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Case Report

Pregnancy in a Woman with Alagille Syndrome, Combined Liver–Kidney Transplantation, and Stage 4 Chronic Kidney Disease: Therapeutic Challenges—A Case Report

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Abstract

Background: Pregnancy following liver and kidney transplantation is rare. The presence of a rare genetic disorder and advanced chronic kidney disease (CKD) further complicates clinical management, for which evidence-based guidelines are limited. Case presentation: A 29-year-old woman with Alagille syndrome underwent combined liver and kidney transplantation in early childhood. She had stage 4 CKD, and her baseline creatinine was around 250 umol/L. Her pregnancy was unplanned and diagnosed at 19+1 weeks of gestation. After the diagnosis of pregnancy, immunosuppressive therapy was promptly adjusted, and potentially teratogenic medications were discontinued. At 21+1 weeks' gestation, creatinine and urea levels rose despite multidisciplinary management, and she started renal replacement therapy. Despite ongoing multidisciplinary care, the pregnancy was complicated by placental abruption at 24+5 weeks, requiring a preterm cesarean section. A live-born female infant weighing 590 g was delivered. Discussion: The coexistence of CKD, long-term immunosuppression, and high obstetric risk requires early multidisciplinary assessment and individualized management. Currently, standardized protocols for monitoring and treatment are lacking in this rare population, making clinical decision-making particularly challenging, especially regarding CKD progression. Conclusion: Pregnancy in women with combined liver and kidney transplantation and advanced CKD carries a high risk of severe renal and obstetric complications. Preconception counseling and early referral to multidisciplinary teams may help improve management in similar rare clinical scenarios.

Keywords: pregnancy; Alagille syndrome; liver–kidney transplantation; chronic kidney disease; renal replacement therapy

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1. Introduction

Recent advances in transplant care, obstetric surveillance, and immunosuppressive therapy have improved maternal and fetal outcomes, resulting in more pregnancies among

women with solid organ transplants [1–4]. Despite these advances, pregnancy in transplant recipients remains high-risk, especially for preeclampsia, fetal growth restriction, and preterm delivery [1,5–7]. These risks are even greater in women with impaired kidney function or proteinuria [8,9]. Among reproductive-age women with a kidney transplant, pregnancy rates are estimated at 1–4% per year based on national registry data [3,4]. International guidelines recommend a minimum interval of 12–24 months between kidney transplantation and conception, stable graft function, immunosuppression modulation, and absence of active rejection [10,11]. In women with advanced CKD, however, these recommendations may be insufficient, given the risk of progression to end-stage kidney disease due to pregnancy-induced hyperfiltration superimposed on reduced functional renal reserve [12–14].

Pregnancy after multiorgan transplantation is uncommon and more challenging compared to single-organ transplants [15–18]. These pregnancies present complex clinical issues that demand multidisciplinary management, yet evidence remains limited to small case series and case reports [17,19–21].

This situation is even less common in women with Alagille syndrome (ALGS) [22], a rare genetic disorder affecting multiple organs: liver, heart, skeleton, vasculature, and kidneys [23–25]. A recent report estimated the prevalence of ALGS at 1:30,000–70,000 live births [24]. It is caused by mutations in JAG1 (~95% of cases) or NOTCH2 (~2%) [25], resulting in impairment of intrahepatic bile duct morphogenesis, renal vasculogenesis, and podocyte differentiation, leading to a multisystem phenotype. The condition follows an autosomal dominant inheritance pattern with approximately 97% penetrance but markedly variable expressivity [24,25]. The diagnosis requires bile duct paucity on liver biopsy combined with at least three of five major criteria: chronic cholestasis, congenital cardiac defect, posterior embryotoxon, butterfly vertebrae, and characteristic triangular facies [26], as reported in Table 1. Notably, kidney impairment does not constitute a traditional diagnostic criterion. Given the peculiar abnormalities of the kidneys and vasculature (often in the head and neck) in ALGS, these clinical features have recently led to an expansion of the phenotypic criteria for ALGS, such that three of seven characteristic clinical criteria are sufficient for a clinical diagnosis [26]. Hepatic disease is the main feature and may progress to end-stage liver failure requiring transplantation [25,27]. Renal involvement occurs in about 40% of cases, including kidney dysplasia, tubular acidosis, and obstructive nephropathy [28].

Table 1. Traditional diagnostic criteria of Alagille Syndrome.

