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Pregnancy in Patients with End-Stage Kidney Disease

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Abstract

Introduction. Pregnancy in patients with end-stage renal disease (ESRD) is rare but possible. Fertility may be affected by both hormonal and non-hormonal factors. However, after kidney transplantation, reproductive function often improves, and many women resume regular menstrual cycles. Despite the potential for complications, successful pregnancies can occur in these patients with careful, multidisciplinary management.

Methods. A study conducted at the University Hospital Centre Zagreb from 1988 to 2024 analysed 15 pregnancies among 12 women aged 25 to 43 years. Of these pregnancies, two occurred while the patients were on hemodialysis, one during continuous ambulatory peritoneal dialysis, and 12 after kidney transplantation. Transplant recipients were treated with immunosuppressive medications such as cyclosporine combined with azathioprine and prednisone, or tacrolimus combined with azathioprine and prednisone.

Results. Eleven pregnancies resulted in deliveries via cesarean section, while four were delivered vaginally. There were four miscarriages. Five pregnancies were preterm, with deliveries occurring between 31 and 36 weeks of gestation. Six children were born with low birth weight (less than 2500 grams), although only three of these were preterm.

Obstetric complications included umbilical cord issues in four deliveries. Three newborns experienced complications: one had a Bochdalek hernia, another was suspected of having necrotizing enterocolitis, and one suffered from asphyxia and sepsis, requiring successful resuscitation. Maternal complications were rare, with one patient experiencing elevated blood pressure and another suffering from a urinary tract infection.

Conclusion. In conclusion, while pregnancy in patients with ESRD on dialysis or after kidney transplantation carries significant risks, it is not impossible. Advances in dialysis and immunosuppressive therapy have improved outcomes for both mothers and their children. A multidisciplinary approach is essential to provide the best possible care and outcomes for these high-risk pregnancies.

Keywords: pregnancy, dialysis, kidney transplantation, chronic kidney disease

Introduction

Fertility in women with chronic kidney disease (CKD) is generally reduced, although the exact cause is not fully understood. Studies show that several factors may be responsible for this condition, including dysfunction at the hypothalamic-pituitary-ovarian axis, sexual dysfunction, oxidative stress, and effects of certain medications [1]. One of the key indicators of fertility in women with CKD is a lower level of Anti-Müllerian Hormone (AMH), regardless of the stage of the disease, which indicates a reduced ovarian reserve [2]. In addition to the decreased AMH levels, these patients also have a reduced number of antral follicles, as determined by transvaginal ultrasound. Although they have elevated estradiol levels, FSH levels and ovarian volume are similar to those in women without CKD [3]. As glomerular filtration rate (GFR) decreases, the frequency of oligomenorrhea increases, and at GFR values below 4 ml/min, amenorrhea may occur [4]. Elevated prolactin levels, common in women with CKD, may affect the pulsatile secretion of hypothalamic gonadotropins, leading to anovulation and irregular menstrual cycles [5]. Hyperprolactinemia is caused by decreased prolactin clearance and increased secretion from the pituitary due to insufficient dopaminergic inhibition [6]. When evaluating female sexual function indices, which assess sexual desire, arousal, lubrication, orgasm, and pain/discomfort, women with CKD scored lower than controls, indicating sexual dysfunction [7]. Sexual dysfunction even worsens when patients begin dialysis [4].

Fertility in women with CKD who are on hemodialysis may be influenced by several factors. In women with CKD on hemodialysis who have regular menstrual cycles, Anti-Müllerian Hormone levels are not significantly different from those of women without CKD who also have regular menstrual cycles [8]. However, AMH levels are significantly lower in CKD patients on hemodialysis who have irregular menstrual cycles [8]. Overall, there is no significant difference in AMH le-

