”CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

DOCTORAL SCHOOL

MEDICAL FIELD

Diagnostic and treatment guidelines in pregnancy associated with renal failure and the impact of therapeutic attitude on maternal-fetal prognosis

PHD THESIS SUMMARY

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Introduction

Pregnancy-associated renal failure is a significant public health problem, being one of the leading causes of maternal and fetal mortality and morbidity [1-4]. Establishing the diagnosis and incidence of this pathology can be difficult and challenging for obstetricians due to the structural and functional physiological changes in the renal system in pregnancy [4-8].

In the absence of a consensus on diagnostic criteria, serum creatinine remains the most effective element to identify this condition [1].

The physiological changes to the renal system that occur in pregnancy may make the diagnosis of acute kidney injury difficult, particularly in situations where they overlap or contribute to impaired renal function. Therefore, a diagnostic guideline is useful in differentiating pregnancy-induced physiologic renal changes from pathologic renal changes, leading to the institution of a rapid therapeutic course of action that decreases the incidence of maternal-fetal complications. Early diagnosis and initiation of appropriate treatment also prevent the progression of acute kidney injury to chronic forms, leading to improved survival and quality of life.

Therapeutic management of associated pathologies that increase the risk of developing kidney injury during pregnancy (diabetes mellitus, hypertension, autoimmune diseases) should be included in the guidelines for the treatment of pregnancy-associated renal failure, emphasizing the importance of clinical and paraclinical changes with multisystem involvement.

Maternal and fetal mortality and morbidity can be significantly reduced by timely and correct therapeutic management. It is imperative to standardize this, especially in a multidisciplinary approach (obstetrician, nephrologist), in order to ensure a high-quality, unitary medical act that prioritizes the patient but also makes optimal use of available medical resources. In conclusion, recognizing the risk factors and symptoms and establishing treatment strategies can make a considerable contribution to improving the quality of care for pregnant women with renal failure.

GENERAL PART

Chapter 1. Renal system changes in pregnancy

During term pregnancy, increased cardiac output causes an increase in renal plasma flow and glomerular filtration rate (GFR) by up to 50%, reducing plasma urea and creatinine levels by 40-50% [9-13]. Serum creatinine is the main parameter for monitoring renal function and values above 0.87 mg/dL require further investigation [14-16]. Increased GFR and elevated glucose levels lead to glycosuria, and increased protein excretion is also an effect of increased GFR [9-13,17]. After 12 weeks of pregnancy, progesterone-induced changes favor dilation of the ureters and renal calices, increasing the risk of urinary tract infections [9,12,13]. Pregnant women are also at increased risk of developing renal lithiasis, which may lead to an increased frequency of renal colic, ureteral obstruction and, consequently acute kidney injury [18].

Chapter 2. Pregnancy-associated renal failure

2.1. Acute renal failure associated with pregnancy

2.1.1. Definition of pregnancy-associated acute renal failure

Pregnancy-associated acute kidney injury (AKI) is a complex condition with multiple underlying causes, having a major impact on maternal and fetal health [2,19]. Although manifested by elevated serum creatinine, standard diagnostic criteria (RIFLE, AKIN, KDIGO) are not validated in pregnancy due to the physiologic decrease of this parameter [20,21]. According to ACOG, AKI in pregnancy is defined by an increase in serum creatinine above 1.1 mg/dL [22,23].

2.1.2. Incidence of acute renal failure in pregnancy

The incidence of this condition varies according to demographic factors, with significant differences between developed and developing or poorly developed countries.

Studies detail an increase in the incidence of pregnancy-associated AKI in developed countries (1%-2.8%). These figures remain well below those in developing and underdeveloped countries, where the incidence can range between 4% and 26% [24-27].

2.1.3. Etiopathogenesis of acute renal failure in pregnancy

Pregnancy-associated acute renal failure may occur antenatally, peripartum or postpartum and is a potentially life-threatening condition for both mother and fetus. Usually, the main pathologies leading to AKI are obstetric causes such as septic abortion, emetic dysgravid dysgravidity, preeclampsia and associated complications, preterm placental abruption of the normally inserted placenta (PPIP), intrauterine fetal death (IUFD), hemorrhage or puerperal sepsis and develop in patients who previously had no renal pathology [28,29]. The etiology of pregnancy-associated AKI can be categorized according to the stage of pregnancy or its form - prerenal, intrinsic or postrenal [1,2,30,31].