Diagnosis	**Bile Duct Paucity Demonstrated on Liver Biopsy + 3–5 of Major Criteria**
Domain	**Feature**
Hepatic	Cholestasis, jaundice, pruritus, progression to end-stage liver disease
Cardiac	Peripheral pulmonary artery stenosis (most common), tetralogy of Fallot, VSD, PDA
Ocular	Posterior embryotoxon (anterior chamber anomaly)
Skeletal	Butterfly vertebrae, other vertebral anomalies
Facies	Triangular face, broad forehead, deep-set eyes, pointed chin, bulbous nose tip

Footnotes: VSD: ventricular septal defect; PDA: patent ductus arteriosus.

Experience with pregnancy in women with ALGS is very limited; the few reported cases suggest increased risk of adverse obstetric and neonatal outcomes, including fetal growth restriction, preterm birth, and small-for-gestational-age infants [22,29]. Data are

especially lacking for women with both liver and kidney transplants complicated by advanced chronic kidney disease (CKD).

We report this case as, to our knowledge, the first documented pregnancy in a patient with ALGS following combined liver–kidney transplantation, in whom pre-existing stage 4 chronic kidney disease progressed to the need for initiation of renal replacement therapy during gestation. The coexistence of multiple factors—including a rare underlying genetic syndrome, advanced graft dysfunction, late recognition of pregnancy, and dialysis initiation during the second trimester—highlights critical gaps in evidence-based guidance for such complex clinical scenarios. We believe this case may serve as a reference for clinicians facing comparable scenarios.

2. Case Report

The present case report adheres to the CARE (CAse REport) guidelines [30]. The corresponding CARE checklist is included in Table S1.

2.1. Clinical History

AA is a 29-year-old woman with a diagnosis of ALGS made in early infancy. At the age of 2 years, she underwent combined liver and kidney transplantation due to end-stage disease. Table 2 reports her clinical characteristics according to expanded diagnostic criteria, focusing on the relevance in the presentation of this case.

Table 2. Diagnostic criteria and clinical features in the case report.

Domain	Feature	Frequency (%)	Relevance to Present Case
Genetics	JAG1 mutation (94%), NOTCH2 (~2%); autosomal dominant [25]	~95% JAG1	50% fetal transmission risk; addressed in genetic counselling at 19 weeks
Diagnosis	Bile duct paucity (liver biopsy) + ≥3/5 major criteria [26]	Criteria-based	Confirmed in infancy; led to combined transplantation at age 2
Hepatic	Intrahepatic bile duct paucity, cholestasis, jaundice, pruritus, progression to end-stage liver disease	>90	End-stage liver disease—liver transplantation performed
Cardiac	Peripheral pulmonary artery stenosis tetralogy of Fallot, VSD, PDA	90–95	Cardiac evaluation unremarkable; fetal cardiac scan normal at 20 weeks
Renal	Dysplasia, tubular acidosis, obstructive nephropathy [27]	~40	CKD stage 4 (eGFR ~24 mL/min); kidney transplantation; central to this case
Ocular	Posterior embryotoxon	78–89	Present; part of diagnostic criteria at presentation
Skeletal	Butterfly vertebrae, other vertebral anomalies	33–87	Incidental finding; not clinically significant in this patient
Facies	Triangular face, broad forehead, deep-set eyes, pointed chin, bulbous nose tip	~95	Characteristic facies contributed to clinical diagnosis in infancy
Vascular	Intracranial and visceral arterial anomalies; increased cerebrovascular risk	~15	Relevant to anaesthetic risk stratification and anticoagulation decisions

Footnotes: VSD: ventricular septal defect; PDA: patent ductus arteriosus, CKD chronic kidney disease.

During long-term follow-up, she developed diabetes, dyslipidemia, hypertension, and recurrent urinary tract infections. She also had polycystic ovary syndrome (PCOS).

At the end of April 2025, during a routine visit to the kidney transplant outpatient clinic, she reported no significant clinical changes. Blood tests were stable with only a mild increase in uric acid and a worsening lipid profile. Two weeks later, she discovered she was pregnant and informed the transplant team. Notably, her last menstrual period was at the beginning of 2025, but she had not considered this unusual, given her history of irregular cycles.

She was referred to the obstetrics team, where the pregnancy was dated at 19 weeks' gestation. She received counseling about the risk of ALGS in the fetus and possible teratogenic exposures. Nutritional advice was provided, and screening for cystic fibrosis and hemoglobinopathies was offered. After the discussion, she chose to continue the pregnancy.

