CASE REPORT

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Pregnancy after kidney transplantation complicated by severe preeclampsia – case report

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Abstract

Pregnancy after kidney transplantation carries a high risk of hypertensive disorders, particularly preeclampsia with severe features, which remains a major contributor to maternal and perinatal morbidity. Diagnostic complexity arises from overlap between preeclampsia findings and chronic kidney disease or graft dysfunction. This case report presents a rapidly progressive form of preeclampsia superimposed on impaired allograft function, underscoring limited therapeutic options and the need for vigilant assessment. The clinical course highlights the importance of preconception counseling, adherence to immunosuppressive therapy, and strict blood pressure control. It also emphasizes the role of multidisciplinary management and timely identification of maternal and foetal deterioration. The presented case illustrates key risks and complications encountered in clinical practice.

Key words

kidney transplant, pregnancy, preeclampsia

INTRODUCTION

Severe kidney failure is associated with metabolic and endocrine disorders which can cause infertility and decreased libido. A successful kidney transplant can gradually normalize the body's condition, restore ovulatory cycles, and thus increase the possibility of having biological offspring. Kidney transplantation can restore fertility in over 50% of women with chronic kidney disease [1]. According to statistics, an average of 12–20% of women become pregnant after kidney transplant [1, 2]. Unfortunately, many pregnancies end in spontaneous or surgical miscarriage, and it is estimated that over 90% of pregnancies that last through the first trimester end successfully [3].

Pregnant women after a kidney transplant should be provided with special, multidisciplinary medical care by a nephrologist, obstetrician-gynecologist, and neonatologist. In order to increase the chances of having a healthy offspring after a kidney transplant, the following conditions must be met: stable kidney function – serum creatinine <2 mg/dl, no recent episodes of acute graft rejection, manifested by increased serum creatinine levels, proteinuria, hypertension, fever, or tenderness over the graft site; reasonable control of blood pressure – RR ≤ 140/90 mmHg; strict control of proteinuria – <500 mg/24 h, and a normal ultrasound image of the transplant [4, 5]. Pregnancy should be planned no earlier than 1 year after transplantation. Obstetric and nephrology check-ups in the 1st and 2nd trimester of pregnancy should take place every 2 weeks, while in the 3rd trimester every week [5].

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Pregnancy in kidney transplant recipients carries a significant risk of graft dysfunction. The risk of immune-mediated transplant rejection increases when immunosuppressive agents are not taken regularly, or when their doses are not adjusted to the required effective concentrations. Mohammadi et al. demonstrated that approximately 33% of pregnant kidney transplant recipients experienced a decline in graft function during pregnancy. Of these, more than 60% did not regain their original kidney function after pregnancy. Pregnant women with kidney transplants are at increased risk of complications such as anaemia, hypertensive disorders of pregnancy, including preeclampsia (PE), foetal growth restriction (FGR), preterm birth, especially before 32 weeks of gestation, caesarean delivery, gestational diabetes, urinary tract infections, and metabolic disorders. These metabolic disorders include dyslipidaemia, post-transplant diabetes mellitus (PTDM), abnormalities in calcium-phosphate metabolism, and electrolyte imbalances like hyperkalaemia and hypomagnesaemia [6, 7]. Intrauterine exposure to immunosuppressive drugs may increase the risk of congenital disabilities in the foetus [8]. The rate of preterm birth, particularly before 32 weeks of gestation, remains high and is associated with increased risks of respiratory distress syndrome (RDS), adaptive disorders, and higher perinatal mortality and morbidity [9].

Immunosuppressive drugs used by pregnant women after kidney transplantation may impact foetal development and neonatal health. Calcineurin inhibitors (CNIs), such as cyclosporine and tacrolimus, are fundamental immunosuppressive agents for most transplant patients. These drugs cross the placenta, reaching foetal blood at concentrations similar to those in maternal blood, and are associated with increased risks of FGR, prematurity, and low birth weight [10, 11]. Rarely, newborns may experience

transient renal failure and electrolyte imbalance, including hyperkalaemia and hypomagnesaemia, with temporary abnormal glucose levels, particularly noted with tacrolimus. Glucocorticosteroids, frequently used for maintenance therapy, as well as azathioprine, are generally considered safe to use during pregnancy. Azathioprine use, however, may lead to temporary leukopenia, thrombocytopenia, and reduced immunity in newborns, necessitating haemodynamic monitoring after delivery [8, 9]. Similarly, mycophenolate mofetil (MMF) is contraindicated during pregnancy because of its significant teratogenic effects [12, 13], and its discontinuence is recommended least 6 weeks before planning conception. In addition, mTOR inhibitors, such as sirolimus and everolimus, are not recommended during pregnancy. Although clinical data are limited, preclinical studies suggest these medications may lead to FGR and foetal malformations [14, 15].