2.1.4. Diagnostic criteria for acute renal failure in pregnancy

There are currently no standard criteria to define pregnancy-associated acute renal failure [2,32,33]. Physiological changes that occur in pregnancy lead to a drop in serum creatinine level below 0.8 mg/dL [1,14,29,34]. Currently, assessment of serum creatinine value is the most effective marker for the diagnosis of pregnancy-associated AKI [1].

In addition to serum creatinine, multiple investigations can be performed in case of suspected AKI in pregnancy: urinalysis, metabolic evaluation or coagulogram.

Ultrasonographic evaluation may be necessary to confirm or exclude obstructive pathologies or the presence of hydronephrosis [1]. Renal biopsy can be safely performed in the first and second trimester of pregnancy with minimal risk of complications up to 25 gestational weeks [1,35].

2.1.5. Maternal-fetal complications in pregnancy associated with acute renal failure

Maternal complications of acute renal failure associated with pregnancy

According to the literature, the pregnant patient who develops acute renal failure has a 10-fold increased risk of developing cardiovascular complications and may require prolonged hospitalizations [1,36]. In addition, this condition increases the risk of developing chronic kidney disease [1].

A study conducted from June 2019 to October 2020 in India on a group of 150 pregnant patients with AKI revealed 34% maternal deaths due to direct or indirect cause of acute kidney injury [28]. The leading cause of mortality was sepsis accounting for 49% of cases, followed by preeclampsia or eclampsia (41%) and obstetric hemorrhage (35.3%) [28].

Fetal complications of acute renal failure associated with pregnancy

Pregnancy-associated fetal complications aggravated by acute kidney injury are of particular importance. According to the literature, they include preterm delivery, low birth weight, the need for admission to the Neonatal Intensive Care Unit or perinatal death [1,2]. The risk of preterm delivery and intrauterine growth restriction (IUGR) is estimated to be 3-5 times higher in pregnant patients with AKI [1,37].

2.1.6. Predictors of adverse maternal-fetal prognosis

Risk factors associated with AKI during pregnancy include various demographic, clinical and paraclinical parameters, which are essential to identify high-risk pregnancies and to implement preventive measures to reduce maternal-fetal complications.

Demographic risk factors include maternal age over 35 years, race (women of color and Native American women are at increased risk), poor socioeconomic status, and limited access to prenatal care [1,36,38-41]. Smoking, genetic factors and rural background also contribute to higher mortality [21,42-46].

Clinical factors that worsen the prognosis include altered general condition, multiple pregnancies, obesity and associated diseases such as diabetes or hypertension [16,23,30,40, 47-50]. Paraclinically, elevated creatinine levels, severe proteinuria, elevated urea, anemia, thrombocytopenia, and elevated transaminases or CRP are correlated with an increased risk of maternal-fetal complications, including preterm delivery and intrauterine growth restriction [51-57].

2.1.7. Management of pregnancy associated with acute renal failure

General measures in pregnancy-associated AKI therapy include identification of the underlying pathology leading to the renal injury, volemic resuscitation, prevention of future renal injury, early initiation of dialysis when necessary, prompt fetal delivery when appropriate [2]. In terms of volemic resuscitation, it is crucial for prerenal pathologies leading to AKI, but this management should be carefully monitored, as pregnant patients with endotoxin-mediated renal injury or those with preeclampsia can easily develop pulmonary edema [2]. Complications caused by AKI can be treated as in non-pregnant patients, and if the pathology progresses, dialysis may be necessary and should be initiated [2].

2.2. Chronic kidney disease associated with pregnancy

2.2.1. Incidence of chronic kidney disease associated with pregnancy

The incidence of pregnancy-associated chronic kidney disease (CKD) is estimated to be 3%, and 1 in 750 pregnant patients have CKD stages 3-5 [58,59].

Pregnancy in the context of CKD carries multiple risks, including a significantly higher risk of developing preeclampsia and requiring cesarean delivery [3,60]. Also, the most common neonatal complications identified were preterm delivery and low birth weight [3,60].

2.2.2. Etiopathogenesis of pregnancy-associated chronic kidney disease

A wide range of pathologies can lead to the development of chronic kidney disease during pregnancy, many of which are common to those occurring in the general population.

The most common conditions are:

- Congenital renal or urinary tract abnormalities
- Hypertensive nephrosclerosis
- Diabetic nephropathy
- IgA nephropathy
- Lupus nephritis [61].