No acute complication was documented until 21+1 weeks, when her renal function started to worsen. Renal replacement therapy was initiated and continued until delivery at 24 weeks + 5 days. Following an episode of vaginal bleeding, the gynecology team performed an ultrasound scan which showed a placental abruption. An urgent cesarean section was performed, and a live female infant weighing 590 g was delivered. The neonatology team took over immediately after birth. Figure 1 represents a flowchart of management.

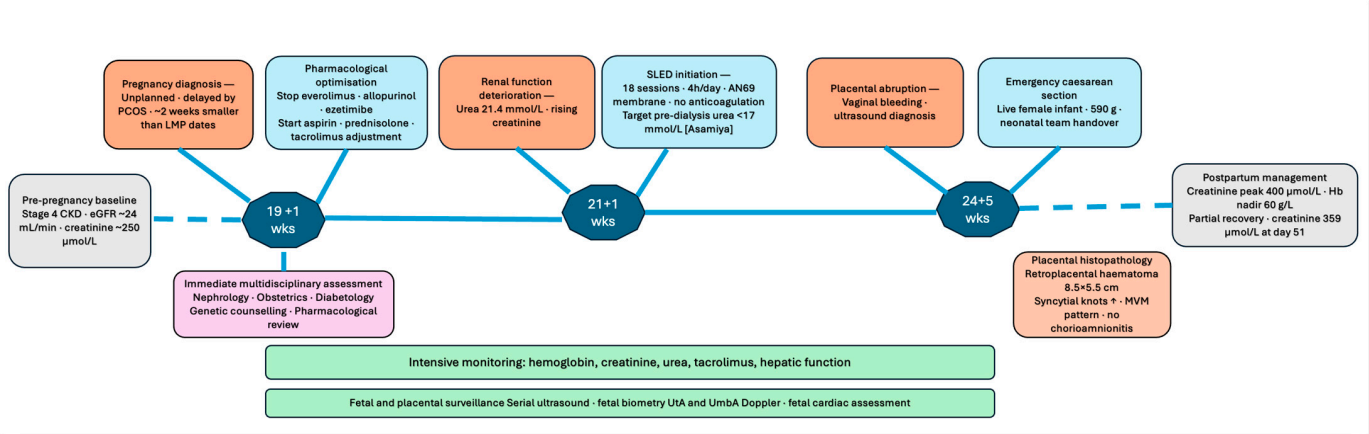
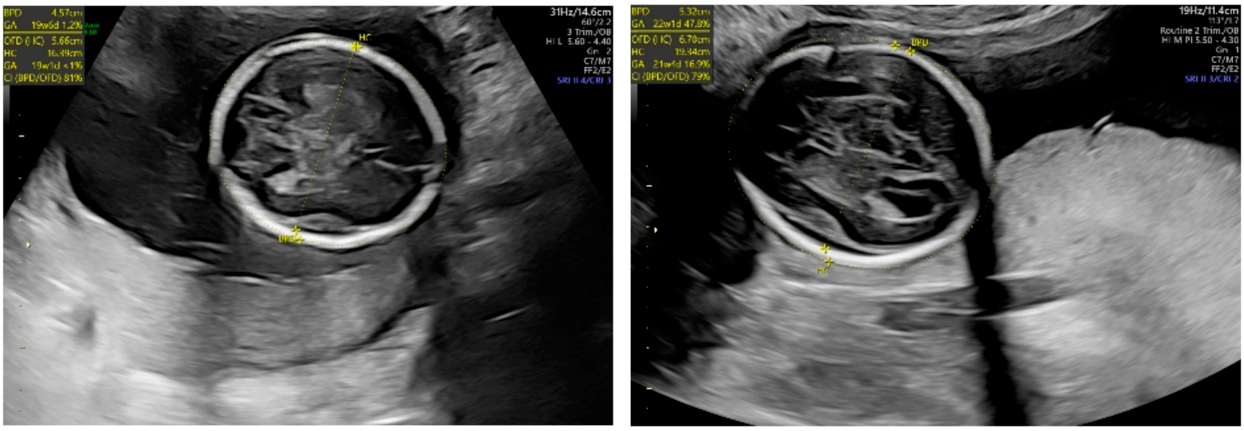


Figure 1. Management flowchart.

