DOI: 10.15825/1995-1191-2022-4-15-23

IVF PREGNANCY AFTER KIDNEY TRANSPLANTATION: CLINICAL CASE AND LITERATURE REVIEW

E.I. Prokopenko[1, 2], V.M. Guryeva[2], V.A. Petrukhin[2], K.V. Krasnopol'skaya[2], F.F. Burumkulova[2], D.V. Gubina[1]

[1] Vladimirsky Moscow Regional Research Clinical Institute, Moscow, Russian Federation
[2] Moscow Regional Research Institute of Obstetrics and Gynecology, Moscow, Russian Federation

Kidney transplantation (KT), the optimal treatment for stage 5 chronic kidney disease (CKD), restores impaired fertility in most women of reproductive age. However, infertility occurs in some patients after successful KT. We present our own experience of overcoming secondary tubal infertility by in vitro fertilization (IVF). The patient was a 36-year-old with a transplanted kidney, who had lost two pregnancies in the past due to severe preeclampsia (PE). After the second attempt on cryo-thawed embryo transfer against the background of hormone replacement therapy, one embryo was transferred into the uterus, resulting in pregnancy. Gestational diabetes mellitus (GDM) was diagnosed in the first trimester, and a diet was prescribed. Immunosuppression with tacrolimus, azathioprine and methylprednisolone, prophylaxis of PE with low molecular weight heparin and antiplatelet drugs were administered during pregnancy. Elective cesarean section was performed at 37–38 weeks and a healthy boy was born, weighing 2760 g (25th percentile), 48 cm tall (36th percentile). A stay in the neonatal intensive care unit was not required. The baby is growing and developing normally, the mother's renal graft function is satisfactory. So, IVF can be successfully used in post-KT patients with infertility issues, provided that the IVF program is carefully controlled, and the pregnancy is managed in a multidisciplinary manner.

Keywords: kidney transplantation, infertility, pregnancy, assisted reproductive technology, in vitro fertilization.

INTRODUCTION

KT is the most effective treatment for stage 5 CKD. Maintaining a good reproductive function is one of the medical challenges that young women with kidney transplants face. Nowadays, post-KT pregnancy is firmly established in real clinical practice. Since 1958, when a woman with a transplanted kidney first carried a pregnancy and gave birth to a healthy child, thousands of pregnancies after KT have been reported. The outcomes of such pregnancies, despite the increased risk of obstetric and perinatal complications, are generally favorable – the rate of giving birth to live and viable children is over 70%, even taking into account fetal losses in the early gestational period [1, 2].

Our country Russia has also accumulated some experience in pregnancy management in women after KT, including those after simultaneous kidney-pancreas transplant [3–6]. The key points in planning and managing pregnancy in women with a transplanted kidney are pregravid preparation, modification of immunosuppression and other types of drug therapy during planning with exclusion of teratogenic and fetotoxic drugs (mycophenolates and proliferative signal inhibitors, ACE inhibitors, angiotensin receptor blockers, statins, allopurinol, warfarin and new oral anticoagulants), diagnosis at the pregravid stage of post-transplant diabetes (new-onset diabetes mellitus after transplantation, NODAT), careful monitoring of renal function and blood calcineurin inhibitor concentrations during gestation, early detection and treatment of GDM, prevention of placenta-associated complications – PE and fetoplacental insufficiency, and preterm birth. This pregnancy should be managed by an interdisciplinary team of specialists with relevant experience: a nephrologist, obstetrician, gynecologist, in some cases, an endocrinologist, a rheumatologist, a urologist, and other specialists.

CKD is one of the causes of dysregulation in hypothalamic-pituitary-gonadal system, leading to increased levels of follicle-stimulating hormone, luteinizing hormone and prolactin, and as a result of these changes in hormonal background – to infertility [7]. After successful KT, most women of reproductive age recover their regular menstrual cycle and ability to conceive within the first postoperative year due to elimination of uremic toxins and normalization of sex hormone levels. However, hormonal changes, pelvic inflammatory processes and other causes of female infertility may persist or occur de novo in the post-transplant period. The true incidence of infertility in this cohort of patients is difficult to estimate. Apparently, due to anatomical and endocrine abnormalities, fertility disorders in women after KT occur

Corresponding author: Elena Prokopenko. Address: 61/2, Shchepkina str., Moscow, 129110, Russian Federation. Phone: (495) 681-55-85. E-mail: renalnephron@gmail.com

more frequently than in healthy women [8–10]. At the same time, such a modern method of overcoming infertility as the use of assisted reproductive technologies in patients with a transplanted kidney is rarely used in clinical practice.