2.2.3. Maternal complications in pregnancy associated with chronic kidney disease

Studies have shown that there is an increased risk of preeclampsia, especially in cases with associated etiology of glomerulonephritis or polycystic kidney disease [60,62]. CKD is also associated with an increased rate of cesarean section, especially in cases of diabetic nephropathy [62].

Recent analyses of more than 38 million pregnant women in the USA (2010-2020) showed that the maternal mortality rate is highest in patients with stage 5 CKD stage 5, whereas pregnant women with stage 1 CKD stage 1 had no deaths [63]. In the UK, a study conducted between 2003-2017 in specialized centers demonstrated that chronic hypertension and proteinuria before or at the onset of pregnancy are major predictors of a poor prognosis in CKD stages 3-5 [58].

According to the data presented, it can be stated that the most common maternal complications that may occur in pregnancy-associated CKD associated with pregnancy are:

- Preeclampsia
- Cesarean delivery
- Death
- Renal replacement therapy - depending on the stage of CKD[58,62,63].

2.2.4. Fetal complications in pregnancy associated with chronic kidney disease

Among the most common fetal complications are preterm delivery, low birth weight and the need for admission to the Neonatal Intensive Care Unit [61,64].

Fetal complications also depend on the mother's CKD stage: preterm delivery, intrauterine fetal death, the need for admission to the NICU [58].

Birth weight and gestational age were lower the more advanced the CKD stage. Chronic arterial hypertension is the strongest predictor for preterm delivery before 34 weeks' gestation [58]. Proteinuria > 1g/24 h before or early in pregnancy is the strongest predictor for birth weight below the 10th percentile. Neonatal mortality has occurred among patients with CKD stage 4 and 5 [58].

2.2.5. Management of pregnancy associated with chronic kidney disease

Preconception counseling involves a rigorous clinical and paraclinical evaluation, with urinary tests such as proteinuria and blood pressure being among the most important parameters that should be investigated and optimized preconceptionally [65]. Assessment of serum creatinine and GRF is also important, especially in patients with CKD stages 3-5 [58].

General data from studies of patients with different etiologies and an increased risk of developing preeclampsia suggest that starting low-dose aspirin before 16 weeks' gestation decreases the risk of early preeclampsia [65-67].

Patients with CKD should be assessed at least monthly, with increasing frequency of visits depending on blood pressure, renal pathology activity and fetal needs [65,68,69].

Delivery should be at term in the absence of maternal or fetal indication requiring emergency cesarean section [60,65,70-72]. According to the literature, CKD is not an indication for cesarean section, but nevertheless, surgery is more common in patients with CKD [62,65].

Chapter 3. Working hypothesis and general objectives

The present paper "Guidelines for diagnosis and treatment in pregnancy associated with renal failure and the impact of therapeutic attitude on maternal-fetal prognosis" aims to analyze demographic, clinical and paraclinical parameters in order to establish a diagnostic plan and therapeutic conduct, in relation to the risk of maternal-fetal complications. The thesis is structured in three research directions, aimed at investigating the influence of the severity of renal disease in the prediction of maternal-fetal outcome.

The first research direction is represented by a descriptive statistical analysis of the patients included in the study, while the second research direction with the main role in the research aimed to identify the predictors associated with an increased risk of maternal-fetal complications (demographic, clinical and paraclinical variables), emphasizing the parameters of severity of renal disease in relation to the occurrence of maternal death or intrauterine fetal death. The third, secondary line of research describes a comparative statistic between patients

with renal injury and a control group, whose serum creatinine values on admission were prespecified to be between 0.8 mg/dL - 1.1 mg/dL.

Therefore, the research objectives can be described as:

1. To describe the demographic profile of pregnant women at risk of developing acute kidney injury
2. To identify maternal factors leading to an unfavorable prognosis of pregnancy associated with kidney injury
3. Identification of paraclinical parameters associated with unfavorable pregnancy outcome
4. Assessment of fetal prognosis in pregnancies associated with acute/chronic renal injury
5. Description of some diagnostic criteria for pregnancy-associated renal injury, in particular in relation to paraclinical parameters whose threshold value associates maternal-fetal complications
6. Correlations between different risk variables

Chapter 4. General research methodology

The research in the present thesis is based on a descriptive, observational, non-randomized, observational analysis, as well as on a retrospective and prospective case-control study, with the aim of identifying risk factors influencing the maternal-fetal prognosis in patients with renal injury, compared to those with nitrogen retention parameters below the diagnostic limit of renal failure.