2.2. Fetal Features and Doppler Assessment

The first ultrasound examination at 19 weeks showed no structural abnormalities, approximately two weeks smaller than expected based on gestational age calculated from the last menstrual period. The estimated fetal weight was 275 g, with normal movements and heart rate for gestational age. At 20 weeks, a detailed fetal cardiac evaluation was performed and was unremarkable. A subsequent ultrasound at 22 weeks showed a regular growth, with an estimated weight of 440 g. Notably, between the first and last examinations, we observed a progressive decline of some morphological measures such as head circumference (from the 23rd to the 7th percentile) and femur length (from the 21st to the 10th percentile). These findings suggested a trend toward suboptimal fetal growth in the context of maternal advanced CKD, pre-existing proteinuria, and a suboptimal intrauterine environment. This observation was clinically significant and was incorporated into the multidisciplinary assessment of the optimal timing for initiating renal replacement therapy. Figure 2 reports ultrasound images of biparietal diameter captured at 19+1 and at 23+5 weeks of gestation.



(**a**) (**b**)

Figure 2. (**a**) Biparietal diameter at 19+1 weeks of gestation; (**b**) biparietal diameter at 23+5 weeks of gestation.

Serial Doppler assessments of the uterine and umbilical arteries were conducted during gestation, enabling longitudinal characterization of uteroplacental and fetoplacental hemodynamics. At 19 weeks, the mean uterine artery (UtA) pulsatility (PI) measured 1.11, which is within the normal range for gestational age, and protodiastolic notching was absent bilaterally. Notably, we observed a clinically significant difference between the left and right UtA-PIs. At 23 weeks and 5 days, seven days prior to the acute event, repeat UtA Doppler assessment revealed marked and clinically significant deterioration of the left UtA-PI with new-onset protodiastolic notching, exceeding the 95th percentile for gestational age as reported by Cavoretto et al. [31]. Umbilical artery (Umb-A) Doppler was performed at 20 and 23+5 weeks with PIs of 1.33 and 1.14, respectively. Both values were within the normal range for gestational age, with a physiologically appropriate decline in resistance over time and preserved end-diastolic flow at both assessments. Detailed measurements are reported in Table 3.

Table 3. Fetal biometric measurements and Doppler findings.

Parameter	19+1 Weeks of Pregnancy	22+1 Weeks of Pregnancy	23+5 Weeks of Pregnancy
Biparietal diameter mm(percentile)	45.7 (51)	53.2 (29)	56.5 (19)
Head circumference mm(percentile)	160.6 (23)	192.3 (12)	206 (7)
Transverse cerebellar diameter mm(percentile)	19.2 (51)	22.7 (39)	25.6 (66)
Femur length mm(percentile)	28.7 (21)	36 (11)	39.8 (10)
Abdominal circumference mm(percentile)	140.2 (49)	167.6 (31)	191 (48)
Humerus length mm(percentile)	28.2 (49)	36.7 (67)	37.1 (22)
Weight g (percentile)	275 g	440 g (23)	585 g (34)
UtA mean PI	1.11	Not reported	1.59
UtA right PI/UtA left PI	0.88/1.33	Not reported	1.11/2.06
UtA right RI/UtA left RI	0.56/0.67	Not reported	Not reported
Notching right/Notching left	Absent/Absent	Not reported	Absent/Present
UmbA PI		1.33	1.14

Footnotes: UtA = uterine artery; UmbA = umbilical artery; PI = pulsatility index; RI = resistance index.

2.3. Blood Tests

Before the diagnosis of pregnancy, laboratory findings were consistent with stable stage 4 chronic kidney disease and moderate proteinuria. Mild metabolic acidosis was present, together with worsening hyperuricemia and dyslipidemia.

At 21 weeks' gestation, renal function deteriorated, with a rise in urea levels. The nephrology team therefore decided to initiate renal replacement therapy to support maternal metabolic control and optimize the intrauterine environment. Daily short dialysis sessions were planned via a central venous catheter. Hemoglobin progressively decreased from 111 g/L to 91 g/L at 23 weeks, consistent with pregnancy-related hemodilution superimposed on anemia of chronic kidney disease. It subsequently fell to 60 g/L postpartum, following hemorrhagic blood loss due to placental abruption. Tacrolimus trough levels fluctuated between 2.8 and 4.8 ug/L before delivery, requiring close therapeutic drug monitoring and dose adjustment. Liver function tests remained stable throughout pregnancy. Proteinuria peaked at 3.2 g/day at 19 weeks, with partial improvement before delivery. All laboratory values are summarized in Table 4.