The methods used to treat infertility in renal transplant recipients are generally the same as those used in the general population. The choice of method should be based on the nature of the diagnosed disorders and include ovulation induction or more advanced assisted reproductive techniques, if necessary [11]. Indications for intrauterine insemination or in vitro fertilization (IVF) are determined by existing guidelines, and the goal of IVF is to achieve a singleton pregnancy and deliver a healthy baby at term.

Data are not available on the number of the entire cohort of post-KT women who have undergone IVF, as only those cases in which a pregnancy has occurred following an IVF are routinely published. The first successful case of an IVF pregnancy in a patient with a transplanted kidney was described by Lockwood et al. in 1995 [12]. In the following years, we were able to find 11 more publications in the literature describing individual clinical cases or their small series (Table) [9, 12–22].

As shown in the table, a total of 27 kidney transplant patients who underwent IVF had 31 pregnancies and 30 live births, including 4 twins, i.e., 26 patients carried a pregnancy to the age of fetal viability. Development of PE has been described in 8 pregnancies out of 31 (26%), so the incidence of this complication is approximately 8 times higher than in the population. Gestational and chronic hypertension were present in 6 (22%) pregnant women, a rate about 2-fold higher than in the general population. GDM occurred in only 3 cases out of 31 (10%). Fetal growth restriction was observed in 8 cases (26%), which is about 5 times higher than the rate of this complication in the general population. Fifteen women (58%) delivered prematurely, with PE and impaired renal graft function being the main indications for preterm delivery. Only 3 of 26 pregnant women (11%) delivered through natural delivery routes; in the remaining cases, a C-section was performed. It should be noted that despite elevated serum creatinine levels before delivery among a significant proportion of the patients, there were

Table

Obstetric outcomes in IVF pregnancy in kidney recipients (based on 1995–2021 literature)

Authors, year of publication	Patient / pregnancy count	Living children count	Preterm birth	Gestational or chronic hypertension	PE*	FGR**	GDM***	C-section
Lockwood G.M., Ledger W.L., Barlow D.H. 1995 [12]	1/1	2 (twins)	1 (100%)	0	0	1 (100%)	–	Vaginal delivery
Furman B., Wiznitzer A., Hackmon R. et al. 1999 [13]	1/1	2 (twins)	1 (100%)	1 (100%)	1 (100%)	–	1 (100%)	1 (100%)
Khalaf Y., Elkington N., Anderson H. et al. 2000 [14]	1/1	2 (twins)	1 (100%)	–	–	–	–	Vaginal delivery
Tamaki M., Ami M., Kimata N. et al. 2003 [15]	1/1	1	1 (100%)	1 (100%)	–	–	–	1 (100%)
Rao N.N., Wilkinson C., Morton M. et al. 2011 [16]	1/1	1	1 (100%)	1 (100%)	0	0	1 (100%)	1 (100%)
Nouri K., Bader Y., Helmy S. et al. 2011 [17]	1/1	1	0	0	0	0	–	1 (100%)
Norrman E., Bergh C., Wennerholm U.B. 2015 [18]	7/8	9 (one set of twins)	3 (42.9%)	2 (26%)	1 (13%)	1 (13%)	–	8 (100%)
Pietrzak B., Mazanowska N., Kociszewska-Najman B. et al. 2015 [19]	1/1	1	1 (100%)	1	–	1 (100%)	–	1 (100%)
Warzecha D., Szymusik I., Grzechocińska B. et al. 2018 [20]	3/3	3	3 (100%)	–	3 (100%)	1 (33.3%)	1 (33.3%)	3 (100%)
Yaprak M., Dogru V., Sanhal C.Y. et al. 2019 [9]	8/11	6	3/6 (50%)	–	3/8 (37.5%)	3/8 (37.5%)	–	6 (100%)
Kosoku A., Uchida J., Maeda K., Yoshikawa Y. et al. 2019 [21]	1/1	1	0	0	0	0	0	1 (100%)
Gastañaga-Holguera T., Calvo M., Gómez-Irwin L. et al. 2021 [22]	1/1	1	0	0	0	1 (100%)	0	Vaginal delivery

Note. * PE, preeclampsia; ** FGR, fetal growth restriction; *** GDM, gestational diabetes mellitus.

no cases of renal graft loss in the outcome of pregnancy in the presented observations.

