DOI: 10.20514/2226-6704-2023-13-4-294-301
УДК 618.2-06:616.61-002.2-085
EDN: QJHNAB

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УСПЕШНОЕ ВЫНАШИВАНИЕ БЕРЕМЕННОСТИ ПРИ ТЕРМИНАЛЬНОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТИ: МИФ ИЛИ РЕАЛЬНОСТЬ (НА ПРИМЕРЕ КЛИНИЧЕСКОГО НАБЛЮДЕНИЯ)

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Successful Pregnancy with Terminal Renal Failure: Fiction or Reality (on the Example of Clinical Observation)

Резюме

195 миллионов женщин на Земле страдают от хронической болезни почек, что не препятствует им планировать материнство. Даже у абсолютно здоровых женщин беременность сопряжена с рисками. Эти риски увеличиваются, когда речь заходит о патологии почек. Известно, что беременность у женщин с заболеваниями почек даже при сохранной почечной функции сопровождается серьезными проблемами как для матери, так и для плода. Нами представлено клиническое наблюдение успешно выношенной беременности пациентки 23-х лет, имеющей терминальную почечную недостаточность. Коморбидность пациентки (хроническая болезнь почек, язвенный колит, анемия и др.) требовало комплексной терапии и междисциплинарного подхода, что было реализовано с первых дней наблюдения женщины. Высокопрофессиональная работа команды специалистов (нефрологи, реаниматологи, акушеры-гинекологи, гастроэнтерологи, инфекционисты, врачи функциональной диагностики, урологи и др.) определила успешный исход настоящего наблюдения. В статье расставлены акценты на факторах, отягощающих течение данного наблюдения, а также имеющих благоприятное влияние на исход.

Ключевые слова: *хроническая болезнь почек, беременность, гемодиализ, заместительная почечная терапия*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Благодарность за помощь

Коллектив авторов выражает благодарность специалистам ФГБУ «НМИЦ акушерства, гинекологии и перинатологии имени академика В.И. Кулакова», Центру помощи беременным с патологией почек и мочевыводящих путей Государственного бюджетного учреждения здравоохране-

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ния города Москвы «Городская клиническая больница имени А.К. Ерамишанцева Департамента здравоохранения города Москвы» в лице профессора, д.м.н. Козловской Натальи Львовны, Бюджетному учреждению Ханты-Мансийского округа-Югры «Окружная клиническая больница» в лице к.м.н., главного внештатного нефролога ХМАО-Югры Пьянкиной Оксаны Владимировны за сотрудничество и оказанную помощь на всех этапах ведения пациентки, а также к.м.н., главному врачу Сургутской окружной клинической больницы Шестаковой Галине Никандровне, заведующему Центром диализа Сургутской окружной клинической больницы Малашенко Сергею Михайловичу и всем специалистам Центра диализа, где пациентка получала и продолжает получать помощь, главному акушер-гинекологу Сургутской окружной клинической больницы Денисовой Ольге Леонидовне и специалистам Бюджетного учреждения Ханты-Мансийского автономного округа-Югры «Сургутский окружной клинический центр охраны материнства и детства», а также всем докторам, консультирующим и наблюдающим пациентку, мультидисциплинарная высококомпетентная помощь которых определила успешный исход настоящего наблюдения.

Статья получена 02.01.2023 г.
Принята к публикации 25.05.2023 г.

Для цитирования: Вишняк Д.А., Каримова А.Х., Кулай Ю.А. и др. УСПЕШНОЕ ВЫНАШИВАНИЕ БЕРЕМЕННОСТИ ПРИ ТЕРМИНАЛЬНОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТИ: МИФ ИЛИ РЕАЛЬНОСТЬ (на примере клинического наблюдения). Архивъ внутренней медицины. 2023; 13(4): 294-301. DOI: 10.20514/2226-6704-2023-13-4-294-301. EDN: QJHNAB

Abstract

195 million women on Earth suffer from chronic kidney disease — some of them are planning to become mothers. Even in absolutely healthy women, pregnancy is fraught with risks. These risks increase when it comes to kidney pathology. It is known that pregnancy in women with kidney diseases, even with preserved renal function, is accompanied by serious problems for both the mother and the fetus. We present a clinical observation of a 23-year-old patient with terminal renal insufficiency who successfully carried out the pregnancy. The patient's polymorbid condition (chronic kidney disease, ulcerative colitis, anemia, etc.) required complex therapy and an interdisciplinary approach, which was implemented from the first days of the woman's observation. The highly professional work of a team of specialists (nephrologists, resuscitators, obstetricians-gynecologists, gastroenterologists, infectious disease specialists, functional diagnostics doctors, urologists, etc.) determined the successful outcome of this observation. The article focuses on the factors aggravating this observation, as well as determining, on the contrary, a favorable outcome.