Table 4. Laboratory findings during pregnancy and postpartum.

Variable	17 Weeks *	19 Weeks	21 Weeks	23 Weeks	Postpartum Day 1
Creatinine (µmol/L)	302	283	299	275	381
Urea (mmol/L)	15.9	15.9	21.4	15.1	19.7
Hemoglobin (g/L)	111	114	98	91	60
Glucose (mg/dL)	106	124	123	87	58
Sodium (mmol/L)	137	137	137	134	133
Potassium (mmol/L)	4.1	4.2	4.7	4.2	4.4
Calcium (mmol/L)	2.37	2.37	2.23	2.3	2.11
Phosphate (mmol/L)	1.31	1.16	1.43	1.25	1.8
Uric acid (mmol/L)	0.51	0.49	0.55		0.33
Bicarbonate (mmol/L)	17.9	16.9	19.5		
AST (U/L)	10	10	13		14
ALT (U/L)	15	13	9		13
GGT (U/L)	14	12	11		41
ALP (U/L)	55	56	36		10
FK 506 (µg/L)	1.6	2.1	2.8		1.8
Everolimus (µg/L)	1.5	<0.5	<0.5		
Urine output (mL/day)	2200	2300	3400	2000	
U-protein (g/day)	2.11	3.2	2.79		1.67

Footnotes: week of pregnancy, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase, FK506: basal tacrolimus levels. * before pregnancy diagnosis.

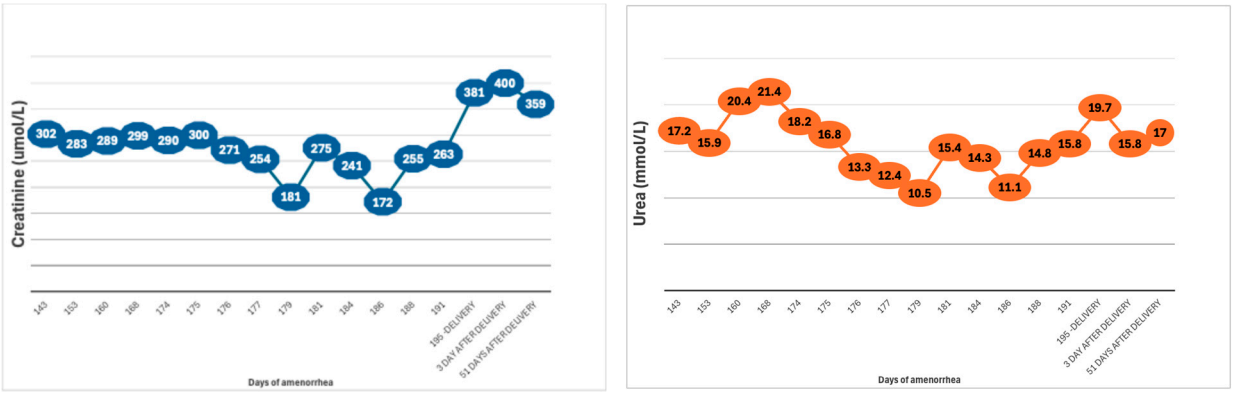
2.4. Pharmacological Treatment

Baseline treatment included tacrolimus 1 mg twice daily, everolimus 1 mg twice daily, long-acting insulin (5 units daily), omega-3 fatty acids (2 g daily), and cholecalciferol (100,000 IU every 3 months). At the last visit before the pregnancy diagnosis, tacrolimus and everolimus did not require any dose adjustment. Ezetimibe 10 mg daily and allopurinol 100 mg daily were added at that time. After confirmation of pregnancy, everolimus, allopurinol, and ezetimibe were discontinued. Tacrolimus dosage was adjusted, and low-dose prednisolone and aspirin were introduced to optimize immunosuppressant therapy and reduce the risk of preeclampsia (PE). Insulin therapy was also modified by adding rapid-acting insulin before dinner. Notably, exposure to everolimus occurred throughout the entire embryonic and early fetal period.

2.5. Renal Replacement Therapy

She underwent 18 sessions of sustained low-efficiency dialysis (SLED), performed daily and lasting about 4 h each, through a temporary internal jugular catheter. Dialysis was performed using an AN69 membrane, with a blood flow rate of 200 mL/min and a dialysate flow rate of 4000–6000 mL/h, without anticoagulation.