Successful pregnancy outcomes after IVF in simultaneous pancreas-kidney transplantation has also been described [23]. However, such pregnancies should be considered separately because of the additional risks associated with diabetes, especially in patients with a long history of diabetes before pancreas transplantation (it is known that long-term complications of diabetes persist for a long time after successful transplantation and complete normalization of carbohydrate metabolism, and, in some cases, are unable to completely regress).

In Russian literature, we were unable to find descriptions of IVF in patients after KT. We present our own observation of successful IVF in a woman with a transplanted kidney.

CLINICAL CASE

Patient A., born in 1985, was diagnosed with changes in urine tests as a child, but the medical records of that time were not preserved. In 2011–2012, routine check-up showed she had traces of protein in her urine, but she was not diagnosed with kidney disease. In 2013, her first pregnancy occurred spontaneously, a multiple pregnancy (twins). At 10 weeks of pregnancy, hypertension, proteinuria 1.4 g/l, microhematuria, an increase in serum creatinine to 216 μmol/l with progressive increase were detected. Clinically (without morphological verification), the patient was diagnosed with chronic glomerulonephritis, stage 3b CKD. At 16–17 weeks of gestation, the pregnancy was terminated by a small C-section. After delivery, serum creatinine level was 214 μmol/l. Subsequently, the patient received ACE inhibitor perindopril for nephroprotection, as well as a preparation of keto-analogues of amino acids. No kidney biopsy was performed.

The second pregnancy occurred spontaneously in 2017, the patient was taking oral iron (III) hydroxide polymaltose, prenatal vitamins, dipyridamole, micronized progesterone, and dopegyt on her own from early terms. At the time of registration for pregnancy at 15–16 weeks, her blood pressure (BP) was elevated to 145/90 mmHg, hemoglobin level was 97 g/l, serum creatinine level was 308 μmol/l, and urea was 17.8 mmol/l. Proteinuria was relatively low – 0.5–0.8 g/day.

The patient was explained the risks of pregnancy with CKD: risk of maternal mortality and fetal death, risk of worsening hypertension, development of early severe PE, fetal growth restriction, further deterioration in renal function during pregnancy up to the need for emergency hemodialysis, accelerated progression of CKD in the postpartum period. However, the woman strongly insisted on prolonging the pregnancy.

Amlodipine (to correct elevated BP), low molecular weight heparin, and intravenous injection of iron preparations were added to the treatment. At 19–20 weeks, renal replacement therapy (hemodialysis) had to be started due to a further increase in azotemia. Despite the treatment, the patient had a progressive increase in BP, an increase in proteinuria from 0.8 g/day to 15 g/day (her urine output remained intact after hemodialysis was initiated), platelet count decreased and was considered to be a manifestation of severe PE. At 22 weeks, a small C-section was performed due to the futility of pregnancy and high risk of maternal mortality. Subsequently, hemodialysis was discontinued due to stabilization in glomerular filtration rate (GFR) at 16–18 ml/min/1.73 m^2; the patient was put on the kidney transplant waiting list.

Deceased-donor KT was performed in April 2018, graft function was immediate, serum creatinine levels decreased rapidly to 90–95 μmol/L. Immunosuppression was induced by basiliximab according to the standard scheme, the patient received long-acting tacrolimus, mycophenolic acid and methylprednisolone orally as baseline immunosuppression. Prophylaxis for cytomegalovirus infection with valganciclovir and prophylaxis of pneumocystis with trimethoprim/sulfamethoxazole were given for 6 months after transplantation. In July 2018, a urological complication – ureteral stricture and graft kidney hydronephrosis – was diagnosed. Immediate ureteral stenting was performed, and in November 2018, reconstructive surgery – laparoscopic revision, Boari flap ureteroneocystostomy. In January 2019, the ureteral stent of the transplanted kidney was removed. A single episode of graft pyelonephritis was noted, no recurrent urinary infection thereafter. Ultrasound images of the transplanted kidney after the reconstructive surgery confirmed the absence of urodynamic disorders.