In the present research, medical data were extracted from the patient's observation sheets, as well as from the InfoWorld computer system of the Obstetrics-Gynecology Clinic of the University Emergency Hospital of Bucharest. Anamnesis and the medical records of the dispensed pregnant women were also important ways of obtaining information about the medical history and pathology associated with pregnancy. At the same time, the information collected involved a multidisciplinary analysis, including the Neonatology Department, the Nephrology Department, the Central Laboratory, the Pathologic Anatomy Department and the Radiology and Imaging Department.

The research in the present thesis was performed on a sample of 112 pregnant women with renal insufficiency and a group of 267 pregnant women with serum creatinine values below

the diagnostic value of renal injury (between 0.8-1.1 mg/dL) who gave birth in the Obstetrics-Gynecology Clinic of the University Emergency Hospital Bucharest between 01.01.2017 and 31.12.2024.

Inclusion criteria:

- Pregnant women with chronic kidney disease, regardless of the underlying pathology (glomerulonephritis, systemic lupus erythematosus, chronic pyelonephritis, etc.)
- Pregnant women with acute renal failure, irrespective of the triggering factor (sepsis, hypovolemia due to severe hemorrhage)
- Birth in the Obstetrics-Gynecology Clinic of the University Emergency Hospital Bucharest

Exclusion criteria:

- Absence of informed consent of the patient
- Pregnant under 18 years of age
- Pregnant women with acute renal failure due to first trimester septic abortions
- Cases of renal failure associated with ectopic pregnancies

The research was carried out with the approval of the Ethics Committee of the University Emergency Hospital of Bucharest no. 26407/17.05.05.2021. The use of the data provided by the patients was exclusively for scientifical purposes, with the guarantee of confidentiality of the information presented when explaining the objectives of the study.

Chapter 5. Results

5.1. First line of research

The first line of research aimed at a comparative statistical analysis of groups of pregnant women with acute and chronic renal failure, following demographic parameters, obstetric and pathologic personal history, paraclinical and fetal parameters - Apgar index (AI) at 1 minute, fetal birth weight, fetal intrauterine growth restriction, MFIU.

Age-specific analysis of patients with acute kidney injury showed that the highest serum creatinine values were recorded in patients under 20 years of age (2.17 ± 1.18 mg/dL). However,

in the age group 35-39 years, the need for dialysis and maternal mortality were significantly higher (6.67% and 4.44%, respectively).

With respect to background, rural patients had higher serum creatinine values (1.75 ± 0.93 mg/dL versus 1.51 ± 0.61 mg/dL in urban areas). However, maternal mortality was higher in urban areas (14.29%), while the number of cases of intrauterine fetal death was significantly higher in rural areas (19.51% vs. 6.12% in urban areas).

There were no statistically significant differences in body mass index (p=0.98) between the analyzed groups, most of the patients being normal weight. Also, gestational age at delivery was similar between the AKI group (34.1 ± 4.7 weeks) and group B (33.7 ± 3.9 weeks).
In terms of parity, the primiparous B group had lower serum creatinine values (2.33 ± 1.97 mg/dL) than the multiparous group (3.88 ± 2.79 mg/dL). Also, multiparas required dialysis in a higher percentage (66.67% vs. 46.15%), but the only death was among primiparas.

Dispensing pregnancy did not show a significant difference between the analyzed groups (p=0.71). However, patients with AKI who received adequate prenatal care had a lower serum creatinine value on admission (1.53 ± 0.72 mg/dL) compared to those who were not discharged (1.82 ± 0.88 mg/dL), suggesting a benefit of pregnancy monitoring on renal function.

In the group of patients with acute kidney injury, the majority were primiparous (68.69%) and from urban areas (61.29%), with a mean age significantly higher than those from rural areas. Similarly, in the group of patients with chronic kidney disease (CKD), the majority were also primiparous and the mean age of those from urban areas was higher than those from rural areas.

Pregnancy hypertension and its complications were common in both groups (82% in AKI and 63% in CKD). There were no significant differences in patient age or admission serum creatinine values according to the presence of hypertension. However, patients with CKD without hypertension had higher creatinine values compared with hypertensive patients. Thrombophilia did not significantly influence the length of hospitalization of hypertensive patients.

