Reproduction in Women with End-Stage Renal Disease and Effect of Kidney Transplantation

Shirin Ghazizadeh,[1] Mahboob Lessan-Pezeshki[2]

[1]Department of Obstetrics and Gynecology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Nephrology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

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Menstrual problem is common among women with chronic kidney disease, and patients with end-stage renal disease usually have amenorrhea. The rate of pregnancy in women on dialysis is low. Fetal survival in this population has improved, with half of such pregnancies resulting in delivery of a live infant. However, prematurity remains common and accounts for the low-birth weight of these infants. Intensifying hemodialysis by increasing the frequency of treatments is associated with longer gestation and increased likelihood of a successful pregnancy. Intense hemodialysis also improves the control of maternal intravascular volume and reduces the risk of hypotension due to excessive ultrafiltration.
Women with chronic kidney disease tend to experience decreased libido and reduced ability to reach orgasm. Sexual difficulties in uremic patients are often worsened by hemodialysis, with a lowered frequency of intercourse, reduced sexual desire, and an increased incidence of sexual failure. There have been ongoing improvements in survival and quality of life after kidney transplantation. In most patients, sexual desire increases significantly after successful transplantation; however, improvement in the frequency of sexual activity and the overall sexual satisfaction is not as high as that in sexual desire. These have been accompanied by an improvement in reproductive function. Pregnancy success rate exceeds 90% after the first trimester in women with kidney transplant. Contraceptive counseling should be provided before transplantation, because ovulatory cycles may begin within 1 to 2 months after transplantation in women with functioning grafts. Breastfeeding is discouraged for patients taking any immunosuppressive drugs.

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INTRODUCTION

The purpose of this review was to examine the impact of end-stage renal disease (ESRD) on the reproductive performance of women, including sexual health and fertility. We reviewed the menstrual cycle irregularities and sexual dysfunction in women with ESRD, maternal and fetal complications of pregnancy in these patients, and the role of successful kidney transplantation in restoration of reproductive health, with a focus on pregnancy outcomes and the currently suggested management strategies such as contraception counseling.

MENSTRUAL CYCLE IRREGULARITIES

Menstrual problem is common among women with chronic kidney disease (CKD). It is partly because of abnormal bleeding due to platelet dysfunction and also because of failure to ovulate or sustain adequate corpus luteum function.

Amenorrhea is common by the time the patient reaches ESRD. Menstrual cycle typically remains irregular with scanty flow after the initiation of maintenance dialysis, although normal menstruation is restored in some women.[1] In others, menorrhagia develops, sometimes leading to significant blood loss and increased transfusion requirements.

Oligo-ovulation or anovulation is the major factor for these menstrual cycle abnormalities in uremic women. Uremia is associated with hypothalamic-pituitary-gonadal dysfunction. Leptin is one of the responsible factors involving in this cycle abnormality. In general, serum leptin levels are significantly elevated in patients with kidney failure compared with age- and body mass index-matched controls.[2] Leptin appears to be one of the several factors that influence maturation of the gonadotropin-releasing hormone pulse generator. Hyperprolactinemia is common in women with CKD, due to the increased secretion and decreased metabolic clearance of prolactin.[3] Elevated serum levels of prolactin may impair the hypothalamic-pituitary function and contribute to sexual dysfunction and galactorrhea in these patients.

Although kidney transplantation greatly improves the menstrual pattern, irregular bleeding is still a major concern among women with a transplanted kidney. In a study on menstrual problems after kidney transplantation, we found normal menstruation in 49%; oligomenorrhea, hypomenorrhea, or amenorrhea in 31.2%; and hypermenorrhea in 19.8% of our 114 patients.[4]

SEXUAL DYSFUNCTION

Sexual desire or sexual drive is defined as the frequency or intensity of a person's desires to participate in sexual activity. Both organic and psychological variables contribute to this interest. Hormones can act on sexual behavior indirectly by influencing the general mood. They can influence the levels of sexual interest in a woman by their peripheral action, such as increasing genital vasocongestion, increasing sexual sensation, and enhancing sexual attractiveness by means of smell. Women with CKD are likely to experience decreased libido and reduced the ability to reach orgasm.[5] Sexual difficulties of uremic patients are often worsened by hemodialysis with a lowered frequency of intercourse, reduced sexual desire, and an increased incidence of sexual failure.[6] Initial treatment goals for uremic women with sexual dysfunction include increasing the adequacy of dialysis and correcting their anemia.[7]

Patients on dialysis who are amenorrheic may have low levels of serum estradiol; this may lead to vaginal atrophy and dryness, thereby, resulting in discomfort during intercourse. Such patients may benefit from local estrogen therapy or vaginal lubricants. Successful transplantation is clearly the most effective means to restore normal sexual desire in women with ESRD.[8] Sexual desire increases significantly after successful transplantation in most patients; however, improvement in the frequency of sexual activity and the overall sexual satisfaction is not as high as that in sexual desire. Low-dose testosterone may be effective, but due to potential toxicity, it is rarely used. Administration of bromocriptine may help restore sexual function in patients with hyperprolactinemia.[9]

PREGNANCY IN END-STAGE RENAL DISEASE

Fertility is reduced in the presence of ESRD. Conception is rare for women on dialysis and occurs at a rate of 1 in every 200 patients.[10] Pregnancy is often diagnosed late because of menstrual irregularities; thus, early spontaneous abortion may be overlooked. Diagnosis of pregnancy may be difficult in women with ESRD, particularly because serum levels of β-human chorionic gonadotropin may be increased in the absence of pregnancy.