CASE REPORT

A 29-year-old patient was diagnosed with renal failure in childhood and treated with haemodialysis. She also had hypertension, managed with 3 hypotensive agents for adequate blood pressure control. At the age of 12 years, she underwent a left kidney transplant and started immunosuppressive therapy with tacrolimus, azathioprine, and prednisone, after which hypotensive treatment was no longer necessary. Her first pregnancy at 27 ended in spontaneous miscarriage at 8 weeks. Later, her creatinine level exceeded 2.8 mg/dL, indicating renal transplant failure. The patient was counselled on absolute contraindications to conceiving, effective contraception, and the risks of pregnancy. Nevertheless, she did not comply with medical recommendations and self-reduced the doses of her immunosuppressive medications after obtaining a positive pregnancy test.

During the current pregnancy, the patient required four hospitalizations. The first hospitalization aimed to assess kidney function and pregnancy development. Gestational age according to the last menstrual period was 6–8 weeks. The patient had reduced her tacrolimus dose on her own a month earlier, and did not consent to the recommended increase in the dose of the drug. The patient was fully functional with respect to circulation and respiration, with no generalized oedema. Renal function, although limited, as confirmed by creatinine concentration and reduced eGFR (estimated glomerular filtration rate) was stable. Blood pressure was normal (118/70 mmHg), without the need for antihypertensive drugs. After laboratory testing, E. coli bacteriuria (107 CFU/mL) was found, and the patient received cefuroxime based on the antibiogram. The results of the most relevant laboratory tests are shown in Table 1.

The patient presented with minor genital tract bleeding, and the ultrasound examination confirmed a live pregnancy of 8 weeks (CRL 22.5 mm) (Fig. 1). During this hospitalization, the patient was administered immunosuppressive medications to prevent transplant rejection. The regimen included tacrolimus 2.5 mg twice daily, azathioprine 50 mg once daily, and prednisone 5 mg once daily. Additionally, the patient received folic acid (5 mg) once daily and progesterone (100 mg) intravaginally twice daily.

The purpose of the second hospitalization at 11–12 weeks' gestation was to assess renal function, pregnancy development and to verify an abnormal cervical cytology result (HSIL-high-grade squamous intraepithelial lesion). During this hospitalization, the patient received immunosuppressive medications as outlined above. Blood pressure values were within the norm, without the need for antihypertensive drugs. In accordance with current recommendations for patients at high risk of preeclampsia, low-dose aspirin (150 mg daily) was initiated at this stage of pregnancy. The results of the most relevant laboratory tests are shown in Table 2. Ultrasound confirmed a live pregnancy, and foetal biometry corresponded to 12 hbd (Fig. 2).

Table 1. The laboratory tests' results – first hospitalization

PARAMETER [unit]	VALUES
CREATININE [mg/dL]	1.70
D-DIMERS [ng/mL]	437
URIC ACID [mg/dL]	6.5
UREA [mg/dL]	72
DAILY PROTEINURIA[mg]	553.8
EGFR [mL/min/1.73m2]	37.8
HEMOGLOBIN [g/dL]	11.5

Figure 1. Ultrasound examination, first hospitalization

Table 2. The laboratory tests' results – second hospitalization

PARAMETER [unit]	VALUES
CREATININE [mg/dL]	1.56
D-DIMERS [ng/mL]	476
URIC ACID [mg/dL]	6.8
UREA [mg/dL]	51
DAILYPROTEINURIA[mg]	270.1
EGFR [mL/min/1.73m2]	41.7
HEMOGLOBIN [g/dL]	11.9

A colposcopic examination was performed and targeted biopsy specimens taken under colposcopic guidance. Histopathological examination confirmed a high-grade squamous intraepithelial lesion (HSIL) with p16 and Ki-67 expression. HPV 16 (humanpapillomavirus) infection was confirmed.