In May 2019, the patient expressed a desire to get pregnant. There were no absolute contraindications to pregnancy: her graft function was satisfactory (serum creatinine 90 μmol/l, estimated GFR 69 ml/min/1.73 m^2), daily proteinuria 0.15–0.18 g, BP was normal (120/80–110/70 mm Hg) without taking antihypertensive drugs, no recurrent urinary infection, and no obesity – body weight 56 kg at height 165 cm (BMI 20.57). In order to prepare for pregnancy, the patient was successfully converted from mycophenolic acid, a drug prohibited for use during gestation, to azathioprine. In 2019, an endometrial polyp was removed at her place of residence.

However, the patient did not become pregnant for a year despite discontinuation of contraception. Hysterosalpingography revealed blocked fallopian tubes. In 2020, a case conference consisting of a nephrologist, transplantologist, obstetrician/gynecologist physician, reproductive endocrinologist, and the head of the Moscow Regional Research Institute of Obstetrics and Gynecology, decided to use IVF in the patient with a well-functioning transplanted kidney and tubal infertility.

In October 2020, the IVF program was performed with mild stimulation according to a protocol with gonadotropin-releasing hormone antagonists, 14 oocytes

were obtained by transvaginal puncture, 3 embryos were cryopreserved on day 5 of cultivation. In December 2020, cryo-thawed embryo transfer was performed against the background of hormone replacement therapy, one embryo was transferred into the uterus, pregnancy did not occur. In January 2021, cryo-cycle IVF was repeated against the background of hormone replacement therapy, one embryo was transferred into the uterus, resulting in pregnancy.

Immunosuppressive therapy during gestation was performed with long-acting tacrolimus with gradual dose escalation due to decreasing blood concentrations, a small dose of azathioprine 50 mg/day and oral methylprednisolone 4 mg/day. The course of pregnancy from the first trimester was complicated by early GDM, which was compensated by diet, and gestational hypothyroidism, for which the patient was prescribed levothyroxine under thyroid-stimulating hormone control for continuous use. The woman had no clinical and laboratory manifestations of secondary hyperparathyroidism. An endocrinologist was involved in the management of the pregnancy, monitoring the achievement of glycemic and thyroid hormone targets.

In the first trimester, high BP values were noted during outpatient visits. However, daily BP monitoring and analysis of self-monitoring diary showed that there was no evidence of hypertension, and that episodes of BP increase were due to the patient's psycho-emotional lability. This allowed antihypertensive therapy to be discontinued. Since the first trimester, the patient received antiplatelet agents (dipyridamole) and low-molecular-weight heparin in a prophylactic dose to prevent placental-associated and thromboembolic complications, as well as for nephroprotection. At 13 weeks of gestation, dipyridamole was replaced by acetylsalicylic acid 150 mg/day, which was continued until week 36 according to a preeclampsia prevention protocol. The patient was also given recommendations on physical activity (aerobic exercise – walking 25–50 minutes daily), which were followed.

The course of GDM against the background of diet was compensated, fetal size on routine ultrasound examinations showed no abnormalities. BP in the second and third trimesters according to a self-monitoring diary remained normal, the values of the PE marker (angiogenic factor sFlt-1/PlGF), which were monitored during pregnancy, did not exceed the reference values. Gestational proteinuria was noted, which did not exceed 1 g/day in most studies. Bacteriuria was constantly monitored; fortunately, there were no episodes of pyelonephritis, and a one-week course of oral cefixime was administered for a single episode of asymptomatic bacteriuria. Mild anemia was treated with oral iron supplements.

At 37 weeks of pregnancy, the patient had her BP increasing to 145–155/90–100 mmHg, mostly against the background of psychoemotional stress (scheduled hospitalization at an obstetric hospital, preparation for delivery), which were regarded as moderate PE by doctors at the obstetric department. At the same time, there was no increase in proteinuria over time, no significant increase in serum creatinine levels, the sFlt-1/PlGF indicator was 10.0 (normal for this gestational age).