Key words: *chronic kidney disease, pregnancy, hemodialysis, renal replacement therapy*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

The authors declare no funding for this study

Gratitude

The team of authors expresses gratitude to the specialists of the Federal State Institution "Research Center for Obstetrics, Gynecology and Perinatology" Ministry of Healthcare of Russian Federation, the Center for Pregnant Women with Renal and Urinary Tract Pathology of the City Clinical Hospital named after A.K. Eramishantsev in represented by Head of the Center, Professor, MD Kozlovskaya Natalia Lvovna, the District Clinical Hospital of the city of Khanty-Mansiysk in the person of PhD, Chief freelance nephrologist of KhMAO-Yugra Pyankina Oksana Vladimirovna for cooperation and assistance at all stages of patient management, as well as PhD, Chief physician of the Surgut Regional Clinical Hospital Shestakova Galina Nikandrovna, head of the Dialysis Center of Surgut Regional Clinical Hospital Malashenko Sergey Mikhailovich and all specialists of the Dialysis Center, where the patient received and continues to receive, to the chief obstetrician-gynecologist of Surgut Regional Clinical Hospital Denisova Olga Leonidovna and specialists of the Surgut District Clinical Center of Maternity and Childhood Health Care, as well as to all doctors consulting and observing the patient, whose multidisciplinary highly competent assistance determined the successful outcome of this observation.

Article received on 02.01.2023
Accepted for publication on 25.05.2023

For citation: Vishnyak D.A., Karimova A.H., Kulai Yu.A. et al. Successful Pregnancy with Terminal Renal Failure: Fiction or Reality (on the Example of Clinical Observation). The Russian Archives of Internal Medicine. 2023; 13(4): 294-301. DOI: 10.20514/2226-6704-2023-13-4-294-301. EDN: QJHNAB

CKD-EPI — Chronic Kidney Desease Epidemiology Collaboration, Hb — hemoglobin, Fe — serum iron, AV — arteriovenous fistula, IBD — inflammatory bowel disease, RRT — replacement renal therapy, BMI — body mass index, LK — left kidney, MBD — mineral and bone disorders, NCVI — novel coronavirus infection Sars-CoV2, LMH — low molecular heparin, NMRC — National Medical Research Center, TSI — transferrin saturation with iron, RK — right kidney, TIBC — total iron-binding capacity, PTH — parathyroid hormone, PU — proteinuria, eGFR — estimated glomerular filtration rate, PT — parenchyma thickness, ESRD — end stage renal disease, US — ultrasonic examination, CKD — chronic renal disease, UC — ulcerative colitis

Introduction

195 million of women all over the earth suffer from chronic kidney disease (CKD); however, it does not prevent them from planning pregnancy. The incidence of stage 1, 2 and 3 CKD in women of childbearing age is at least 3 %, while the incidence of stage 3–5 CKD is approx. 0.6–0.7 % [1, 2].

For the first time, a successful pregnancy in a hemodialysis female patient was described by P. Confortini et al. (1971). The authors described a 35-year-old woman who carried pregnancy to term and gave birth to a 1950 g infant, the woman was undergoing hemodialysis for 24 hours weekly [3].

While earlier a pregnancy in kidney insufficiency patients was no less than a miracle and a rare event, now this scenario is possible; there are more and more foreign and Russian authors describing epidemiology, outcomes and management of pregnancies in CKD

patients, as well as in patients with end stage renal disease (ESRD) who undergo replacement renal therapy (RRT) [4, 5, 11, 19, 21]. The rate of success of such pregnancies increased from 25 % in 1980s to over 80–90 % at the present time [3]. In the Australia and New Zealand Dialysis and Transplant Registry, the rate of pregnancies in such patients was 3.3 per 1000 patient/year in 1996–2008 vs. 0.54 and 0.67 in 1976–1985 and 1986–1995, respectively [6, 7].