The indication for the third hospitalization was to assess renal function and pregnancy development. The maternal bradycardia was observed (an average rate of 63 beats/minute during the day and 44 beats/minute at night) with numerous

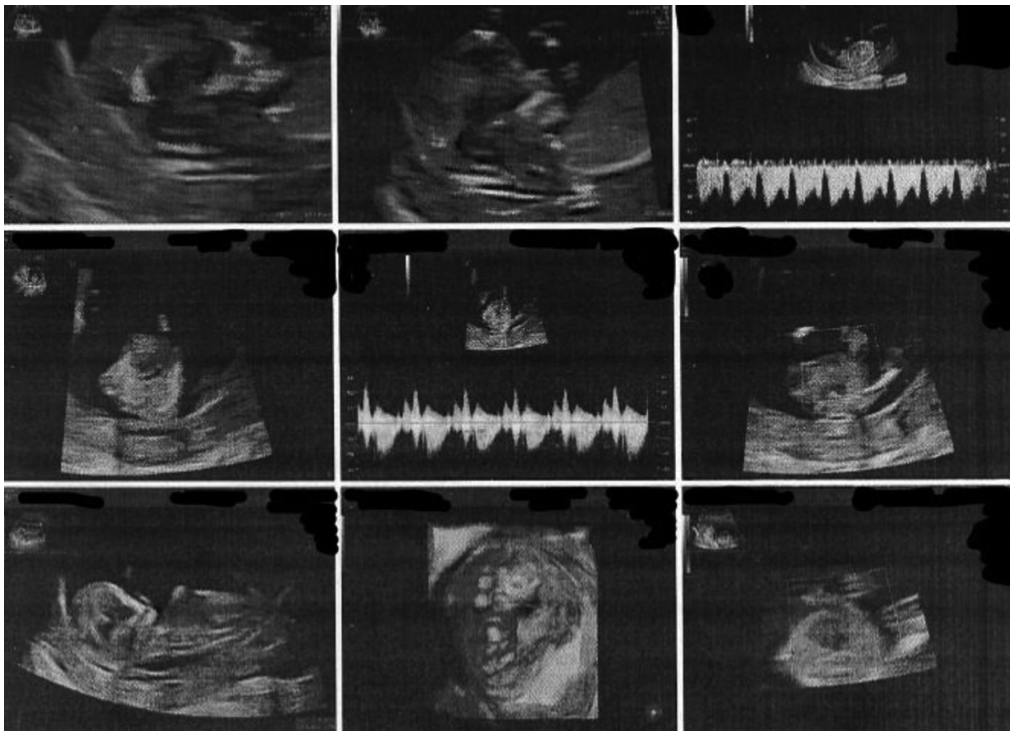

Figure 2. Ultrasound examination, second hospitalization

premature supraventricular beats of approximately 7,000 per day. Due to the bradycardia, antiarrhythmic treatment was not introduced. Blood pressure values remained within the normal range without the need for antihypertensive medications. The results of the most relevant laboratory tests are shown in Table 3.

Table 3. The laboratory tests' results – third hospitalization

PARAMETER [unit]	VALUES
CREATININE [mg/dL]	1.83
D-DIMERS [ng/mL]	3367
URIC ACID [mg/dL]	8.6
UREA [mg/dL]	85
DAILY PROTEINURIA[mg]	1330
EGFR [mL/min/1.73m2]	34.7
HEMOGLOBIN [g/dL]	11.3

Ultrasound confirmed the presence of a live foetus with biometry corresponding to the 19th week of pregnancy (MVP 3.4 cm) (Fig. 3). The immunosuppressive treatment regimen was maintained with an increased tacrolimus dose to 3 mg twice daily.

The patient was admitted to the hospital for the 4th time as an emergency at 21 weeks of gestation due to hypertensive crisis with a blood pressure of 180/110 mmHg. She also exhibited generalized oedema, and periodically experienced shortness of breath. An intensive antihypertensive regimen was promptly initiated, involving increasing doses of methyldopa, amlodipine, and occasionally nifedipine. However, despite these interventions, blood pressure remained unstable, renal function began to decline rapidly, with rising creatinine and urea levels. The patient's condition was significantly worsened by hydrothorax, ascites and pericardial effusion, which was confirmed by imaging studies. By the 22nd week of pregnancy, dialysis had become unavoidable, requiring 6 sessions per week. Severe proteinuria and anaemia developed. Serial ultrasound examinations revealed an early and rapidly worsening form of FGR with associated significant abnormalities in uteroplacental blood flow.