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vels between women on hemodialysis and those without CKD. When examining hormone levels in premenopausal women on hemodialysis, they are mostly similar to those in healthy women, except for elevated LH. Although normal estradiol levels are described during the follicular phase of the menstrual cycle, these levels do not reach the peak necessary for ovulation, and thus the LH surge does not occur, causing anovulation. Also, patients on hemodialysis with amenorrhea have lower estradiol levels, which further indicates ovarian dysfunction. If a woman had oligomenorrhea or amenorrhea before starting dialysis, it is very likely that these problems will persist after dialysis begins [4]. Elevated prolactin levels are common in women with CKD on hemodialysis. Although prolactin is significantly higher than in healthy women, no clear correlation has been found between prolactin levels and gonadotropins [9]. One reason for elevated prolactin is the decreased prolactin clearance [10].

Kidney transplantation can have a significant impact on the fertility in women. Although prolactin levels usually normalize after transplantation, the same does not fully apply to sex hormones. Estrogen and FSH levels are higher in transplanted women than in healthy women [11]. Conversely, some studies report no significant differences in estradiol and FSH levels in women before and after transplantation, with values comparable to those in healthy women [12]. Unlike estrogen and FSH concentrations, progesterone and LH levels are lower in transplanted women. The differences in hormone concentrations even after transplantation suggest that there is no complete recovery of the menstrual cycle [11]. This is also influenced by the fact that women after kidney transplantation have been found to have reduced AMH levels compared to the healthy population [8]. In more than half of the women who had dysfunctional menstrual cycles, the cycle stabilized after transplantation [4,13]. Although pregnancy in women with a transplanted kidney is four times more common than in those on dialysis, it is still ten times less frequent than in the healthy women [6]. This cluster of hormonal changes and cycle alterations indicates that kidney transplantation may have a positive effect on fertility, but ovarian function may still differ from that of healthy women.

Material and methods

This retrospective study was conducted as part of the project "Complications after Kidney Transplantation and Immunosuppressive Therapy". The study was approved by the Ethics Committee under number 02/21 AG. Data were collected by searching the database of the Department of Nephrology, Arterial Hypertension, Dialysis, and Transplantation at the Clinical Hospital Center Zagreb for the period from 1988 to 2024.

The main objective was to examine the course and outcomes of pregnancies in patients with CKD who are on dialysis or have undergone transplantation, and to assess the frequency and types of complications in mothers and newborns.

Initially, 14 patients with CKD who had documented pregnancies during this period, either while on dialysis treatment or after kidney transplantation, were included. Two patients were excluded from the analysis due to insufficient data following death (it was recorded that one of them had two deliveries after transplantation, and the other had one delivery during hemodialysis treatment), resulting in a final analysis cohort of 12 patients.

The following data were collected: underlying kidney disease, duration and type of dialysis (hemodialysis or peritoneal dialysis), time of kidney transplantation and type of donor (cadaveric or living), immunosuppressive therapy used, number of pregnancies per patient, pregnancy outcomes (delivery or miscarriage), patient age at delivery, gestational age at delivery, mode of delivery (vaginal or cesarean section), APGAR score, newborn's birth weight and length, obstetric complications, neonatal complications, and maternal complications during or after pregnancy. Renal function of the patients was also monitored during and after the pregnancy. In all subjects, renal function remained stable throughout and after pregnancy, without significant deterioration in GFR or increase in proteinuria.

Results

This study included 12 patients treated at the Clinical Hospital Center Zagreb from 1988 to 2024.

Out of a total of 15 analysed pregnancies, 12 occurred after kidney transplantation, while 3 were recorded during dialysis treatment (2 on hemodialysis and 1 on peritoneal dialysis). This aligns with findings from previous studies that show a higher frequency and better pregnancy outcomes after transplantation, which is attributed to the stabilization of hormonal status and the recovery of the ovulatory cycle following kidney transplantation.

All pregnant women with transplanted kidneys were on immunosuppressive therapy. The most commonly used combinations were cyclosporine + azathioprine + corticosteroids, and tacrolimus + azathioprine + prednisone. One patient used tacrolimus and everolimus. Despite the known teratogenic potential of some of these drugs, no increase in the number of congenital malformations related to the therapy was observed in this sample. One case of diaphragmatic hernia was recorded, but it cannot be directly associated or considered as a consequence of the therapy.