In 2022, the search for "pregnancy with chronic kidney disease" in the PubMed returned 2755 publications. In 1955–2022, the number of manuscripts on this topic grew, with the majority of articles, reviews, case studies falling on the recent decade. In Russia, there are still very few publications describing such cases, with a majority of publications (both in Russia and abroad) being dedicated to pregnancies in pre-dialysis CKD patients. Publications about the features of pregnancies in women undergoing RRT can be counted on one hand.

It is obvious that introduction of dialysis was revolutionary for the management of patients with end stage renal disease; however, this method does not allow to fully recover and restore a number of normal physiologic processes, including reproductive function. Despite numerous advances, pregnancies in women undergoing dialysis are rare and are high risk. Currently, it is acknowledged that all forms of early CKD are associated with a higher risk of unfavourable pregnancy outcomes, and it is true even for such basic conditions as a history of stone disease, underlying acute kidney injury or stage 1 CKD [8, 9].

According to the 2011 systematic review, the rate of unfavourable maternal outcomes in CKD patients was 11.5 %, i. e., more than 5 times higher than in healthy women (2 %) [1, 2]. The real incidence of pregnancy complications in pregnant women with CKD can be significantly underestimated [1]. The rate of complications grows with the renal function deterioration. In 1950, perinatal mortality in a group of patients with serum creatinine of 132.5–265 μmol/L was 58 %, while with creatinine of > 265 μmol/L the mortality was 100 %, by 1980, the rates decreased to 10 % and 53 %, correspondingly. According to the 1985–2007 data, perinatal mortality in women with serum creatinine of 125–180 μmol/L was 5 %, with persistent postpartum loss of renal function of over 25 % vs. the baseline value (20 %), the incidence of ESRD one year after delivery was 2 %. With an increase in plasma creatinine to > 180 μmol/L, these values increased to 10 %, 50 % and 35 %, respectively [10].

Therefore, pregnancy management of patients undergoing the replacement therapy with long-term hemodialysis is a current problem of the modern healthcare, the nephrological point of view of which is described in the case study below.

Clinical Case Report

Patient M., 23 years of age. Born in Tajikistan. G1.

Upon admission to the Nephrology Unit of the Budgetary Institution of the Khanty-Mansiysk Autonomous Region — Yugra Surgut Regional Clinical Hospital in November 2021, the pregnant patient complained of marked fatigue.

The medical record shows that in June 2018 the patient had loose stool up to 10 times a day with otherwise satisfactory condition, accompanied by non-specific mild extended abdominal pains. She consulted a GP at the place of her residence. An examination revealed abnormal laboratory findings: mild anemia (Hb 98–103 g/L), hyperazotemia (urea 13.7–14 mmol/L, createnine 297–308 μmol/L), reduced Chronic Kidney Desease Epidemiology Collaboration (CKD-EPI) estimated glomerular filtration rate (eGFR) up to 15.9 mL/min, GFR (Rehberg Test) — 12 mL/min, hyperuricemia (384 μmol/L), spot urine proteinuria (PU) 300 mg/L, microscopic hematuria, sclerotic kidney (right kidney — 70*37 mm, parenchyma thickness — 11 mm, left kidney — 69*41 mm, parenchyma thickness — 11 mm), renal cysts, evidencing a chronic kidney pathology and criteria for CKD diagnosis. During examination, differential diagnosis included primary and secondary glomerulopathy, abnormal urinary system development. Sclerotic kidney was a contraindication for renal biopsy [11] and hindered verification of the true cause of ESRD in this case study.

Taking into account that the patient was complaining mostly of GIT problems, she was treated in the Gastroenterology Unit. An endoscopic examination revealed pathognomonic signs of inflammatory bowel disease (IBD). Biopsy material morphology confirmed ulcerative colitis. Baseline therapy with mesalamine was initiated. During the inpatient treatment and examination in the Nephrology Unit, consistent results were obtained. After discharge, the patient was dynamically followed up by the Centre for IBD and CKD Office of the Surgut Regional Clinical Hospital. Of note, medical records for this period are not complete.

