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The impact of chronic kidney disease on pregnancy

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ABSTRACT

Background. Renal chronic disease can be categorized as an uncommon pathology associated with pregnancy, with a real incidence difficult to estimate. The significant risk for adverse outcomes can be translated into a high degree of occurrence of preeclampsia, fetal growth restriction, preterm delivery, and, also, progression of underlying renal dysfunction. The purpose of the article is to review the data from specialty literature, regarding the correlation between renal function and the pregnancy's prognosis, so the best management can be implemented to improve the outcomes.
Material and methods. We performed a research project conducted in Emergency University Hospital in Bucharest, regarding the impact of chronic renal disease on maternal and fetal outcome. The retrospective and prospective study extends over a period of over 4 years, between 2017 and 2021 and it is currently ongoing with the involvement of the Nephrology Department, the Dialysis Department and the Medical Laboratory.
Results. We enrolled 12 pregnant women diagnosed with chronic renal disease. In all cases included in this research the mean 1-minute Apgar Index was 7. The rate of cesarian section was 95%, due to severe preeclampsia in 58% cases, fetal bradycardia in 33.33% cases and placentae abruption in 8.66%. In our study the most frequent risk factor was systemic lupus erythematosus (25%). The risk factors associated with the progression of renal disease in pregnancy were age < 24 years, nephrotic syndrome, hypertension, hematocrit <= 26%, serum creatinine > 1.4 mg/dl, prednisone monotherapy. The blood urea nitrogen had an average of 57 mg/dl, ranging between 26 and 173 mg/dl.
Conclusions. The prognosis of pregnancy-associated with renal chronic disease is burdened by the appearance of serious fetal and maternal complications. Thus, special regard should be given to the management of this pathology during pregnancy, so that therapeutic criteria can be easily adopted, taking into consideration that, nowadays, the diagnosis is still a challenge due to the overlapping psychological changes.

Keywords: renal chronic disease, pregnancy, renal transplant, diagnosis, outcome

INTRODUCTION

The incidence of chronic renal disease in pregnancy, which varies between 2 to 12 per 10,000 women, is difficult to assess, due to the fact that many women with significant renal failure are infertile or beyond childbearing age [1-3]. Thus, the diagnosis and management of this pathology associated with pregnancy remain a challenge, due to the reduced number of reported cases and the overlapping physiological changes. The main predictors of complications in this category of population: the stage of chronic renal disease, pre-existent hypertension and proteinuria [4,5,6]. Also, the tendency for pregnancy at advanced maternal age and poorly controlled underlying primary renal disease contributed to the higher prevalence of pregnancies complicated by this pathology [7,8].

The underlying pathology of chronic renal disease in pregnancy is similar with the one in general population, including primary glomerulonephritis, lupus erythematous systemic, diabetic nephropathy, chronic pyelonephritis, congenital abnormalities of the kidney and urinary tract. The risk of adverse pregnancy outcomes is increased, including preeclampsia, progression of underlying renal dysfunction, fetal growth restriction, fetal loss and preterm delivery [9].

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The classic definition as an alteration in renal function, characterized by a glomerular filtration rate<60 mL/min for a minimum of 3 months, is not accurate in pregnancy due to the increase of renal blood flow and glomerular hyperfiltration [7]. The most frequent involved pathologies which led to chronic renal disease are diabetes, lupus erythematous systemic, primary glomerulonephritis, polycystic renal disease and pyelonephritis. Pregnant women with polycystic kidney disease have increased risk for pyelonephritis, preterm birth and preeclampsia, independent of the presence of previous proteinuria and hypertension [10]. Pregnancy associated with chronic kidney disease involves numerous maternal-fetal complications: preeclampsia, intrauterine growth restriction, intrauterine fetal death, premature birth, aggravation of declining renal function, gestational diabetes or anemia, caesarean operation [4].

The aim of our study was to assess the impact of chronic kidney disease on pregnancy.

MTERIAL AND METHODS

We performed a clinical trial at Emergency University Hospital in Bucharest, regarding the impact of chronic renal disease on maternal and fetal outcome.

The retrospective and prospective study extends over a period of over 4 years, between 2017 and 2021, and it is currently ongoing with the involvement of the Nephrology Department, the Dialysis Department and the Medical Laboratory.

The study has the approval of The Ethics Council and all enrolled patients signed the informed consent.

We included in our study only pregnant patients with chronic kidney disease. Preoperative assessment included routine blood tests and biochemical urine tests, summary and urinalysis. Also, all patients underwent computerized tomography. The parameters considered were age, complete blood tests, urine tests, symptoms at presentation such as fever and pain location, affected sides, associated disease, gestational age, preeclampsia, intrauterine growth restriction, intrauterine fetal death, premature birth, aggravation of declining renal function, gestational diabetes or anemia, caesarean operation.