As shown in Figure 3a, creatinine levels rose progressively from 21 weeks of gestation (evaluated by ultrasound biometry), peaking at 400 µmol/L in the immediate post-partum period (day 1) with partial recovery to 359 µmol/L by day 51. This post-partum deterioration is consistent with the hemodynamic and inflammatory stress of emergency cesarean delivery for placental abruption, superimposed on pre-existing graft dysfunction. As shown in Figure 3b, urea levels peaked at 21.4 mmol/L at the time of dialysis initiation, were maintained between 12 and 16 mmol/L throughout the SLED period, and rose transiently to 19.7 mmol/L on post-partum day 1, reflecting the catabolic stress of the immediate post-operative period.



(**a**) (**b**)

Figure 3. (**a**) Creatinine levels during pregnancy and in post-partum period; (**b**) Urea levels during pregnancy and in post-partum period.

2.6. Histopathological Examination of the Placenta

Macroscopic Examination: The placenta and membranes weighed 232 g and measured 11 × 9 cm. The placental disc weighed 195 g, with variable thickness ranging from 0.5 to 1.9 cm and an irregular shape. The umbilical cord measured 21 cm in length without any structural abnormality. The fetal surface exhibited regular morphology, while the maternal surface presented regularly shaped cotyledons with a large adherent blood clot measuring 8.5 × 5.5 cm. On sectioning, no focal lesions were identified.

Microscopic Examination: Placental sections show normal representation and branching of chorionic villi, with minimal perivillous and subchorial fibrin deposition, increased syncytial knots, and deposition of haematic material in continuity with the basal decidua. Fetal membranes without significant inflammation. Umbilical cord with normal vascular representation.

3. Discussion

This case report highlights the limited evidence available about the best therapeutic strategy for pregnancy in multiorgan transplant recipients. It underscores several open questions in pregnancy management. Current knowledge on ALGS in pregnancy is limited [22]. The safety of pharmacological treatment, the timing of renal replacement therapy, and the role of conservative management in pregnant women with stage 4–5 CKD remain insufficiently defined. The optimal therapeutic approach, therefore, remains unclear. The

impact on the mother's health and fetal survival also remains uncertain. We share this case report to highlight these knowledge gaps in reproductive medicine and to offer insights for future cases, particularly given the condition's rarity and the limited evidence.

3.1. Alagille Syndrome and the Baseline Chronic Disease

ALGS is a rare genetic disease [23,24]. Combined liver and kidney transplants for end-stage disease are uncommon [32], making our case significant but less generalizable. The rarity of such cases in women limits the available evidence. However, it allows consideration of the impact of rare genetic syndromes on pregnancy outcomes. The nature of the underlying disease in liver–kidney transplant recipients may influence the risk of disease relapse during pregnancy [33,34]. This factor affects both risk assessment and treatment decisions. For example, an autosomal dominant disease like polycystic kidney disease [35–39] may carry different pregnancy risks compared to autoimmune conditions such as vasculitis [40–44] or lupus [45–48], or diseases prone to frequent relapse such as atypical hemolytic uremic syndrome [49–52]. Thus, the knowledge of underlying disease may influence the pregnancy risk profile, particularly when the likelihood of relapse is high even after kidney transplantation.

3.2. Uncertain Fetal Effects of Pharmacological Exposure

The evaluation of drug side effects in the mother and fetus in this population is limited by ethical constraints. Many drugs avoided during pregnancy have not been adequately studied in humans, and available information often comes from animal studies suggesting teratogenic effects [53–55]. In our patient, only limited human data were available for the drugs in use. Allopurinol, a xanthine oxidase inhibitor, crosses the placenta. Most reported pregnancies exposed to allopurinol do not show a clear increase in major birth defects, but a few cases of malformations have raised safety concerns, particularly in the first trimester [53,56,57]. Everolimus is generally contraindicated in pregnancy due to evidence of fetal risk in animal models [58–63]. Human data on everolimus remain limited, but some reports suggest possible adverse pregnancy outcomes [64]. Ezetimibe also has very limited safety data in pregnant women. Animal studies do not show major teratogenic effects, but it is not recommended during pregnancy due to the lack of controlled human data and concerns about cholesterol's role in fetal development [65–67]. Given the limited evidence in humans, the decision to discontinue certain medications may be debated. However, a cautious approach to drug use during pregnancy remains appropriate.