This pregnancy started in August 2021 without any sound pre-conceptional preparation. First visit to the maternity welfare clinic was on time.

Upon physical examination the following findings were obtained: height — 153 cm, weight — 35 kg, body mass index (BMI) — 14.9 kg/m^2; skin of lower limbs with areas of hyperkeratinization (fish-skin disease); according to the patient, diuresis is normal (1500–2500 mL/day). During the follow-up period, blood pressure was normal and did not require management with medicines.

Upon examination during hospitalisation into a specialised unit because of a first pregnancy and concomitant somatic pathology (IBD) in September–October 2021 on

week 4–8 of gestation, the negative laboratory parameters were evidencing condition severity: Hb — 80–100 g/L; serum iron (Fe) — 5.3 μmol/L; total iron-binding capacity (TIBC) — 46 μmol/L; transferrin saturation with iron (TSI) — 11.5 %; creatinine — 305–415 μmol/L; urea — 13–17 μmol/L; GFR (Rehberg Test) — 12 mL/min; vitamin D — 13 ng/mL; parathyroid hormone (PTH) — 608 ng/mL; albumin-adjusted Ca — 1.18 mmol/L; phosphorus — 1.47–1.93 mmol/L. Anemia was treated in accordance with clinical guidelines for anemia in chronic kidney disease patients, taking into account iron exchange parameters and blood count. The patient received ferric carboxymaltose to correct iron deficit. Once iron levels were normal, alpha-1-erythropoietin (erythropoiesis-stimulating agent) was added to the therapy. The obstetrician-gynaecologist recommended acetylsalicylic acid and magnesium hydroxide starting from week 12 of pregnancy.

It is obvious that the severe decompensated somatic pathology and comorbidities were associated with a high risk of complications both for the mother and the foetus, and pursuant to Order No. 736 of the Ministry of Health and Social Development of Russia dated December 3, 2007, On Approval of the List of Medical Indications for Induced Abortion, these findings were an absolute indication and a reason for termination of this pregnancy. The Order envisages that chronic renal insufficiency of any origin, with pre-conception createnine levels of over 200 μmol/L or a progressive increase in creatinine levels at any period of gestation, is a direct indication for pregnancy termination; and this conclusion was approved by the interdisciplinary medical team meeting. Besides, the patient was remotely consulted by specialists from the Federal State Budgetary Institution Academician V. I. Kulakov National Medical Research Center for Obstetrics, Gynaecology and Perinatal Medicine. They recommended to terminate the pregnancy and initiate RRT. If the patient refuses to terminate the pregnancy, RRT of at least 20 h/week should be initiated. The method of choice is long-term hemodialysis. However, the situation was complicated not only because the patient refused to terminate her pregnancy, but she also refused to initiate RRT, leading to clinical condition deterioration. On November 6, 2021, the patient refused to terminate her pregnancy, to initiate RRT, and to stay for any further inpatient treatment.

Next time she was hospitalised to the Nephrology Unit one month later, when she was 12 weeks pregnant, for additional examination, determination of the management strategy, and identification of the possibility to prolong this pregnancy, as well as for deciding on RRT initiation. The examination showed progressive system complications of end stage renal disease: anemia (Hb — 98–77 g/L), hyperazotemia (creatinine — 380–449 μmol/L; urea — 18–24 mmol/L), metabolic acidosis (blood pH — 7.2); hyperparathyroidism (PTH — 193 ng/mL); GFR (Rehberg Test) — 11.3 mL/min, proteinuria (PU 1.95 g/s). Another multidisciplinary medical team meeting was held; a remote consultation was sought from leading specialists and institutions specialising in expert assistance to this group of patients (V. I. Kulakov National Medical Research Center for Obstetrics, Gynaecology and Perinatal Medicine, Center for Pregnant Women with Kidney and Urinary Tract Pathologies at the State Budgetary Healthcare Institution of the City of Moscow A. K. Eramishantsev City Clinical Hospital of the Moscow Healthcare Department (Prof. N. L. Kozlovskaya, Dr. Med. Sci.), Budgetary Institution of the Khanty-Mansiysk Autonomous Region — Yugra Regional Clinical Hospital O. V. Pyankina, Cand. Med. Sci.). Taking into account the refusal to terminate the pregnancy and consent to RRT, long-term hemodialysis was initiated on December 15, 2021, at ween 19 of pregnancy, using a permanent dialysis catheter inserted in the internal jugular. Bicarbonate dialysis with ultrafiltration to 0.05–0.1–0.2 L (Elisio 13M dialysis unit) was performed 6 times weekly for 2–3 h; interdialytic weight gain was 0.04–0.12–0.6 kg. Dry weight was adjusted weekly taking into account blood pressure, oedema, weeks of pregnancy, foetus weight, and amniotic fluid volume. When the target blood urea levels were achieved, hemodialysis duration was reduced to 2—3 hours daily. On December 28, 2021, an arteriovenous (AV) fistula was formed in the lower third of left forearm. In December 2021, when the patient was 17–19 weeks pregnant, she had mild novel coronavirus infection Sars-CoV2 (NCVI), no antivirals were prescribed (Fig. 1). The entire pregnancy was associated with constant hospital admissions, examinations and treatment in the Nephrology Unit of the multidisciplinary inpatient clinic.