Urinary tract infections were associated with higher creatinine values on admission in the AKI group, but during hospitalization, this value decreased more significantly in patients

with infection than in those without. In contrast, in the CKD group, the presence of genital infections resulted in a significantly longer duration of hospitalization.

Severe pre-eclampsia was the main indication for caesarean section in both groups (34.57% in AKI and 59.09% in CKD). 23.33% of patients with AKI required dialysis, and maternal mortality in this group was significantly higher compared to patients who did not need renal replacement (38.10% vs. 5.80%).

ROC curve analysis revealed threshold values for some biological parameters correlated with a poor prognosis: hemoglobin below 9 g/dL, hematocrit below 25%, leukocytes above 17,000/μL, INR >1.05, APTT >32 sec, proteinuria above 200 mg/L, serum creatinine above 1.15 mg/dL, urea above 48 mg/dL and GRF below 58 mL/min/1.73m². C-reactive protein values above 7 mg/L and blood glucose above 90 mg/dL were also associated with increased maternal and fetal mortality.

Mean fetal weight was higher in the AKI group compared with the CKD group, but intrauterine growth restriction was significantly more frequent in the CKD group (82% vs. 53%). Patients with AKI and creatinine below 1.15 mg/dL had a favorable outcome, with no maternal deaths and a significantly lower need for ICU admission compared with patients with creatinine above this threshold.

5.2. Second line of research

The second line of research focused on determining the factors leading to an unfavorable maternal and fetal prognosis.

The study found that adequate prenatal care is associated with a favorable prognosis in pregnancies with acute or chronic renal failure, reducing the risk of maternal and fetal death. The mean age of patients with creatinine values below 1.15 mg/dL was higher, and each additional week of pregnancy was correlated with a 14% reduction in the risk of death. Lack of antenatal monitoring increased the risk of mortality almost threefold, and an earlier delivery was associated with a 40% increased risk of an unfavorable outcome.

Biological parameters demonstrated significant correlations with maternal-fetal prognosis. A hemoglobin above 9 g/dL and a hematocrit above 25% significantly reduce the risk of death, while leukocytes above 17,000/μL and high CRP values (>7 mg/L) are strongly associated with poor prognosis. Also, glycemia above 90 mg/dL increases the risk of death by

6.2-fold, and high INR (>1.09) and APTT (>32.6) values are correlated with a higher likelihood of severe outcome.

Urinary tract infections did not significantly influence the overall prognosis, but resulted in a higher rate of Neonatal Intensive Care Unit admissions. In contrast, other types of infections were associated with an increased risk of maternal and fetal mortality. Caesarean delivery was correlated with a more favorable outcome, whereas natural childbirth had a four-fold higher risk of poor prognosis. These factors emphasize the importance of close monitoring and early intervention in pregnancies complicated by renal failure.

5.3. Third line of research

The comparative study between patients with pregnancy-associated kidney disease (group A) and those with serum creatinine between 0.8-1.1 mg/dL (group B) revealed significant differences in pregnancy outcome and fetal prognosis. The mean gestational age was lower in group A (34 ± 4.5 weeks) compared to group B (37.2 ± 3.0 weeks), and extreme prematurity was 12.5% in group A compared to only 1.87% in the control group. Antenatal care was also poorer in group A (26% of patients without antepartum medical check-up compared to 15% in group B, p=0.009).

Among hypertensive patients, the mean fetal weight was significantly lower in group A (2032.06 ± 822.65 g) than in group B (2508.64 ± 978.88 g). The Apgar index at 1 minute was also lower in group A (5.83 ± 3. 10) compared to group B (7.39 ± 2.49), and intrauterine growth restriction was more frequent in group A (66.23% vs. 52.43%). Intrauterine fetal mortality (IUFM) was almost double in hypertensive patients with renal injury (9.09% vs. 4.85%).

Duration of hospitalization was significantly longer in group A (12 ± 13 days) compared to group B (6 ± 6 days). Fetal weight was influenced by hemoglobin level, values above 9 g/dL being associated with higher newborn weight (2197.83 ± 966.31 g in group A and 2878. 42 ± 780.06 g in group B). The Apgar index was lower in cases with hemoglobin below 9 g/dL, and patients with leukocytes above 17,000/μL had a lower gestational age in group A (32.42 ± 4.86 weeks) compared to group B (36.68 ± 3.15 weeks). These results emphasize the impact of renal failure on maternal-fetal prognosis and the importance of careful monitoring of these pregnancies.