The clinical picture and laboratory findings (Tab. 4) justified the diagnosis of preeclampsia with severe findings superimposed on renal failure according to Mustafa et al. [15]. Recognizing the imminent risk of extremely premature birth and its consequences, at the 24th week the patient was administered betamethasone to prevent prematurity complications Renal failure was a contraindication to the administration of magnesium sulphate. Caesarean section at 25+4 weeks was indicated due to the ongoing progression of preeclampsia, with severe findings with life-threatening symptoms (neurological symptoms, severe, untreatable hypertension) in severe renal failure, and the worsening disruptions in uteroplacental blood flow (the absence of late diastolic flow and finally the presence of reverse flow in the late diastolic phase of the umbilical artery). The results of renal function tests during pregnancy are summarised in Table 5.

The patient gave birth to a live, extremely premature male newborn with a birth weight of 490 grams (<3rd percentile). On the APGAR scale, he scored 3 points in 1 min, 5 points

Table 4. The patient's examination results – IV hospitalization

PARAMETER [unit]	AT ADMISSION	BEFORE DELIVERY
CREATININE [mg/dL]	2.03	3.31
D-DIMERS [ng/mL]	677	2266
URIC ACID [mg/dL]	3.0	9.9
UREA [mg/dL]	28	85
DAILY PROTEINURIA [mg]	748	10160
EGFR [mL/min/1.73m2]	30.8	17.5
HEMOGLOBIN [g/dL]	11.7	9.0

Table 5. The comparison of renal function parameters during subsequent hospitalizations

PARAMETER [UNIT]	I HOSPITALISATION	II HOSPITALISATION	III HOSPITALISATION	IV HOSPITALISATION
SERUM CREATININE [mg/dL]	1.7	1.56	1.83	3.61
EGFR [mL/min/1.73m^2]	37.8	41.7	30.8	17.5
SERUM UREA [mg/dL]	72	51	62	85
24-hour PROTEINURIA [mg]	554	270	748	10 160

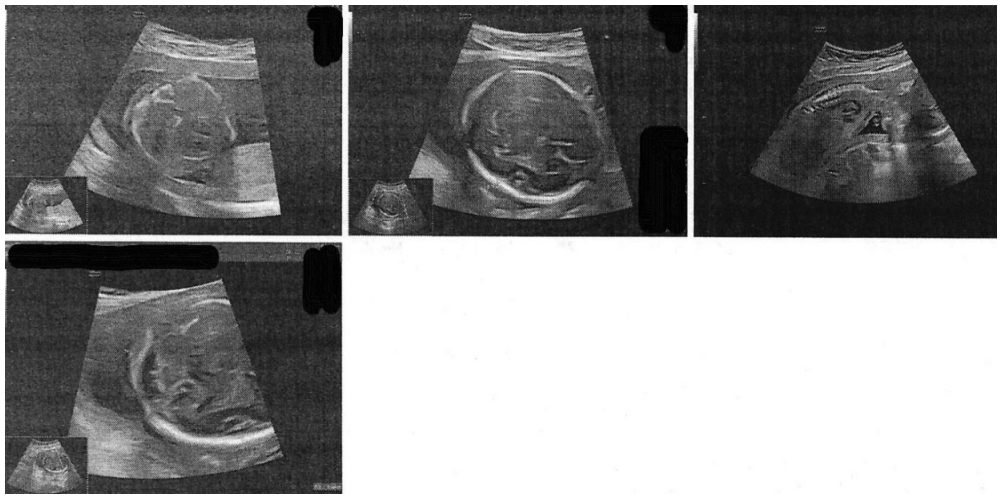

Figure 3. Ultrasound examination, third hospitalization.

Table 6. Postpartum laboratory test results

Parameter [units]	Values
Hemoglobin [g/dL]	9.5
Erythrocytes [m/uL]	2.8
Hematocrit [%]	28.1
Daily Proteinuria[mg]	7521
Urea [mg/dL]	45
Creatinine [mg/dL]	2.6
Uricacid [mg/dL]	3.3

in 3 min, 5 points in 5 min and 5 points in 10 min. Physical examination and laboratory tests revealed signs of profound multi-organ failure, which was the cause of death on the 1st day of life despite intensive medical treatment.