On May 12, 2022, the patient underwent term Stark C-section at 37 weeks and 3 days of pregnancy at the Budgetary Institution of the Khanty-Mansiysk Autonomous Region — Yugra Surgut Regional Clinical Centre for Mother and Child Protection. The newborn weighted 2980 g, Apgar scale — 8–9 points. After 10 months of dynamic follow-up, the baby boy's development corresponds to the age and gender standards.

After the operative delivery, the patient stayed in the Nephrology Unit, where she had hemodialysis for 2–4 hours 3 days a week. The woman was added to the kidney transplant waiting list.

Clinical diagnosis:

Primary diagnosis: unspecified nephropathy evolving to C5D A2 CKD. Long-term hemodialysis from December 15, 2021. Vascular access: AV fistula in the lower third of left forearm from December 28, 2021.

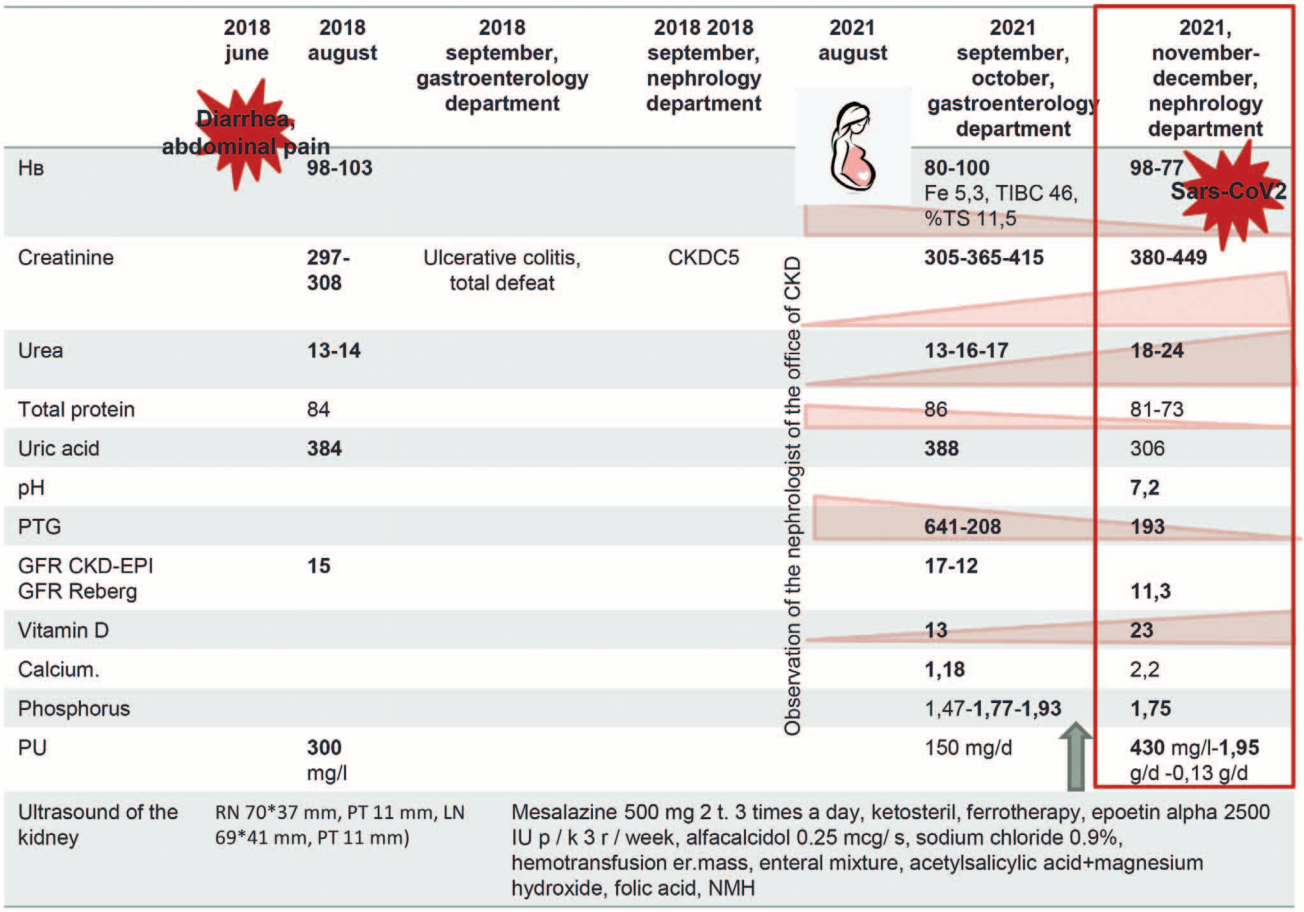

Figure 1. *Anamnesis of patient M., 23 years old*

Primary disease complications: Mineral and bone disorders (MBD) CKD: hyperphosphatasia, secondary hyperparathyroidism, vitamin D deficit. Secondary hyperuricemia. Mixed origin anemia (iron-deficient anemia and anemia of chronic diseases), moderate. Metabolic acidosis.

Secondary diagnosis: Ulcerative colitis (total), partial clinical remission. Helicobacter pylori-associated duodenal ulcer, clinical remission. Weight deficit. Mild protein-energy malnutrition. Acquired fish-skin disease, remission. Renal cysts. Mild coronavirus infection with identified virus (PCR, positive result dated December 17, 2021), survivor. Asymptomatic bacteriuria. Secondary functional ureterohydronephrosis.

First-time term operative delivery at 37 weeks and 3 days of pregnancy. Joel-Cohen incision. Stark C-section on May 12, 2022.

