
Review article

Kidney Transplant and Pregnancy

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Abstract

The prevalence of chronic kidney disease (CKD) worldwide is increasing. According to a simulation study published in the American Journal of Kidney Disease in the following 20 years the number of people with chronic kidney disease (CKD) will notably increase, and more than half of the people affected will be from 30 to 64 years of age. The number of pregnant women with various degrees of kidney dysfunction is expected to grow. Even mild kidney dysfunction can increase considerably the risk of adverse maternal and fetal outcomes. There is a bidirectional relationship between CKD and pregnancy. The pregnancy can have a deleterious impact on various aspects of CKD and renal dysfunction negatively affects pregnancy outcomes.

Key words: chronic kidney disease, transplantation, pregnancy

Introduction

Chronic kidney disease (CKD) affects almost every organ and tissue leaving consequences on structure and function, moreover it significantly affects quality of life [1]. Loss of fertility is considered to be one of the features of CKD [1,2]. It is estimated that approximately 4% of women of childbearing age have certain degree of CKD [2]. Female patients with CKD have elevated levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin. Uremia is known to promote premature aging in humans, so female patients may also be affected with premature menopause [3]. Besides the CKD itself, there are other causes of the disturbance, such as vasomotor dysfunction, medications used in treatment and prevention of complications of CKD and psychological changes [4]. Dialysis worsens the fertility issue due to chronic inflammation and protein malnutrition. Pregnancies in women on maintenance dialysis are rare.

Chronic kidney disease

Female patients with end stage renal disease (stage 5) that undergo dialysis have decreased rate of fertility with an annual possibility of pregnancy from 0.3% to 12.5% [5]. Confirming the pregnancy can be challenging due to false positive results of beta-Human Chorionic Gonadotropin testing in women that undergo dialysis. If the patient that undergoes dialysis gets pregnant then more intensive dialysis schedule with blood urea nitrogen below 17 mmol/L is needed what may be achieved by increasing the frequency of hemodialysis sessions or switching to prolonged nightly hemodialysis. In patients on peritoneal dialysis lowering the volume of dwells to 800 mL and raising their frequency is recommended [1].

Renal transplantation

Renal transplantation is an optimal replacement of kidney function. Renal transplantation increases the possibility of pregnancy in women with end stage renal disease, however adverse effects regarding mother and fetus are more often. It is of utmost importance to control and observe the pregnancy from a multidisciplinary point of view. First successful pregnancy after kidney transplantation was documented in 1958 [6]. Since then there are data for hundreds of successful pregnancies. Davison and Baylis gathered information in 2001 for 14 000 pregnancies after kidney transplantation [7]. Until today the number of successful pregnancies has drastically increased, however it is hard to determine exactly how much regarding the fact that there are many centers around the world that deal with this kind of patients. Hormonal changes amend after successful kidney transplantation as well as ovulation and menstrual cycle, patients have stronger sexual desire and higher fertility rates [8]. Due to everything mentioned above every patient of childbearing age should be warned about the changes in order to start contraception to avoid unwanted pregnancies.

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The effects of immunosuppressive therapy on fertility

Little is known about the effects of some immunosuppressants on fertility after kidney transplantation [9-11]. Detailed review of literature suggests just that immunosuppressive therapy with mTOR inhibitors (sirolimus, everolimus) can affect menstrual cycles during the first year after the transplantation and can cause forming of ovarian cysts that are reversible. It is considered that other immunosuppressants used after transplantation do not affect the hypothalamic-pituitary-gonadal axis or gametogenesis. In pregnant women after kidney transplantation (including other organs) or in women with autoimmune diseases (such as SLE and lupus nephritis) immunosuppressive therapy is continued during the pregnancy [12,13]. Pregnancy planning and drug choices for prevention of complications in mother and fetus are very important [12]. Until recently, pregnancy was not recommended in first two years after transplantation. Nowadays number of clinicians consider pregnancy safe for mother and fetus already at six months after the transplantation [10]. Every patients, not only in transplantation medicine, has to be carefully assessed for potential risks. Sexuality is very important for the quality of life. Patients should be well educated about every method of contraception due to necessity of pregnancy planning [14]. The use of intrauterine device is increasing the possibility of infections. Hormonal contraceptives can interfere with the metabolism of immunosuppressive therapy. Protection (male condoms) are recommended contraceptive options because they are efficient birth control and they protect from sexually transmitted diseases [14]. Barrier methods and intrauterine devices are not optimal birth control methods because they are not safe enough [14]. Intrauterine devices require healthy immune system to work properly, so the recommendations are to use hormonal contraceptives along with good regulation of hypertension.

When to recommend pregnancy after the transplantation?

Pregnancy can be recommended in patients with good graft function (serum creatinine levels below 132 $\mu\text{mol/l}$, steady doses and concentrations of immunosuppressive therapy, proteinuria less than 500 mg/day, and without recent transplant rejection or infections [8]. Blood pressure has to be below 140/90 mmHg with antihypertensive drugs. Patients have to have normal ultrasound findings of transplanted kidney, moreover treatment with mycophenolate mofetil and mTOR inhibitors should be ceased at least six weeks before pregnancy due to known teratogenic effects [9]. It is clear that the first couple of months after transplantation are not good for pregnancy planning because of the intense immunosuppressive therapy and high risk of acute transplant

rejection. Pre-existing kidney disease is a risk factor for preeclampsia, whereas proteinuria above 500 mg/day increases the risk of chronic dysfunction of transplanted organ [15]. Hypertension is very common (up to 75% patients during pregnancy) and results from existing disorder or can develop during pregnancy.

Mother and fetal complications

According to the data from literature around 12% of women of childbearing age that underwent kidney transplantation can get pregnant. Miscarriage happens in about 11% to 26% of patients. Successful pregnancies happen above 90% after the first trimester [10,15]. Average duration of pregnancy in transplanted patients is around 34 weeks. Most common complications that affect the mother are preeclampsia, arterial hypertension, reversible dysfunction, transplant rejection and infections [10,16]. Low birth weight happens in around 50% of newborns. Newborn survival rate is very high, while the rates of miscarriages and malformations are low [10]. Although cesarean section is more common there are no medical barriers for natural birth since transplanted kidney is located in pelvic region. Illness that caused the transplantation affects the pregnancy and complications during the period.

Discussion

In the years 2020 and 2030 the number of people with CKD will increase from 13.2% in the present to 14.4% and 16.7%, respectively [17]. It is considered that around 4% of women of childbearing age have a certain degree of CKD [1]. The risk for the development of CKD is higher in women than in men (14% to 12%) [18]. Low birth weight happens in around 50% of newborns, premature children is common condition in pregnancy of transplant woman. Minor reductions in nephron numbers that are seen in low-birth weight and small for gestational age newborns are emerging as important predisposing factors to CKD in adult age [19]. It is very important that in humans, all of the branches of the ureteric bud (UB) and the nephrons have been formed by the 32nd to 36th week of gestation. The capacity of generating new nephrons is lost at the time of birth so that human kidneys have an estimated number of nephrons of one million per kidney or more [20]. It is an important issue for all nephrologists as the number of premature children continues to grow [20]. During pregnancy issues of women with transplant kidney as patients particularly stand out and require a multidisciplinary approach.

Conclusion

Around 50% of pregnancies after kidney transplant end with pre-term birth. Younger patients with good

transplant function and good regulation of arterial hypertension have better pregnancy outcomes. Longer period of time between pregnancy and transplantation has better outcomes. Comprehension of the necessity of continuous healthcare for women from pregnancy to kidney disease is improving.

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