The patient delivered a baby in September 2021 at 37–38 weeks, an elective C-section was performed due to uterine scar. The baby was born male, weighing 2760 g (25th percentile), height 48 cm (36th percentile), Apgar score 7–8. The baby's condition after birth was satisfactory; he was discharged home with his mother on day 5 after surgery. Lactation in the mother was suppressed in order to quickly restore immunosuppressive therapy in full, with resumption of mycophenolate administration. Although, it is currently believed that breastfeeding in women receiving tacrolimus, small doses of corticosteroids, azathioprine, is possible [24]. The boy is growing and developing normally; renal graft function in the mother is satisfactory.

DISCUSSION

The case we presented clearly illustrates that in young women, kidney disease can be diagnosed for the first time during pregnancy, although changes in urine tests had been noted earlier (A.'s first pregnancy), and that the course of pregnancy complicated by PE can significantly accelerate the progression of renal dysfunction and rapidly lead to end-stage CKD (A.'s second pregnancy). It should be noted, however, that prior to KT, our patient had spontaneous pregnancies within a short period of time after discontinuation of contraception. After successful KT, we encountered the problem of secondary infertility, which was related to the tubal factor. Repeated abdominal surgical interventions: two small cesarean sections, the Boari operation, which uses transperitoneal access, might have been the cause of the blocked fallopian tubes. As in the general population, ovarian or tubal factors, as well as male factors may be the cause of infertility in renal transplant recipients [24].

Given the patient's age (35 years), we decided not to postpone IVF since the effectiveness of this method of overcoming infertility decreases sharply with increasing age. In patients after organ transplantation, the most important goal of IVF is not only to achieve pregnancy, but also to prevent possible complications: IVF uses mild ovarian stimulation to reduce the risk of ovarian hyperstimulation syndrome (OHSS); one embryo is typically transferred, as multifetal gestation complications can negatively affect both the gestation outcome and the transplanted organ [13].

Khalaf et al. described a patient after kidney transplantation who developed OHSS in an IVF cycle with worsening graft function – an increase in serum creatinine to a maximum of 230 μmol/L [14]. In the pathogenesis of renal dysfunction in the described case, compression

of the renal graft by the enlarged ovary and hypoperfusion of the transplanted kidney against the background of hypovolemia, typical for this complication, played a role. Conservative treatment of OHSS was effective, graft function normalized; three months later, she had two frozen–thawed embryos transferred that resulted in a twin pregnancy and subsequent birth of two living children. In the second published observation of OHSS in a patient after KT, the complication was also successfully managed, but embryo transfer was never performed subsequently [26].

In recent years, due to improvements in IVF protocols, the incidence of OHSS has been decreasing, resulting in a lower risk of IVF, including in patients with transplanted organs [27]. An important point when preparing for IVF is the withdrawal of mTOR inhibitors sirolimus and everolimus used for immunosuppression in some patients, which not only have teratogenic effects, but can also reduce the effectiveness of IVF due to their negative impact on oocyte maturation [28].

In our observation, the kidney disease was not hereditary, and IVF was used to overcome secondary infertility. But it should be remembered that assisted reproductive technology is used not only in infertility: IVF with preimplantation genetic testing and selection of healthy embryos can be successfully used in patients with monogenic renal diseases, including patients with a renal transplant, to obtain healthy offspring. This applies primarily to women with the most common monogenic renal diseases – autosomal dominant or autosomal recessive polycystic kidney disease and Alport syndrome [29, 30].

In our patient, IVF resulted in a pregnancy, but early GDM was already detected in the first trimester, which manifested as clinically significant fasting hyperglycemia. The true incidence of GDM in pregnant women after IVF with a transplanted kidney is not known; in our opinion, it should exceed the population rate by at least 2–4 times, because both the IVF procedure (estrogens, ovulation induction) and the immunosuppression drugs have a strong diabetogenic potential. In the presented observation, early GDM, in whose pathogenesis the contra-insulin effect of placental hormones is minimal, developed.

However, the literature does not allow an objective assessment of GDM incidence in this group of pregnant women, since different countries and at different times used different diagnostic criteria. Nevertheless, modern studies have shown the high importance of achieving normoglycemia in pregnant women with GDM for a good perinatal outcome, including by reducing the incidence of PE [31, 32]; so, identification and effective treatment of GDM in women with a transplanted kidney is very important.