The main risks for a fetus are death, prematurity, and growth retardation. In a review of 37 pregnancies associated with chronic dialysis, Hou found that 75% to 80% ended up with spontaneous abortion, stillbirth, or neonatal death.[11] Placental abnormalities included abruption, infarction, and microscopic areas of necrosis. No developmental abnormalities were reported and the incidence of congenital abnormalities appeared to be no greater than that for pregnancies in healthy individuals.

Hypertension is a major problem and may prove very difficult to control. Forty-nine percent of the patients reviewed by Hou became hypertensive during pregnancy.[11] An increased dose of dialysis appears to be beneficial, with reports of Kt/V values of 6 to 8 on hemodialysis, 5 to 6 day per week , with the blood urea nitrogen being maintained under 50 mg/dL or even under 45 mg/dL.[12] Ameliorating the uremic milieu can avoid polyhydramnios,

help control hypertension, and improve maternal nutrition. Increased dose of erythropoietin is required to maintain hemoglobin levels within an acceptable range (10 g/dL to 11 g/dL) and transfusions are sometimes required.[12] Metabolic acidosis and hypocalcemia should be corrected. Careful uterine and fetal monitoring during hemodialysis, such as assessment of the fetal heart rate (particularly during the last trimester), combined with measures aimed at preventing dialysis-induced hypotension, should be performed. In many cases, patients are hospitalized around week 20 of gestation for the management of blood pressure, dialysis fluid balance, nutrition, and anemia.[12]

Since 1976, chronic ambulatory peritoneal dialysis (CAPD) has been increasingly used to manage ESRD. In theory, it has several advantages over hemodialysis for the management of pregnant patients.[13] A more constant intrauterine environment without rapid shifts in fluid, solutes, and electrolytes may benefit a fetus. Redrow and colleagues compared 8 patients with pregnancy that were on CAPD with 8 managed by hemodialysis.[14] Less frequent hypotensive episodes, higher hematocrit levels, and more precise control of insulin and glucose levels were seen in patients on peritoneal dialysis. Further experience is needed to determine if CAPD is the preferred mode of dialysis in pregnancy.

PREGNANCY IN KIDNEY TRANSPLANTATION

Fertility is usually restored in women with kidney allografts and pregnancy is common, reported to occur in 12% of women at childbearing age in one study.[15] However, the recovery of fertility is less common in women who undergo transplantation close to the end of their childbearing years.[11] Pregnancy success rate exceeds 90% after the first trimester.[16] The first reported successful pregnancy was in a recipient of a kidney transplant from an identical twin sister performed in 1958.[17] Since then, there have been hundreds of successful pregnancies reported in kidney transplant recipients,[18] and during the last decade, there has been a steady increase in the number of pregnancies following kidney transplantation.[19] Pregnancy in transplant recipients provides an opportunity to investigate biological processes that may have an impact on graft outcome as well as pregnancy outcome. For example, immunologic adjustments are believed to be involved in the implantation as well as a successful acceptance of the allogenic fetuses by their mothers.

Although pregnancy can cause an increase in the glomerular filtration rate, which could theoretically lead to hyperfiltration and resultant glomerulosclerosis, the hyperfiltration of pregnancy is flow related with no concomitant increase in the intraglomerular pressure.[20] In cyclosporine-treated patients, graft dysfunction following pregnancy was seen in those with higher serum creatinine levels and lower cyclosporine doses on average prior to conception.[21] Overall, in the majority of recipients studied, pregnancy does not appear to cause excessive or irreversible problems with graft outcome if the function of transplant organ is stable prior to pregnancy.[22]

The long-term effect of pregnancy on kidney function is less clear. Conflicting results were reported in 2 small-scale studies in which matched nonpregnant controls were used: no deleterious effect on one with 15-year follow-up, and an increase in the serum creatinine concentration (0.5 mg/dL to 0.7 mg/dL) at 3 months to 12 months in the other.[15,23] The latter report also suggested that a second pregnancy might carry a greater risk, as the kidney function deteriorated in 3 out of 7 women.[23] The incidence of acute rejection is not greater than expected for nonpregnant transplant patients.[24] The incidence of acute rejection during pregnancy and 3 months after delivery varies between 9% and 14.5% in the published series.[24,25] Rejection is sometimes difficult to diagnose and an ultrasonography-guided biopsy may be helpful to identify acute pyelonephritis, recurrent glomerulonephritis, and severe preeclampsia. Renal biopsy should be performed before starting antirejection therapy, and a high-dose of steroid is the first line of treatment. It has been suggested that acute rejection during the puerperium may be due to a return to a normal immune status or to a rebound effect from the altered gestational immune responsiveness. Therefore, immunosuppression should be readjusted immediately after delivery.

Overall, contraceptive counseling should be provided before transplantation surgery, because ovulatory cycles may begin within 1 to 2 months after transplantation in women with grafts that are functioning well. It is strongly advised that every sexually active transplant recipient attend a

family-planning counseling session, ideally before transplantation. Breastfeeding is discouraged for patients taking any immunosuppressive drugs.

CONCLUSION

There have been ongoing improvements in survival and quality of life after kidney transplantation. Sexual desire increases significantly after successful transplantation in most patients. These have been accompanied by an improvement in the reproductive function. Pregnancy success rate exceeds 90% after the first trimester. Because the outcome of pregnancy in transplanted women is so different from that in women on chronic dialysis, it is advisable to treat patients with ESRD by transplantation and wait until kidney function is stable for 1 year to 2 years before undertaking a planned pregnancy. Such planned pregnancies offer to the mother and fetus the best chance of a favorable outcome.

CONFLICT OF INTEREST

None declared.

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Correspondence to:
Shirin Ghazizadeh, MD
Department of Obstetrics and Gynecology, Imam Khomeini Hospital, Tohid Sq, Tehran, Iran
Tel: +98 21 8895 5549
Fax: +98 21 6693 7766
E-mail: shirin_ghazizadeh@yahoo.com

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