceeds, it may be necessary to reduce the volume and to increase the exchange rate. Redrow *et al.* [7] were able to demonstrate that the peritoneal membrane retains both clearance and ultrafiltration capabilities in pregnancy.

Peritoneal dialysis offers a number of potential advantages in the management of pregnant patients. It may minimize significant shifts in fluid and electrolytes, reduce the risk of hypotension, more effectively control hypertension, and eliminate the need for systemic heparin. Intraperitoneal insulin can also be used to maximize glucose control in the diabetic patient. Hemoperitoneum may serve as the initial indication of placental abruption. Finally, it has been shown that intraperitoneal magnesium administration can be used to inhibit premature labor, though its use in renal failure requires meticulous monitoring.

Peritonitis is always a risk in peritoneal dialysis, and several cases have been reported in pregnant women. Though at least 1 patient experienced a stillbirth several months later, other reports suggest that peritonitis can be treated successfully during pregnancy [7,12].

Several problems occur frequently in these pregnancies, regardless of dialysis modality. Anemia is present in almost all of the patients and worsens during pregnancy. Erythropoietin has now been safely used in many pregnant patients. It has reduced the need for blood transfusions, though the re-

sponse to it appears blunted, and higher doses are usually required [9,19]. Erythropoietin does not appear to cross the placenta; erythrocytosis in the fetus has not been a problem. No adverse effects to the fetus have been reported in any erythropoietin-treated pregnancies, and improvement in survival has been seen with its use. Erythropoietin should, therefore, be used during pregnancy, though meticulous care must be employed in maintaining adequate iron supplies.

Hypertension should also be anticipated when women with renal disease become pregnant. Hypertension, including malignant hypertension, has been reported to complicate 49% – 100% of pregnancies of women on dialysis [2,11]. Treatment of hypertension in these patients should follow previously established guidelines with methyldopa, beta blockers, and labetalol as the initial agents of choice. Angiotensin converting enzyme inhibitors and diuretics should be avoided, as should magnesium infusion.

Another important problem that occurs with increased frequency in pregnant patients is maternal sensitization to antigens, which may limit access to kidneys for transplantation. Changes in calcium and phosphorus metabolism may also be aggravated by pregnancy. While no established guidelines exist for the use of calcium or vitamin D supplementation during pregnancy, it would seem prudent to administer sufficient calcium and vitamin D<sub>3</sub> supplementation to ensure that patients remain in positive calcium balance throughout their pregnancies. Adequate protein intake is also essential, particularly for women on peritoneal dialysis. Likewise, women should receive supplemental water-soluble vitamins, including folic acid.

Premature delivery occurs in most of these pregnancies and may be precipitated by fetal distress, *abruptio placentae*, severe maternal hypertension, or premature rupture of membranes. Whether dialysis itself contributes directly to premature labor is unclear. Some success has been reported with the use of indomethacin to treat premature labor in these women [19].

Fetal growth retardation commonly occurs. Another potential problem is an osmotic diuresis in the fetus, because the neonatal levels of urea nitrogen and creatinine may be similar to those of the mother. Despite the azotemic milieu, few if any fetal consequences have been attributed to the environment. Most reviews reported no increase in congenital anomalies, but 11 anomalies were reported in Okundaye's survey [12]. High rates of *abruptio placentae* and polyhydramnios have also been reported [11,12,20].

Fetal wastage, however, has been the most significant problem. The true incidence of fetal wastage in pregnant women on dialysis is unknown, because early spontaneous abortion may be overlooked. The spontaneous abortion rate is approximately 50%; but, in pregnancies that continue, overall fetal survival ranges from 19% to 75% [2]. The latter figure was reported in a group of patients managed primarily with hemodialysis 6 days per week at one hospital in Brazil [11]. Overall, however, the live birth rate has improved as

experience in the management of the pregnant dialysis patient grows.

Care of pregnant dialysis patients must emphasize a comprehensive and coordinated approach between the obstetrician and the nephrologist. Appropriate pediatric care must also be available for the neonate. All of these women must be followed in high-risk obstetric clinics, with appropriately trained maternal–fetal specialists and provision of meticulous prenatal care. As patients approach term, frequent non-stress testing and biophysical profiles are necessary. When patients begin labor spontaneously, vaginal delivery should be attempted. Though many of the pregnancies reported have been delivered by Cesarean section, more recent reports suggest indications for this mode of delivery should be the same as are applied to women not on dialysis.

Of equal concern is the emotional stress that pregnancy creates for the dialysis patients and their families. These women undergo more frequent prenatal evaluations, risk significant hypertension and anemia, and have to be prepared to accept a significant risk of an unsuccessful pregnancy. These women also have a less-than-average life expectancy; their ability to raise their children may be impaired by the demands of their dialysis schedules. All of these issues must be considered and discussed with the patient.

## Conclusion

Current methods of dialysis and obstetric management can provide an opportunity for successful outcome in a dialysis patient who becomes pregnant.

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