Discussion

Modern literature sources describe just a few cases of pregnancy during RRT. The study by I. G. Nikolskiy et al. (2011–2017) presents data on pregnancy complications and outcomes in 311 women with various CKD stages. However, only 7 and 6 patients in this large population had stage 4 and 5 CKD, respectively (4 %). In a similar study by Chinese authors who analysed the course and outcome of pregnancy in 293 patients with CKD, stage 4 was diagnosed only in 5 patients [12]. It is worth mentioning that healthcare providers in Surgut had not have any experience in managing such patients; therefore, this clinical observation was of utmost interest for various specialists in the region.

It is obvious that RRT in this case was strictly necessary. Hemodialysis was an optimal RRT method. However, selection of an RRT method for pregnant women is polemical. There are both pros and contras of hemodialysis and peritoneal dialysis (Table 1). All publications dedicated to this matter state that it is imperative to initiate RRT before or in the first trimester of pregnancy as soon as possible [13, 14]. Hemodialysis intensification improves pregnancy outcomes (better results for the foetus are achieved with 24–28 hours of hemodialysis per week [15] of 24–36 hours of hemodialysis per week) [16]. Alternative strategies are also possible (introduction of intermittent hemodialysis to peritoneal dialysis [17] and transition from peritoneal dialysis to hemodialysis in the second trimester [18]). However, even with

Table 1. *Hemodialysis and peritoneal dialysis pros and cons during pregnancy [2, 3, 6, 7]*