Out of 15 pregnancies, 11 were delivered by cesarean section, while 4 births were vaginal.

Five pregnancies were preterm (between the 31st and 36th week), confirming the presence of a high risk for premature birth.
Six newborns had low birth weight (<2500g) but only three of them were born prematurely, indicating that low birth weight is not necessarily related to the gestational age but also to the specifics of kidney disease and therapy.
Most newborns had satisfactory APGAR scores and a favourable postnatal course. The most serious neonatal complications included asphyxia, sepsis, and congenital diaphragmatic hernia, but all were successfully medically managed. Four deliveries were complicated by the umbilical cord being wrapped around the newborn's neck, but without lasting consequences.

Patient 1
Born in 1965, she suffered from mesangioproliferative glomerulonephritis. In 1990, she started hemodialysis treatment lasting 10 months, after which she was transplanted in 1991. The kidney donor was her mother. The patient had two pregnancies, both after the transplantation. The first delivery occurred at age 30, and the second at age 40. Both deliveries were vaginal. The first delivery was at 40 weeks gestation. The male newborn weighed 3110 grams, measured 51 cm, with an APGAR score of 10. Pregnancy and delivery were without complications. The second pregnancy ended at 39 weeks with an induced vaginal delivery. The female newborn weighed 1910 grams, measured 48 cm, with an APGAR score of 7. The infant was classified as having low birth weight and was diagnosed with congenital diaphragmatic hernia, which was surgically treated the following day. Postoperative recovery was uneventful, and further development was without complications. During both pregnancies, the patient was on standard triple immunosuppressive therapy including cyclosporine, azathioprine, and methylprednisolone.

Patient 2
Born in 1965, she suffered from chronic glomerulonephritis with symptoms appearing at age 16. From 2003, she was treated with continuous ambulatory peritoneal dialysis for ten years until kidney transplantation in 2013 from a deceased donor. She had three pregnancies. The first two deliveries occurred before dialysis and transplantation and were excluded from analysis. The third delivery occurred in 2008 during peritoneal dialysis. The pregnancy was completed vaginally at 41 weeks gestation. The female newborn weighed 2200 grams, measured 46 cm, with an APGAR score of 10. Although classified as having low birth weight, no other complications were noted. Since the patient was not transplanted at the time, she was not on immunosuppressive therapy.

Patient 3
Born in 1975, she had chronic glomerulonephritis. She was on hemodialysis for three years (2001-2004) before receiving a kidney from a deceased donor. She had one pregnancy at age 34. Due to pathological cardiotocography, delivery was performed by emergency cesarean section at 35 weeks gestation. The female newborn weighed 2470 grams, measured 47 cm, and had an APGAR score of 10. The infant was classified as having low birth weight and was diagnosed with necrotizing enterocolitis but without further complications. The patient received immunosuppressive therapy including cyclosporine, azathioprine, and prednisone during pregnancy.

Patient 4
Born in 1975, she had Goodpasture's syndrome at age 13, subsequently developing CKD. She was on hemodialysis from 1998 to 2003, with one failed transplant attempt in 2002, followed by successful transplantation in 2003. She had two pregnancies, both completed by cesarean section. The first pregnancy ended in 2010 at 37 weeks gestation. The male newborn weighed 3260 grams, measured 47 cm, with an APGAR score of 5 at first minute. Asphyxia and sepsis were noted, requiring resuscitation which was successful. The second pregnancy ended in 2012 at 36 weeks. The female newborn weighed 3130 grams, measured 49 cm, with an APGAR score of 10 and no complications. Immunosuppressive therapy during both pregnancies included tacrolimus, azathioprine, and prednisone.