All collected data were analyzed and interpreted using Microsoft Word 2013 and Microsoft Excel 2013. Simple descriptive statistics were calculated. The data collected were compared with those obtained from systematic electronic research was performed using PubMed and UpToDate, aiming for meta-analyses, systematic reviews, randomized controlled trials, clinical trials that are in accordance with the clinical practice guidelines published by American College of Obstetrics and Gynecology and Royal College of Obstetricians and Gynecologists. Search words were "chronic renal failure", "pregnancy", "renal transplant".

RESULTS

In our study we enrolled 12 pregnant women diagnosed with chronic renal disease: three of them with lupus erythematous systemic, three patients with polycystic renal disease, three with glomerulonephritis, two with pyelonephritis and one with renal transplant.

For the first one, maternal age varied between 21 and 28 years old, and all the patients included in the study had anemia (average Hb of 7.5 g/dl), thrombocytopenia (150,000/mm^3), elevated serum creatinine (average of 3.95 mg/dl). All cases resulted in premature births, with an average gestational age of 31 weeks. The average fetal weight was 1,580 grams, with a 1-minute Apgar Index of 7. The risk of flare was also significant, reporting a case of macrophage activation syndrome which led to exitus.

For the group represented by polycystic renal disease, the maternal age varied between 23 and 41 years old and the mean serum creatinine was 1.45 mg/dl. The average gestational ages were 33 weeks with a mean fetal weight of 2,000 grams. The maternal age was correlated with increased rate of complications (placentae abruption, growth restriction, multiple abortions prior this pregnancy). The risk for renal infections was increased, including Proteus and Klebsiella pneumonia.

Unlike the pregnancy associated with lupus erythematous systemic and polycystic renal disease which were related with preterm birth, the average gestational age in glomerulonephritis associated pregnancy was 37 weeks. These pregnancy's outcomes were burdened by the high risk of growth restriction, with a mean fetal weight of 2,200 grams.

In all the cases included in this research the mean 1-minute Apgar Index was 7. The rate of cesarian section was 95%, due to severe preeclampsia in 58% of cases, fetal bradycardia in 33.33% of cases and placentae abruption in 8.66%.

In our study the most frequent risk factor was systemic lupus erythematosus (25%). In these cases, although the morbidity and mortality risk are increased, the pregnancy prognosis is favorable when the autoimmune disease is in remission for at least 6 months prior conception, when there is no superimposed preeclampsia and when antiphospholipid antibody syndrome is negative. The risk factors associated with the progression of renal disease in pregnancy were age < 24 years, nephrotic syndrome, hypertension, hematocrit <= 26%, serum

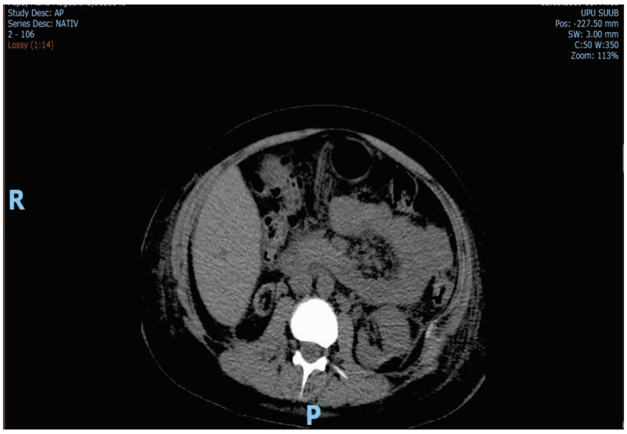

FIGURE 1. CT image of right atrophic kidney; left kidney with variable thickness of cortical index

FIGURE 2. CT aspect- Kidneys with normal shape, position and size, without radio dense lithiasis, with discrete secretion and absent excretion

creatinine > 1.4 mg/dl, prednisone monotherapy. The blood urea nitrogen had an average of 57 mg/dl, ranging between 26 and 173 mg/dl. Also, the factors that increased the risk of prematurity, described before, have all been met in only one case, most patients having a history of spontaneous miscarriages.

Excepting one case of a patient with renal transplant with no nitrogen retention, all the patients in the study were receiving dialysis. Despite that, in 8.33% of cases, the renal function decreased after giving birth, requiring a kidney transplant. The outcome of pregnancy associated with renal transplant was favorable.The average gestational age was 36-37 weeks. Also, the fetal prognosis was favorable, with a mean weight of 2,800 grams and a 1-minute Apgar Index of 9.

The imagistic evaluation performed in our study included computed tomography. The figures 1 and 2 show various aspects of lupus nephritis, belonging to a 25-year-old, respectively 21-year-old patient, both on hemodialysis.

DISCUSSIONS

Because Chronic Kidney Disease Epidemiology Collaboration can underestimate glomerular filtration rate in pregnancy, recent studies suggest that a serum creatinine over 0.87 mg/ml should be consider abnormal and that serial monitoring of this blood parameter should be used for evaluation of renal function in pregnancy [7,8,11].

