European Journal of Obstetrics & Gynecology and Reproductive Biology 180 (2014) 72–76

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Ultra-high-risk pregnancies in women after renal transplantation

Alex Farr [a], Yvonne Bader [a], Peter W. Husslein [a], Georg Györi [b], Ferdinand Mühlbacher [b], Markus Margreiter [c,*]

[a] Department of Obstetrics and Gynecology, Division of Obstetrics and Fetomaternal Medicine, Medical University Vienna, Austria
[b] Department of Surgery, Division of Transplantation, Medical University Vienna, Austria
[c] Department of Urology, Medical University Vienna, Austria

ARTICLE INFO

Article history:
Received 25 March 2014
Received in revised form 18 June 2014
Accepted 26 June 2014

Keywords:
High-risk pregnancy, Pregnancy outcome, Renal transplantation, Transplant outcome

ABSTRACT

Objectives: This study evaluates pregnancy outcomes in renal transplant recipients who have additional obstetrical, surgical, or urological risk factors.
Study design: Data from our transplantation and obstetrical databases were retrospectively analyzed to identify all women of reproductive age who had undergone renal transplantation between 1999 and 2013 at our tertiary referral center and had subsequently become pregnant. Characteristics of pregnancy and perinatal outcome parameters; obstetrical, urological, and surgical risk factors; and graft function were assessed. Descriptive data analysis, Fisher's exact test, unpaired Student's *t*-test and one-way analysis of the variance were performed.
Results: The overall pregnancy rate after renal transplantation was 5% ($n = 13$). 77% of the patients ($n = 10$) had ultra-high-risk pregnancies due to additional risk factors. These included twin pregnancy, placenta previa/percreta, hypertension; previous heart transplantation, previous myocardial infarction; postoperative lymphocele, urinary leakage, hydronephrosis, or vesico-ureteral reflux. Two patients had two consecutive pregnancies. A total of 12 deliveries with 13 newborns were achieved. Cesarean section and preterm delivery rates were 67% and 50%, respectively. Mean gestational week at delivery was 36 ± 3. Mean creatinine levels were higher in women with preterm deliveries and in those of advanced age. Mean time between transplantation and delivery was 79 ± 36 months. All patients had adequate graft function after a mean follow-up of 128 ± 50 months after renal transplantation.
Conclusions: Pregnant women after renal transplantation commonly present with additional risk factors. In these ultra-high-risk pregnancies successful outcomes can be achieved in a multidisciplinary setting. Adequate graft function and urinary tract evaluation is necessary.

Introduction

Although only 2% of women of child-bearing age become pregnant after renal transplantation, the pregnancy rate in transplant recipients has increased during the last years [1]. Pregnancies after renal transplantation are high-risk pregnancies that can cause obstetrical dilemmas, due to side effects of immunosuppressive agents and associated comorbidities. Female renal transplant recipients show higher rates of preeclampsia, small-for-gestational-age (SGA) fetuses, preterm deliveries, and cesarean sections [2,3]. If additional obstetrical risk factors or previous surgical and urological complications exist, the effect on the individual patient is even more serious. Consequently, the potentiated risk for both the mother and the fetus leads to ultra-high-risk pregnancies. Urological complications include ureteral leakage, vesicoureteral reflux (VUR), and hydronephrosis due to ureteral obstruction [4,5]. On voiding cystourethrography, VUR rates of up to 86% have been reported in asymptomatic transplant recipients, causing urinary tract infections (UTIs), graft dysfunction, or even graft loss [6]. Furthermore, postoperative lymphoceles, which have an incidence of up to 20%, can worsen renal function by compressing the pelvicalyceal system, therewith also affecting the pregnancy [7,8]. Further complications in transplant recipients depend on the transplantation-to-conception interval, blood pressure control, and maternal renal function. Hence, high

Abbreviations: IUGR, intrauterine growth retardation; SGA, small for gestational age; UTI, urinary tract infection; VUR, vesicoureteral reflux.

* Corresponding author at: Department of Urology, Medical University Vienna, Währinger Gürtel 18-20, A-1090 Vienna, Austria. Tel.: +43 1 40400 26150; fax: +43 1 40400 23320.
E-mail address: markus.margreiter@meduniwien.ac.at (M. Margreiter).

http://dx.doi.org/10.1016/j.ejogrb.2014.06.031
0301-2115/

creatinine levels during pregnancy, maternal anemia, and uncontrolled hypertension are associated with a high incidence of premature deliveries, as well as SGA or IUGR of fetuses. Other serious comorbidities, including multi-organ transplantation, can potentially increase the risk of these pregnancies that are already at high risk.

The aim of this study was to evaluate pregnancy outcomes in renal transplant recipients who have additional risk factors.

Materials and methods

We retrospectively analyzed our prospective transplantation database, including 1537 consecutive adult patients who underwent renal transplantation at our tertiary referral center between January 1999 and December 2013. A total of 580 female transplant recipients were identified; 248 of these were of reproductive age, defined as age between 18 and 49 years. The data were matched with our obstetrical database to identify all women who had subsequently become pregnant and consulted our perinatal center. Additional risk factors and comorbidities were identified by the review of patient charts.