3.3. Doppler Assessment and Placental Dysfunction

Serial uterine artery Doppler suggested progressive deterioration in uteroplacental perfusion. At 19 weeks, the mean uterine artery PI was normal, though there was a notable difference between the right and left sides without notching. By 23+5 weeks, the mean PI had increased above normal, and notching appeared on the left side. Despite these changes, umbilical artery Doppler readings remained normal throughout, with preserved end-diastolic flow. These findings suggest that, despite worsening uterine artery indices, fetoplacental circulation remained preserved until the acute event. Placental histology was consistent with uteroplacental vascular dysfunction, showing increased syncytial knotting, fibrin deposition, and bleeding at the base of the placenta along with a large retroplacental hematoma (8.5 $\times$ 5.5 cm) and no evidence of infection.

The early inter-arterial asymmetry in uterine artery PI when the mean PI was still normal may have been an early warning sign of defective placentation, as reported in pregnancies with lateral placentas [68]. However, current ISUOG guidelines do not support the routine use of unilateral PI asymmetry as a predictor of adverse outcome [69].

3.4. Renal Replacement Therapy in the Worsening Kidney Function During Pregnancy

AA had a progressive decline in kidney function at 21 weeks of pregnancy, as shown by a marked increase in creatinine and urea levels. Management options include supportive medical treatment or renal replacement therapy. Initiating dialysis during pregnancy in kidney transplant recipients with worsening graft function is a complex and not well-standardized decision [70–73]. Most evidence is derived from studies in women with advanced CKD rather than transplant-specific cohorts, so recommendations are extrapolated [4,74–77]. Early dialysis is typically considered if there is rapid kidney function decline, worsening uremic symptoms, refractory metabolic disturbances, or concerns about the intrauterine environment [78,79]. In pregnancy, more frequent low-dose dialysis regimens seem to improve fetal outcomes, such as gestational age at delivery and birth weight, likely due to better uremia and fluid balance management [77,78,80]. For this reason, some authors recommend starting dialysis earlier than in non-pregnant patients, even before classical uremic indications arise, aiming for lower pre-dialysis urea levels (commonly <17 mmol/L) [78,81]. In kidney transplant recipients, decision-making is more complex. There is a need to preserve graft function while minimizing maternal and fetal risks. Declining graft function in pregnancy may result from hyperfiltration, chronic injury, or immune factors [82]. Close monitoring is essential. The threshold for initiating renal replacement therapy should be individualized [80]. Consequently, dialysis prescription should be optimized to preserve residual renal function and urine output, which may help maintain maternal fluid balance [83] and, indirectly, support amniotic fluid volume and the intrauterine environment. In kidney transplant recipients, dialysis adds complexity by impacting immune homeostasis [84] and possibly affecting allograft tolerance and rejection risk. This is especially important when immunosuppressive therapy must be adjusted along with fluid and metabolic management.

Potential alternatives to dialysis may be considered in all cases of pregnancy in a mother with stage 4–5 CKD [85,86]. Conservative management, such as careful fluid balance, blood pressure control, dietary protein modulation, and correction of metabolic acidosis, may help to stabilize the mother and reduce the impact of uremia on fetal development. Nevertheless, it is clinically challenging to assess the optimal protein intake, given the fetal need for protein and its effects on the mother [87]. However, when medical management fails to improve maternal and fetal status, dialysis initiation seems a reasonable choice [82,88].

3.5. Clinical Implications and Suggestions

This case raises several practical points that may be relevant for clinicians managing similar patients. Women with multiorgan transplants and conditions that can mask early pregnancy symptoms—such as PCOS or CKD-related menstrual irregularity—are at risk of late pregnancy diagnosis. For this reason, periodic pregnancy testing may be considered in selected reproductive-age transplant recipients, particularly when menstrual irregularity or teratogenic medications are present. Pre-conceptional counseling on fertility, contraception, pregnancy risk, and medication review should be offered systematically, and not only when a pregnancy is being actively planned.