The literature sources cited above (Table) shows a high incidence of PE, which, in this population of pregnant women, is one of the main causes of early delivery and can lead to deterioration of graft function. Effective PE prophylaxis can both reduce the incidence of PE and increase the gestational age at which PE manifests (if this complication is not completely prevented), which significantly improves pregnancy outcomes for the fetus. For this reason, PE prophylaxis in renal transplant patients (especially after IVF) should be administered as early as possible. In our opinion, the use of aspirin alone to prevent PE is not enough for pregnant women after KT; a combination of low molecular weight heparin and antiplatelet agents is necessary. It should be noted that none of the publications we cited mention any measures taken to prevent placental-associated complications. There are no studies on the effectiveness of PE prophylaxis in patients after KT. However, the results of our earlier study showed that a combined use of heparin and antiplatelet agents significantly increases the frequency of favorable pregnancy outcomes in women with reduced renal function corresponding to stage 3 CKD [33]; renal graft function in most cases corresponds to CKD stage 2–3.

The feasibility of comprehensive PE prophylaxis is partly confirmed by the presented observation. Recall that the patient's two previous pregnancies were complicated by early severe PE, which resulted not only in termination of pregnancy due to vital signs, but also in accelerated progression of CKD. In the third pregnancy, which occurred after KT and IVF, the patient received low molecular weight heparin and antiplatelet agents from the moment the pregnancy was established until it ended; as a result, symptoms that could be attributed to PE appeared only at full-term pregnancy, 2–3 days before delivery, and did not worsen the perinatal outcome. The diagnosis of PE in the case we presented is generally quite controversial because the patient had no proteinuria and the value of biomarker sFlt-1/PlGF remained normal.

Nephrologists, transplantologists, and obstetricians/gynecologists may be wary of kidney transplant rejection during pregnancy and in the postpartum period. However, the risk of rejection in pregnancy is relatively low: according to a 2019 meta-analysis that included 6,712 pregnancies in 4,174 kidney transplant recipients, the rejection rate was about 9%, which is not significantly different from this rate outside of pregnancy [1]. Apparently, with adequate control of immunosuppression, IVF is not an additional factor that increases the risk of rejection.

In our case, the favorable outcome of the IVF pregnancy in the patient with a history of obstetric complications after KT was due to a thorough IVF and pregnancy risk assessment at the planning stage, prevention of placental-associated complications (PE, fetal growth restriction), early diagnosis of GDM and achievement of normoglycemia, control of immunosuppressive therapy, and a multidisciplinary approach to pregnancy management.

CONCLUSION

Literature data and our observation suggest that in the absence of unambiguous contraindications to pregnancy, patients with infertility after KT can be successfully treated with IVF and give birth to healthy children without deterioration in graft function. However, such women have a high incidence of pregnancy complications, primarily PE, which requires prevention. Early detection and treatment of GDM, hypertension, urinary tract infection and anemia are also necessary. Observation by an interdisciplinary team of qualified specialists and optimal tactics for such a pregnancy, taking into account risk factors, can reduce the incidence of preterm birth and achieve satisfactory pregnancy outcomes for both mother and fetus.

The authors declare no conflict of interest.