Patient 5
Born in 1977, she was on hemodialysis from 2001 to 2006, when transplantation was performed. She had three pregnancies; the first two occurred before dialysis and transplantation and were excluded from analysis. The third pregnancy occurred during hemodialysis in 2002. Delivery was by cesarean section at 34 weeks gestation. The male newborn weighed 2100 grams, measured 41 cm, with an APGAR score of 8. Other than low birth weight, no additional complications were noted. The patient was not on immunosuppressive therapy during the pregnancy.

Patient 6
Born in 1979, she suffered from chronic pyelonephritis. She was on hemodialysis from 2003 to 2009, when she received a kidney from a deceased donor. She had three pregnancies-two ended in spontaneous miscarriages, and one was delivered by cesarean section at 31 weeks during hemodialysis at age 29. The female newborn weighed 1980 grams and was classified as having a low birth weight. The umbilical cord was wrapped around the newborn's neck. No other compli-

cations were noted. The patient was not on immunosuppressive therapy at the time of pregnancy.

Patient 7
Born in 1981, she was on hemodialysis for two years before receiving a kidney from a deceased donor in 2002. She had one pregnancy, completed by cesarean section at 39 weeks gestation at age 37. The male newborn weighed 3450 grams, measured 48 cm, with an APGAR score of 10. The patient developed an urinary tract infection after delivery. Immunosuppressive therapy included cyclosporine, azathioprine, and prednisone.

Patient 8
Born in 1982, she suffered from lupus nephritis. She was on peritoneal dialysis for two and a half years before receiving a kidney from a deceased donor in 2007. She had one pregnancy completed by cesarean section at 38 weeks gestation in 2013. The male newborn weighed 2470 grams, measured 46 cm, with an APGAR score of 10. The infant was classified as having a low birth weight without additional complications. Immunosuppressive therapy included cyclosporine, azathioprine, and prednisone.

Patient 9
Born in 1989, she had fibrotic kidney changes and was on hemodialysis from 2016 for one and a half years. Kidney transplantation from a deceased donor was performed in 2017. She had one pregnancy, delivered vaginally at 35 weeks gestation at age 30. The female newborn weighed 2520 grams, measured 46 cm, with an APGAR score of 10. At delivery, the umbilical cord was wrapped around the baby's neck. No other complications were observed. Immunosuppressive therapy during pregnancy included tacrolimus, azathioprine, and prednisone.

Patient 10
Born in 1990, she suffered from juvenile nephronophthisis. She was not on dialysis before transplantation, which was performed in 2016 with a kidney from a deceased donor. She had two pregnancies. The first delivery occurred at 30 years of age at 37 weeks gestation. The delivery began vaginally but was completed by cesarean section due to a pathological cardiotocography. The female newborn weighed 3530 grams, measured 51 cm, and had an APGAR score of 7 at the first minute. The umbilical cord was wrapped around the newborn's neck and oxygen support was required immediately after birth. The second delivery occurred at 39 weeks gestation at age 32, also completed by cesarean section. The female newborn weighed 3200 grams, measured 50 cm, with an APGAR score of 10. Umbilical cord wrapped around the neck was again noted without other complications. The patient received immunosuppressive therapy (tacrolimus, azathioprine, prednisone) during both pregnancies.

Patient 11
Born in 1990, she was on peritoneal dialysis for two years before kidney transplantation from a deceased donor in 2017. She had three pregnancies-two ended in spontaneous miscarriages, and one resulted in delivery by cesarean section at 37 weeks gestation at age 30. The female newborn weighed 2500 grams, measured 48 cm, with an APGAR score of 10. No complications were recorded in the mother or child. Immunosuppressive therapy included tacrolimus, azathioprine, and prednisone.

Patient 12
Born in 1993, she was on hemodialysis for one year before transplantation in 2015 with a kidney from a deceased donor. She had one pregnancy completed by cesarean section at 39 weeks gestation at age 29. The female newborn weighed 2800 grams, measured 47 cm, with an APGAR score of 10. Pregnancy and delivery were uneventful. Immunosuppressive therapy during pregnancy included tacrolimus and everolimus.