When pregnancy is diagnosed late in women with multiorgan transplants and advanced CKD, prompt obstetric assessment is essential. Although first-trimester risk stratification will not be possible in this setting, second-trimester placental surveillance, including serial fetal biometry, umbilical artery Doppler, and uterine artery Doppler, should be considered without delay and repeated at short intervals, given the high risk of uteroplacental complications associated with chronic hypertension and calcineurin inhibitor-related endothelial injury. The sFlt-1/PlGF ratio may provide additional information, although its

interpretation in this population is challenging because baseline values may be influenced by CKD, hypertension, endothelial dysfunction, and immunosuppressive therapy.

Finally, there is a near-complete absence of evidence-based guidance on dialysis initiation in pregnant kidney transplant recipients with advanced CKD. Based on current knowledge, a stepwise approach, starting with dietary support and close monitoring and proceeding to dialysis if kidney function continues to decline, appears reasonable. However, most available data come from non-transplant CKD populations, and direct evidence in transplant recipients remains very limited. Prospective registries jointly managed by nephrology, obstetrics, and clinical genetics services are needed to generate the evidence required to develop specific recommendations for this growing and vulnerable patient population.

3.6. Limitations

In this case, the pregnancy was diagnosed at 19 weeks of gestation, beyond the gestational windows for first-trimester combined screening (11+0–13+6 weeks), first-trimester uterine artery Doppler, and maternal serum placental biomarker evaluation (PAPP-A, free β-hCG, and mean arterial pressure). These investigations represent the current standard of care for placental risk stratification in high-risk pregnancy [78], and their absence constitutes a diagnostic limitation of this case. However, this was not the result of a clinical oversight but an inherent consequence of the late presentation, and itself a central educational message of this report.

Angiogenic biomarkers (sFlt-1/PlGF ratio) were not measured. In the absence of a clinical picture suggestive of preeclampsia before the acute hemorrhagic presentation of placental abruption at 24+5 weeks, prospective biomarker measurement was not performed. In this context, we note that the current UK Renal Association Clinical Practice Guideline on Pregnancy and Renal Disease, endorsed by NICE, suggests but does not formally recommend the use of angiogenic biomarkers in CKD and kidney transplant patients [11], given the limited evidence in these populations.

Not all Doppler indices were systematically recorded at each assessment between 19+1 and 23+5 weeks of gestation, limiting direct comparison between examinations.

The generalizability of this case is inherently limited by its rarity. Despite these limitations, documenting the clinical decision-making process—particularly regarding dialysis initiation and immunosuppressive management in a transplant recipient—provides clinicians with directly useful information when they inevitably encounter similar cases.

4. Conclusions

This case illustrates the complex clinical challenges associated with pregnancy in a woman with ALGS, combined liver–kidney transplantation, and stage 4 chronic kidney disease. It allows us to highlight several critical issues that evidence-based medicine has not fully explored and where diagnostic and therapeutic approaches remain poorly standardized. The late diagnosis precluded first-trimester risk stratification and highlights the need for a strategy to reduce this likelihood. Periodic pregnancy testing in selected reproductive-age transplant recipients, particularly those with menstrual irregularity or exposure to potentially teratogenic medications, may help reduce delayed pregnancy recognition. The rapid progression from advanced CKD to the need for dialysis emphasizes the importance of pre-conceptional nephrology counseling and proactive pregnancy planning in women with an eGFR below 30 mL/min/1.73 m^2. Furthermore, the decision to initiate intensive daily SLED targeting pre-dialysis urea below 17 mmol/L was consistent with extrapolated evidence from pregnant women with advanced CKD, although direct evidence in kidney transplant recipients remains lacking. The use of a biocompatible membrane

(AN69) without anticoagulation may be preferable in a pregnancy complicated by high hemorrhagic risk. The absence of transplant-specific guidelines for dialysis initiation in pregnancy remains a critical and unmet clinical need that this paper and similar cases begin to address. Finally, the occurrence of placental abruption underscores the importance of having validated tools for maternal and fetal risk stratification and surveillance. Given the limited evidence, future collaborative registries should prospectively collect data on pregnancy outcomes in rare patient populations to generate the evidence base required for guideline development.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/reprodmed7020024/s1; Table S1: CARE Checklist of information to include when writing a case report.

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Abbreviations

The following abbreviations are used in this manuscript:

CKD	Chronic kidney disease
ALGS	Alagille Syndrome
SLED	Sustained low-efficiency dialysis
UtA	Uterine artery
UmbA	Umbilical artery
PI	Pulsatility index
RI	Resistance index
PCOS	Polycystic ovary syndrome
PE	Preeclampsia
RRT	Renal replacement therapy

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