All women underwent renal transplantation at our tertiary referral center according to our routine protocol [9]. The medical care of patients followed the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the care of kidney transplant recipients by the American Society of Transplantation [10]. Immunosuppressive drug dosing was maintained at pre-pregnancy levels through frequent monitoring of blood levels [11]. Patient charts were electronically reviewed using View Point™ for Windows, version 5.6.16.917 (GE Healthcare®, Germany). Obstetrical information included gravidity, parity, assisted reproductive treatment, prenatal ultrasound data, date and mode of delivery, gestational week, and fetal outcome parameters. Gestational age was described as weeks plus days after the woman's last normal menstrual period. Pre-existing or pregnancy-induced hypertension were defined as blood pressure higher than 140/90 mmHg diagnosed before or after 20 weeks of gestation, measured on two separate occasions more than six hours apart. Women were diagnosed with gestational diabetes, if the oral glucose tolerance test (75 g), showed a fasting blood sugar level of >92 mg/dL and/or postprandial blood sugar levels of >180 mg/dL and >153 mg/dL after one and two hours, respectively.

Study endpoints included pregnancy and perinatal outcome parameters, as well as graft function. Creatinine levels were measured at the time of admission for delivery and 12 months postpartum.

Statistical analysis

Descriptive data are presented as mean ± SD and median (range), unless otherwise stated. Discrete data are presented as *n* (%). Fisher's exact test was used to compare groups of categorical data. Metric data were compared using the unpaired Student's *t*-test or one-way analysis of the variance. A two-sided *p*-value <0.05 was considered statistically significant. Statistical calculations were performed using SPSS for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA). The study was approved by the appropriate ethics committee (Research ethics reference 1078/2012).

Results

Obstetrical outcome

The overall pregnancy rate in women who underwent renal transplantation at our tertiary referral center was 5% (*n* = 13). Ultra-high-risk pregnancies, defined as having at least on additional risk factor, were seen in, 77% (*n* = 10) of the patients. Risk factors included twin pregnancy, placenta previa/percreta, hypertension; previous heart transplantation, previous myocardial infarction; postoperative lymphocele, urinary leakage, hydronephrosis, or vesico-ureteral reflux. In the ultra-high-risk group, two women had two consecutive pregnancies with an interval of 23 and 31 months between both deliveries. One patient had a dichorial twin pregnancy. A total of 13 neonates were born. The mean age of women at ultra-high-risk was 27 ± 3 years (median, 26; range, 22–34) at the time of transplantation and 34 ± 4 years (median, 33; range, 29–44) at the time of delivery. The mean transplantation-to-delivery time was 79 ± 36 months (median, 80; range, 26–148).

In our study, the preterm delivery rate prior to 37 + 0 (37 weeks and 0 days) gestational weeks was 50% (*n* = 6). Overall, the mean gestational week at the time of delivery was 36 ± 3 (median, 36; range, 30–40). The earliest time of delivery was 30 + 1 gestational weeks in the patient with twins. Another very preterm birth at 31 + 3 gestational weeks occurred due to cervical insufficiency and preterm contractions after antenatal corticosteroid prophylaxis and intravenous tocolysis were administered. The mean birthweight in our cohort was 2467 ± 770 g (median, 2430; range, 1425–3956), corresponding to a mean percentile for gestational age adjusted birthweight of 37 ± 30 (median, 27; range, 11–74). Overall, the rates of pregnancy-induced hypertension, pre-existing hypertension and gestational diabetes were 42% (*n* = 5), 42% (*n* = 5) and 17% (*n* = 2), respectively. Cesarean section was performed in 67% of all women. Table 1 shows the detailed demographics of the patient population.

Selected patients with ultra-high-risk pregnancies

One patient had a myocardial infarction three years prior to the pregnancy (Table 1). At 38 + 0 gestational weeks, this patient presented with high blood pressure, rising levels of creatinine and consequently underwent cesarean section. Prenatal evaluation included three-dimensional-ultrasound and magnetic resonance imaging. Figs. 1 and 2 illustrate the proximity of the renal graft to the uterus. Another woman had undergone combined renal and cardiac transplantation at the age of 26 due to a congenital double-inlet, double-outlet right ventricle. Eight years later, she experienced an uneventful pregnancy and underwent cesarean section at 35 weeks of gestation due to deteriorating graft function.

A woman with placenta previa/percreta underwent hysterectomy due to unmanageable blood loss. Preoperative planning included three-dimensional-ultrasound and magnetic resonance imaging to identify the location of the transplanted ureters. Fig. 3 shows the renal graft in the patient's left iliac fossa and the ureters weaving directly in front of the potential uterotomy site. Consequently, uterotomy for cesarean section was performed more cranially.

Regarding surgical and urological complications following renal transplantation, 20% (*n* = 2) of our patients were diagnosed with grade I VUR. One patient had both hydronephrosis and ureteral leakage, which required further surgical intervention. Following this re-intervention, normal graft function was achieved without evidence of residual hydronephrosis. The rate of postoperative lymphoceles, was 20% (*n* = 2) and could be managed conservatively. The overall incidence of UTIs was 50% (*n* = 6). No relation was found between the diagnosis of VUR and UTI incidence.

Graft outcome

After a mean post-transplantation follow-up period of 128 ± 50 months (median, 134; range, 32–179), all women had adequate graft function. Creatinine levels at the time of admission for delivery and 12 months postpartum were 1.32 ± 0.37 mg/dL (median, 1.1; range,