REFERENCES

1. *Shah S, Venkatesan RL, Gupta A, Sanghavi MK, Welge J, Johansen R et al.* Pregnancy outcomes in women with kidney transplant: Metaanalysis and systematic review. *BMC Nephrol.* 2019; 20 (1): 24. doi: 10.1186/s12882-019-1213-5.
2. *Puthenveettil N, Mohan A, Rahman S, Paul J*. Pregnancy outcomes in renal transplant recipients. *Indian J Anaesth.* 2021; 65 (9): 695–699. doi: 10.4103/ija.ija_362_21.
3. *Murashko LE, Kandidova IE, Sukhikh GT.* Zabolevaniya pochek u beremennyh i beremennost' posle transplantacii pochki. M.: Avtorskaya akademiya, 2012; 246.
4. *Prokopenko EI, Nikolskaya IG, Vatazin AV, Novikova SV, Gurieva VM, Yankovoy AG, Shcherbakova EO.* Povtornaya uspeshnaya beremennost' i neobychnoe techenie preeklampsii u pacientki s pochechnym allotransplantatom. *Klinicheskaya nefrologiya.* 2014; 5: 36–39.
5. *Temirbulatov RR, Bezhenar VF, Reznik ON, Anan'ev AN.* Beremennost' i rody u pacientok s pochechnym allotransplantatom (klinicheskoe nablyudenie). *Uchenye zapiski SPbGMU im. akad. I.P. Pavlova.* 2017; 24 (1): 74–78.
6. *Zagajnov VE, Katkova NYu, Vasenin SA, Kukosh VM, Murtazalieva MS, Pauzina OA i dr.* Sluchaj uspeshnogo vedeniya beremennosti i rodov u pacientki posle transplantacii podzheludochnoj zhelezy i pochki. *Vestnik transplantologii i iskusstvennyh organov.* 2021; 23 (S): 90.
7. *Dumanski SM, Ahmed SB*. Fertility and reproductive care in chronic kidney disease. *J Nephrol.* 2019; 32 (1): 39–50. doi: 10.1007/s40620-018-00569-9.
8. *Sarkar M, Bramham K, Moritz MJ, Coscia L.* Reproductive health in women following abdominal organ transplant. *Am J Transplant*. 2018; 18: 1068–1076. doi: 0.1111/ajt.14697.
9. *Yaprak M, Doğru V, Sanhal CY, Özgür K, Erman M.* In vitro fertilization after renal transplantation: a single-center experience. *Transplant Proc.* 2019; 51 (4): 1089–1092. doi: 10.1016/j.transproceed.2019.01.105.
10. *Kuczera P, Więcek A, Adamczak M.* Impaired fertility in women and men with chronic kidney disease. *Adv Clin Exp Med.* 2022; 31 (2): 187–195. doi: 0.17219/acem/141188.
11. *Szymusik I, Warzecha D, Wielgoś M, Pietrzak B.* Infertility in female and male solid organ recipients – from diagnosis to treatment: an up-to-date review of the literature. *Ann Transplant.* 2020; 25: e923592. doi: 10.12659/AOT.923592.
12. *Lockwood GM, Ledger WL, Barlow DH.* Successful pregnancy outcome in a renal transplant patient following in-vitro fertilization. *Hum Reprod.* 1995; 10: 1528–1530. doi: 10.1093/humrep/10.6.1528.
13. *Furman B, Wiznitzer A, Hackmon R, Gohar J, Mazor M.* Multiple pregnancies in women after renal transplantation. Case report that rises a management dilemma. *Eur J Obstet Gynecol Reprod Biol.* 1999; 84 (1): 107–110. doi: 10.1016/s0301-2115(98)00258-9.
14. *Khalaf Y, Elkington N, Anderson H, Taylor A, Braude P.* Ovarian hyperstimulation syndrome and its effect on renal function in a renal transplant patient undergoing IVF treatment: case report. *Hum Reprod.* 2000; 15 (6): 1275–1277. doi: 10.1093/humrep/15.6.1275.
15. *Tamaki M, Ami M, Kimata N, Tsutsui T, Watanabe Y, Saito T et al*. Successful singleton pregnancy outcome resulting from in vitro fertilization after renal transplantation. *Transplantation*. 2003; 75 (7): 1082–1083. doi: 10.1097/01.TP.0000055984.84947.90.
16. *Rao NN, Wilkinson C, Morton M, Bennett GD, Russ GR, Coates PT, Jesudason S.* Successful pregnancy in a recipient of an ABO-incompatible renal allograft. *J Assist Reprod Genet.* 2011; 28: 351–353. doi: 10.1007/s10815-010-9521-5.
17. *Nouri K, Bader Y, Helmy S, Ott J, Jirecek S, Tempfer CB.* Live birth after in vitro fertilization and single embryo transfer in a kidney transplant patient: a case report and review of the literature. *J Assist Reprod Genet*. 2011; 28: 351–353. doi: 10.1007/s10815-010-9521-5.
18. *Norrman E, Bergh C, Wennerholm UB.* Pregnancy outcome and long-term follow-up after in vitro fertilization in women with renal transplantation. *Hum Reprod.* 2015; 30: 205–213. doi: 10.1093/humrep/deu293.
19. *Pietrzak B, Mazanowska N, Kociszewska-Najman B, Szymusik I, Grzechociska B, Pazik J et al.* Successful pregnancy outcome after in vitro fertilization in a kidney graft recipient: a case report and literature review. *Ann Transplant.* 2015; 20: 338–341. doi: 10.12659/AOT.893735.
20. *Warzecha D, Szymusik I, Grzechocinska B, Cyganek A, Kociszewska-Najman B, Mazanowska N et al.* In vitro fertilization and pregnancy outcomes among patients after kidney transplantation: case series and single-center experience. *Transplant Proc*. 2018; 50 (6): 1892–1895. doi: 10.1016/j.transproceed.2018.02.144.
21. *Kosoku A, Uchida J, Maeda K, Yoshikawa Y, Hamuro A, Shimada H et al.* Successful pregnancy after in vitro fertilization in an ABO-incompatible kidney transplant recipient receiving rituximab: a case report. *BMC Nephrol.* 2019; 20 (1): 206. doi: 10.1186/s12882-019-1396-9.