The early postoperative and postpartum course was uncomplicated. Hypotensive treatment included methyldopa and amlodipine. Dialysis therapy (3 per week) was associated with improved laboratory test results (Tab. 6). Before the diagnostic and therapeutic process was completed, the patient was discharged from the hospital at her own request.

DISCUSSION

Pregnancy after kidney transplantation poses a high risk to both the mother and the foetus. However, with the advances in medicine and improved post-transplant management, it has become increasingly possible to achieve favourable outcomes. The key factors determining success are stable graft function, well-controlled blood pressure, and strict

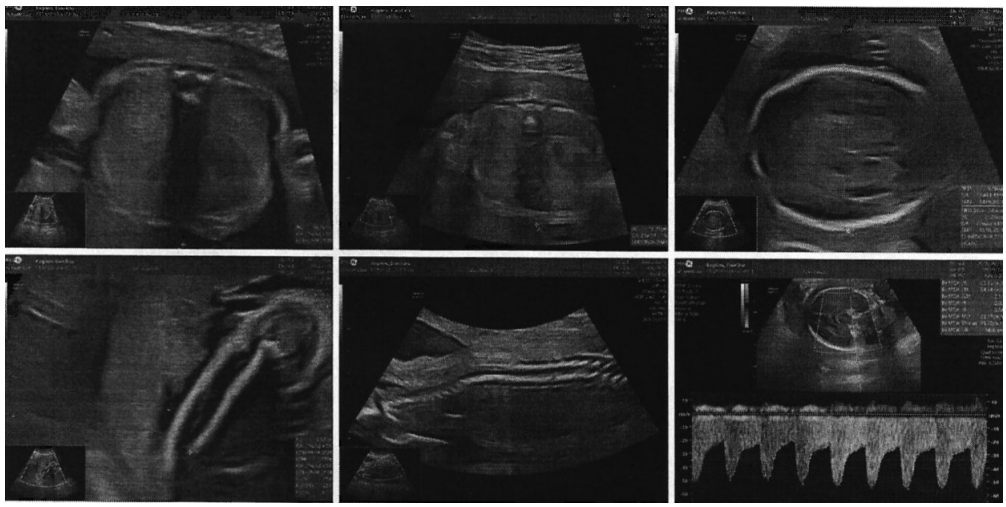

Figure 4. Ultrasound examination, fourth hospitalization

adherence to immunosuppressive therapy. The presented case highlights how serious maternal and foetal complications can develop if absolute contraindications to pregnancy are not taken into account.

European guidelines recommend a 2-year interval between kidney transplantation and pregnancy [7], while the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines suggest a 1-year interval between transplantation and conception [15]. Pregnancy should not occur during the first year after kidney transplantation due to the high doses of immunosuppressive drugs used at that time, the risk of acute rejection, and the high probability of exposure to medications contraindicated in pregnancy [7].

Despite clear recommendations, maternal outcomes in kidney transplant recipients continue to pose a clinical challenge, with consistently elevated risks for chronic hypertension, PE, gestational diabetes, urinary tract infections, acute rejection episodes, and even graft loss within 2 years postpartum [15]. Hypertension is particularly prevalent, affecting 73–85% of pregnant transplant recipients, mainly due to calcineurin inhibitor therapy [16]. Preeclampsia occurs nearly 4 times more frequently in this group, compared to the general obstetric population [17], posing a serious threat to both maternal and fetal health.

During pregnancy, the presented patient developed nephrotic-range proteinuria along with deteriorating function of the grafted kidney. Such reduced renal function markedly increases the risk of PE, FGR, preterm delivery, and peripartum complications [18–21]. The patient's clinical trajectory clearly reflected this risk profile. She underwent a caesarean section and delivered a neonate with an extremely low birth weight due to rapidly progressing PE with severe features, and life-threatening symptoms, in the course of severe and worsening renal failure. This outcome likely resulted from the patient's failure to comply with recommendations regarding the absolute pregnancy prevention. In addition, she independently discontinued immunosuppressive therapy at the beginning of pregnancy, and subsequently used doses that were too low during the first trimester. This highlights the importance of optimizing maternal health before conception and maintaining adequate immunosuppressive therapy in early pregnancy to prevent graft function deterioration and obstetric complications.