Discussion

Pregnancy in women with CKD, especially those on dialysis or after kidney transplantation, represents a significant clinical challenge due to numerous associated complications for both, the mother and child.
This study analysed pregnancies in women with CKD, divided into two groups: those who were on dialysis during pregnancy and those who conceived after kidney transplantation. The results were compared with data from the available literature.
In the transplanted patient group, 14 pregnancies were recorded, of which two (14.3%) ended in spontaneous miscarriage. This frequency is very similar to other studies reporting a miscarriage rate of 12.5%. The average maternal age at delivery was 32.9 years, slightly higher compared to the literature average of 30.3 years [14]. The average time from transplantation to conception was 6.9 years, somewhat longer than the previously reported 5.6 years.
Cesarean section was the most common mode of delivery, performed in 75% of cases, consistent with previous studies reporting a cesarean rate of 68.7%. The average birth weight of newborns in our sample was 2862.5 grams, with an average gestational age of 37.6 weeks, which is considerably more favourable than other studies reporting lower averages, weight 2387.7 g and gestational age 34.3 weeks. Furthermore, preterm deliveries in our sample accounted for 25% of all births, significantly lower than 45.3% reported in previous analyses [14].

Regarding maternal complications, a single case of hypertension (8.3%) was recorded in our group, whereas literature reports such complications in 24.3% of pregnancies. No cases of preeclampsia or gestational diabetes were observed, unlike previous data indicating their prevalence at 20.9% and 5.1%, respectively [14].
In the group of patients who conceived during dialysis treatment, a total of five pregnancies were recorded, of which two (40%) ended in spontaneous miscarriage. This frequency falls within previously reported ranges of 16.9% to 51.7% [15-17]. The average maternal age at delivery was 32.3 years, consistent with earlier studies reporting ages of 34.6 [16]and 35.4 [15] years. Duration of dialysis before pregnancy in our sample was 3.7 years, a way shorter compared to the average of 6 to 8.4 years reported in other studies [15,16].
Of all deliveries, 66.7% were completed by cesarean section, aligning with literature data showing rates between 71.4% and 73.1%. The average birth weight in our study was 2093 grams, slightly higher than those recorded in previous studies (1853 g and 1966 g) [15,16]. All three newborns had low birth weight, accounting for 100%, whereas previous studies reported low birth weight in 78.6% of cases [16].
The average gestational age at delivery in our sample was 35.3 weeks, higher than the averages reported in previous studies (32-33.7 weeks) [15,16]. The proportion of preterm births (66.7%) was lower compared to earlier research where preterm births accounted for 82.8% [17].
In our study, no maternal complications were recorded during pregnancy or postpartum in the dialysis group. In contrast, previous studies reported preeclampsia in 11.9% of cases, gestational hypertension in 7.7%, and anemia in 3.9% of pregnant women treated with dialysis [17].

Conclusion

This study confirms that pregnancy in women with CKD, including those on dialysis and after kidney transplantation, although rare and with a high-risk, can result in favourable outcomes with appropriate medical supervision.
The results showed that the most common complications included preterm birth and low birth weight; however, most infants had satisfactory APGAR scores and good postnatal outcomes. Despite the use of immunosuppressive therapy, a low number of congenital malformations were observed, indicating that safe pregnancy under such therapy is possible with an appropriate drug selection.
Kidney function remained stable in all transplanted patients during and after pregnancy, confirming that carefully planned and monitored pregnancy does not necessarily negatively affect the graft function. At the same time, although less common, successful pregnancies were also recorded in women on dialysis, highlighting the importance of an individualized and multidisciplinary approach to treatment.
In conclusion, with careful planning, adequate therapy adjustment, and continuous collaboration among nephrologists, gynecologists, and neonatologists, pregnancy in women with CKD-whether on dialysis or post-transplantation-is not only possible, but can also have a favourable outcome for both mother and child.

Conflict of interest statement. None declared.

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