The fetal and maternal adverse outcomes are direct correlated with the stage of chronic renal disease. Furthermore, most pregnancies associated with mild alteration of renal function (serum creatinine < 1.24 mg/dl), minimal proteinuria (< 1 g/24 h) and absent or well controlled hypertension, result in live births and no supplementary aggravation of kidney function [12]. Other studies associate the renal function stage three to five to a high risk of preterm births, fetal growth restriction and cesarean delivery [13].

Diabetic nephropathy affects 5-10% pregnancies in women with type 1 diabetes mellitus and it leads to increased risk of complications, such preeclampsia, and a higher risk of congenital defects [7,14]. Women with pregestational diabetes have a variable risk of loss of kidney function, depending on the glycemic control, the degree of proteinuria (microalbuminuria vs. proteinuria>3 g/24 h) [15].

Pregnancy in women on dialysis is associated with a higher risk of adverse events, with an overall successful rate of 89.2%. The risk of perinatal death or extreme prematurity were associated with preeclampsia, primigravida and lupus erythematous systemic. Also, a blood urea nitrogen < 35 mg/dl can be used as an objective for adjusting dialysis and ameliorate the outcomes of pregnancy [16].

New studies confirm that pregnant women on dialysis have a significant risk for preterm births (85%), neonatal intensive care unit (67%) and neonatal death (11%) [17].

Due to disruption of hypothalamic gonadal axis, women with end stage renal disease have impaired fertility. Since there is rapid restoration of fertility, kidney transplantation offers the best hope to women with end-stage renal disease who wish to become pregnant [11].

Maternal kidney transplantation is associated with multiple maternal and fetal complications. Diagnosis of preeclampsia may be difficult in these cases, due to late onset of hypertension and pre-existing proteinuria. A problem is the differential diagnosis between acute rejection and preeclampsia. A study performed by Yin et al. on a group of 26 pregnant women with biopsy-confirmed acute rejection and 78 pregnant women with preeclampsia concluded that the difference can be reported to the higher creatinine levels confirmed in the first group and increased proteinuria in the second group [18]. Also, the risk of prematurity and graft loss is most likely to occur in case of acute rejection [18].

Another meta-analysis and systematic review of pregnancy outcomes in women with kidney transplant, performed by Shah et al., concluded that, although the outcome of live births is favorable, the risk or preeclampsia was 21.5% and the risk of preterm delivery was 43.1%, both with 95% confidence interval [11].

The differential diagnosis between chronic renal disease and preeclampsia is challenging, due to the presence of the hypertension and proteinuria in both cases. Ultrasound studies showed that abnormal flow of the uterine and umbilical arteries is suggestive for preeclampsia, while normal flow confirm the renal disease [19].

Kidney biopsy can be performed during pregnancy, preferably before 25 weeks of gestation, but it must be avoided after 30 weeks of gestation due to the lack of benefits provided by a diagnosis and the uterus' growth [7,20]. Also, it implies risk of renal hematomas and blood transfusion [7,21].

Strategies for improving the pregnancy outcomes in chronic renal disease include management of diabetes, hypertension and proteinuria. The initiation of preeclampsia prevention approaches includes aspirin use, highly recommended between 12 and 36 weeks of gestation. Low-molecular weight heparin is recommended in case of increased proteinuria, because of the high thrombotic risk [15,19,22,23]. Blood pressure control can be achieved with antihypertensive drugs such as metildopa, nifedipine and labetalol. Angiotensin converting-enzyme inhibitors and angiotensin receptor blockers cause intrauterine growth restriction, oligohydramnios and fetal death, especially when administrated in the second and third trimester [21,24,25].

Immunosuppressive drugs as steroids, azathioprine, calcineurin inhibitors, can be used in pregnancy. Avoidance of nephrotoxic and teratogenic medications, as mycophenolate mofetil and cyclophosphamide, is necessary [26,27]. As far as anemia is concerned, erythropoietin, folic acid and intravenous saccharide ferric oxide are recommended [28].

Mode of delivery in women with chronic kidney disease should be based on usual obstetric indications [7,29,30].

CONCLUSIONS

Renal chronic disease, an uncommon pathology during pregnancy, has important implications for maternal and fetal prognosis, correlated with the severity of the disease. Having different underlying pathologies, the management should be directed to each cause, with the aim of reducing the percentage of preterm birth, fetal intrauterine growth restriction, preeclampsia. Also, in addition to these maternal-fetal complications, pregnancy in a kidney transplant recipient continues to remain thought-provoking due to the risk of side effects from immunosuppressive medication and the risk of deterioration of allograft function. More studies are needed to be performed in order to successfully determine the appropriate therapeutic management, so the evolution of pregnancy associated with renal chronic disease should not be burdened by the currently reported incidents.

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