22. *Gastañaga-Holguera T, Calvo M, Gómez-Irwin L, Campo Gesto I, González-González V, Vidaurreta M.* Successful pregnancy and follow-up after in vitro fertilization of a kidney transplant patient with systemic lupus erythematosus, primary biliary cholangitis, and hypothyroidism. *JBRA Assisted Reproduction.* 2021; 25 (4): 657–660. doi: 10.5935/1518-0557.20210052.
23. *Mohammadi F, McDonald S, Clark E, Jesudason S.* Two pregnancies after simultaneous pancreas-kidney transplantation: A case report. *Obstet Med.* 2020; 13 (2): 92–95. doi: 10.1177/1753495X18789584.
24. *Agarwal KA, Pavlakis M.* Sexuality, contraception, and pregnancy in kidney transplantation. *Kidney Med.* 2021; 3 (5): 837–847. doi: 10.1016/j.xkme.2021.05.009.
25. *Mishra VV, Nanda SS, Mistry K, Choudhary S, Aggarwal R, Vyas BM.* An overview on fertility outcome in renal transplant recipients. *J Obstet Gynaecol India.* 2016; 66 (Suppl 1): 330–334. doi: 10.1007/s13224-016-0919-6.
26. *Zheng HH, Song Y, Wu JY.* Critical ovarian hyperstimulation syndrome after in vitro fertilization treatment in a renal transplant recipient: a case report. *Transplant Proc.* 2016; 48 (1): 267–270. doi: 10.1016/j.transproceed.2016.01.008.
27. *Schirmer DA 3rd, Kulkarni AD, Zhang Y, Kawwass JF, Boulet SL, Kissin DM.* Ovarian hyperstimulation syndrome after assisted reproductive technologies: trends, predictors, and pregnancy outcomes. *Fertil Steril.* 2020; 114 (3): 567–578. doi: 10.1016/j.fertnstert.2020.04.004.
28. *Wald K, Cakmak H, Noel M.* mTOR inhibitor sirolimus negatively impacts in vitro fertilization outcomes. *J Assist Reprod Genet.* 2019; 36 (5): 947–950. doi: 10.1007/s10815-019-01439-4.
29. *Snoek R, Stokman MF, Lichtenbelt KD, van Tilborg TC, Simcox CE, Paulussen A et al.* Preimplantation genetic testing for monogenic kidney disease. *Clin J Am Soc Nephrol.* 2020; 15 (9): 1279–1286. doi: 10.2215/CJN.03550320.
30. *Chaperon JL, Wemmer NM, McKanna TA, Clark DM, Westemeyer MA, Gauthier P et al.* Preimplantation genetic testing for kidney disease-related genes: a laboratory's experience. *Am J Nephrol.* 2021; 52: 684–690. doi: 10.1159/000518253.
31. *Jain R, Davey S, Davey A, Raghav SK, Singh JV.* Can the management of blood sugar levels in gestational diabetes mellitus cases be an indicator of maternal and fetal outcomes? The results of a prospective cohort study from India. *J Family Community Med.* 2016; 23 (2): 94–99. doi: 10.4103/2230-8229.181002.
32. *Yang Y, Wu N.* Gestational diabetes mellitus and preeclampsia: correlation and influencing factors. *Front Cardiovasc Med.* 2022; 9: 831297. doi: 10.3389/fcvm.2022.831297.
33. *Prokopenko EI, Nikolskaya IG, Vatazin AV, Novikova SV, Gurieva VM.* Impact of heparin and antiplatelet agents on pregnancy outcome in women with chronic renal failure. *Nephrology and Dialysis*. 2015; 17 (2): 185–192.

The article was submitted to the journal on 20.07.2022