Preeclampsia deserves particular attention in this context. A recent international systematic review comprising 50 studies from 25 countries and analyzing 4,706 pregnancies in 3,570 kidney transplant recipients reported an overall prevalence of 27%, compared to 3.8% in the general population. This increased rate was consistent across all regions – Asia (30%), Europe (32%), North America (27%), Australia (26%), the Middle East (26%), and South America (21%) [15]. These findings underline the global scale of this risk and its central importance in the management of post-transplant pregnancies.

In the presented patient, in accordance with current recommendations, preeclampsia prophylaxis with low-dose acetylsalicylic acid (150 mg daily) was initiated; however, this intervention proved insufficient. The patient developed early-onset preeclampsia with severe features and a fulminant course at 22 weeks of gestation, which became the main reason for extremely premature birth. This may suggest the limited efficacy of aspirin prophylaxis in preventing PE among women with advanced renal insufficiency, as previously reported [15, 17, 20]. From mid-pregnancy onward, the patient's renal function deteriorated significantly, which was consistent with prior studies showing progressive graft dysfunction and worsening hypertension in transplant recipients who develop PE [15, 18, 19]. Both PE and renal failure with nephrotic-range proteinuria are well-recognized causes of FGR [5, 7, 18]. In the presented case, FGR developed early, during the second trimester.

As the pregnancy progressed, the patient's condition worsened further. At 21 weeks, she developed a hypertensive crisis (180/110 mmHg) with generalized oedema, elevated creatinine and urea levels, and massive proteinuria exceeding 10 g per 24 hours. These findings corresponded to the classic presentation of severe preeclampsia superimposed on chronic kidney disease [17, 20]. The decline in renal function with fluid overload, and subsequent advanced renal failure necessitated initiation of chronic hemodialysis, initially 6 sessions per week. Although dialysis during pregnancy after kidney transplantation is rare, it can be a temporary, life-saving measure that allows continuation of pregnancy in selected cases [21]. Despite these interventions, the patient's condition deteriorated consistently and dramatically to such an extent that continuing the pregnancy threatened her life. Additionally, foetal Doppler evaluation revealed critical placental insufficiency. Caesarean section was performed at 25+4 weeks, resulting in the delivery of an extremely premature infant who died shortly after birth. Postpartum, the mother stabilized under antihypertensive therapy, and dialysis frequency was reduced to a standard maintenance regimen (3 sessions per week), with satisfactory fluid and blood pressure control.

Current data clearly show that successful pregnancies are achievable among kidney transplant recipients under optimal conditions. In the same systematic review by Mustafa et al., the live birth rate reached 73.5%, surpassing that of the general population in the USA (66.7%), while miscarriage rates were lower (14.0% vs. 17.1%) [15]. However, these pregnancies are frequently complicated by gestational diabetes (8.0%), preeclampsia (27.0%), caesarean delivery (56.9%), and preterm birth (45.6%). Infants are often born late preterm (average 35.6 weeks) and with low birth weight (mean 2,420 g), reflecting the high-risk nature of such pregnancies [15, 22–26]. Importantly, Devresse et al. reported a live birth rate of approximately 75%, with most infants demonstrating normal postnatal development [5]. Similarly, Stavart et al. found that pregnancies conceived under optimal conditions – stable graft function, controlled blood pressure, and appropriate immunosuppression – were associated with significantly improved neonatal outcomes and lower morbidity [7]. These findings collectively demonstrate that pregnancy after kidney transplantation, although high-risk, can result in successful maternal and neonatal outcomes when managed appropriately.

In summary, pregnancy after kidney transplantation should always be regarded as high-risk and requires meticulous preconception planning, individualized risk stratification, and close multidisciplinary follow-up. Unplanned pregnancies, poor graft function, and discontinuation of immunosuppressive therapy dramatically increase the likelihood of severe complications, such as PE, FGR, and extreme prematurity. However, when optimal clinical conditions are maintained – stable renal function, reasonable blood pressure control, and appropriate immunosuppression

– the results could be favourable maternal and neonatal outcomes.

CONCLUSIONS

The unfavourable outcome of the pregnancy in the presented case was primarily due to significant contraindications to conception. Specifically, the severe and progressive failure of the transplanted kidney led to the development of preeclampsia with severe complications, which posed a threat to the life of the patient and her child.

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