Hemodialysis	
Pros	*Cons*
• Less dietary restrictions • Less water restriction • Less overload using the technique	• Worse metabolic control (intermittent dialysis) • Higher risk of hemodynamic instability • Need for hypocoagulation • Lower autonomy
Peritoneal dialysis	
Pros	*Cons*
• Better metabolic control (continuous dialysis) • Lower risk of hemodynamic instability • Higher degree of autonomy • No need for anticoagulation • Preserving residual kidney function	• Higher risk of infectious complications ¥ • Higher risk of non-infectious complications ¤ • More difficulty managing volume • Higher % of intrauterine growth restriction • Increase in the frequency of exchanges ŧ

Примечания: ¥ — peritonitis/peritoneal dialysis catheter tunnel infection/outlet orifice infection; **¤** — peritoneal dialysis catheter dysfunction caused by obstruction/shifting or associated pain; **ŧ** — volume increase is not tolerated, especially in the last trimester

positive results from hemodialysis or peritoneal dialysis, an ideal RRT strategy during pregnancy may be never identified [19].

In this case study, it should be emphasised that hemodialysis was introduced on the early stages of pregnancy, principles of hemodialysis intensification were followed, the patient was compliant and felt good during the entire pregnancy. The total weight gain was 10 kg, haemodynamics was stable during the entire period of dynamic follow-up, there were no signs of foetus suffering, anemia and mineral and bone disorders were adequately corrected, the patient was under active obstetrical observation. Comorbidities were in remission due to maintenance baseline therapy.

At the same time, lack of adequate pre-conceptional preparation, presence of functional ureterohydronephrosis on week 26–27 of pregnancy (calix extension to 15–17 mm, pelvis extension to 18à24 × 27 mm, extension of upper third of ureter up to 6 mm) (no drainage was performed), COVID infection on week 15–16 of pregnancy, repeated asymptomatic bacteriuria during pregnancy treated with antibacterials after bacteriological urine tests for antibiotic susceptibility (amoxicillin and clavulanic acid, fosfomicin, ceftriaxone), comorbidities (ulcerative colitis, gastric ulcer, fish-skin disease), underlying cachexy, in addition to decompensated extragenital pathology (ESKD) could undoubtedly lead to poor pregnancy outcome both for the mother and the newborn.

Pregnancies in CKD patients are known to be associated with a high risk of perinatal complications; however, recently outcomes of such pregnancies have been quite promising. Favourable pregnancy outcome is possible with a comprehensive risk assessment, pregnancy planning, thorough individualised observation with a dynamic assessment of key blood parameters, prevention and management of complications [20-22]. This is the well-coordinated, highly-professional work of a multidisciplinary team (nephrologists, Ob/Gyn, critical care physicians, gastroenterologists, infection disease doctors, urologists, function test specialists) who followed up the patient during her pregnancy that made the favourable outcome come true.

In order to improve prognosis and prevent fast CKD progression, it is recommended to closely monitor renal disorder patients after delivery [20-22].

Conclusions

Severe comorbidity in this patient necessitated a comprehensive therapy and a multidisciplinary approach, which were implemented from the very first days of observation. Highly professional teamwork of healthcare providers (nephrologists, critical care physicians, Ob/Gyn, gastroenterologists, infection disease doctors, function test specialists, urologists, etc.) resulted in favourable outcome in this case study. Obviously, in case of pregnant women with CKD, basic functional parameters both of the mother and the foetus are regularly followed up. Relatively timely RRT initiation made adequate hyperazotemia correction possible, thus reducing endogenous intoxication and, together with strategies aimed at pregnancy prolongation and maintenance, ensured stable pregnancy and favourable outcome. Currently, we can claim that successful pregnancy and delivery in women with end-stage renal insufficiency are not a myth.

Вклад авторов:

Все авторы внесли существенный вклад в подготовку работы, прочли и одобрили финальную версию статьи перед публикацией

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Authors' contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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Karimova A.H.: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

Kulai Yu.A.: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

Chernobai M.V.: formation of the idea and concept of the manuscript, analysis and systematization of literature data, writing an article, creating graphic material, final approval of the manuscript for publication

Kofeeva V.R.: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

Khairullina G.M.: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

E.T. Mullayarova: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

Isaeva A.G.: formation of the idea and concept of the manuscript, analysis and systematization of data, final approval of the manuscript for publication

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