6. Discussions

The results obtained in the current research can be correlated with specialized studies.

The study reported an incidence of 0.85% for acute kidney injury and 0.16% for chronic kidney disease. The overall incidence of pregnancy-associated AKI has been reported in the literature as 2%, with wide variations reported in developed, developing and underdeveloped countries, while the incidence of CKD as 1.2% [23,72-75].

The median age of patients with AKI was 32 years, and those requiring dialysis were older. A study conducted by Roberto et al. in 2024 described the mean age of patients requiring dialysis was 31.4 years, lower than that reported in the present research [76].

The most common etiology of AKI due to renal cause in the present research was preeclampsia with 26.67%, followed by detachment of normally inserted placenta (10%). The frequency of etiologies described in the present study are consistent with those described by Shija et al. on a group of 51 pregnant women with pregnancy-associated AKI, where preeclampsia was the cause of the onset of renal pathology in 23.5% [77].

Intrauterine growth restriction and intrauterine fetal intrauterine mortality are more common in patients with renal injury compared to those having serum creatinine values <1.1 mg/dL. Also, the duration of hospitalization is much prolonged compared to patients having nitrogen retention parameters within normal limits. Hemoglobin above 9 g/dL was associated with higher fetal weight, and elevated leukocyte values were correlated with lower gestational age.

The study confirmed that dialysis is associated with a favorable maternal prognosis in acute renal failure, with a recovery rate of 61.90%. However, patients with AKI who did not require renal replacement had an even better prognosis (94.20%).

Mortality in the AKI group was 13.33%, lower than that reported by Goplani et al. from a group of 70 patients with AKI, where 18.57% deaths were reported [78].

Increased proteinuria and hyperuricemia were associated with lower fetal weight and unfavorable fetal prognosis. In CKD, patients with creatinine below 1.24 mg/dL, low proteinuria, and well-controlled blood pressure did not have renal decline or increased risk of intrauterine fetal death. Preterm delivery and intrauterine growth restriction were more frequent in advanced stages of CKD, but Apgar index did not vary significantly between subgroups.

Regarding chronic kidney disease, the association with dialysis leads to a negative prognosis, with a success rate of 89.2% and a mean serum urea value of 57 mg/dL [52,79]. Studies show in these cases an increased risk of premature births (85%), neonatal death (11%) or need for neonatal intensive care unit admission of 67% [80]. In the current research, we recorded a 4.54% neonatal death rate in patients with CKD requiring dialysis, a 25% rate of premature births and a 83.33% neonatal intensive care unit admission rate.

7. Conclusions and personal contributions

The results described in the present research led to the following conclusions:

1. The incidence of acute kidney injury in pregnancy was 0.85% and the incidence of cases of chronic kidney disease was 0.16%. The low incidence of cases of acute kidney injury developed postpartum did not allow a proper statistical analysis. The decrease in the incidence of cases with this pathology can also be described by the progressive decrease in the number of births occurring in the Bucharest Emergency University Hospital with the SARS-CoV-2 pandemic
2. The predominant etiology of AKI was preeclampsia (26.67%), while in the CKD group the most frequent cause was membranous glomerulonephritis (31.82%).
3. The maternal age of the pregnant women with AKI and CKD was 31 +/- 7 years, lower than in the control group where we recorded an average of 32 +/- 6 years. Also, in the group of patients with AKI, maternal age under 20 years was associated with the highest mean serum creatinine value (2.17 +/- 1.18 mg/dL), while age between 35-39 years was associated with the highest risk of renal replacement therapy (6.67%) and mortality (6.67%).
4. Urban background is associated in acute kidney injury during pregnancy with a higher risk of maternal death (14.29%), while rural patients had a higher risk of intrauterine fetal death (19.51%).
5. BMI >30 was associated with a higher percentage of cases requiring the institution of renal replacement therapy (69.23% compared to 24.24% in cases with BMI below 30). BMI >30 was not associated with increased mortality.
6. Multiparity was associated with higher hospitalization serum creatinine values compared with primiparous patients in AKI (3.88 +/- 2.79 mg/dL vs. 2.33 +/- 1.97 mg/dL).

7. Multiparity was associated with a higher risk of need for dialysis institution (66.67% vs. 46.15% in primiparous).
8. Increasing parity by 1 was associated with a 40% higher risk of unfavorable maternal-fetal prognosis.
9. Adequate antenatal care is associated with an approximately 3-fold decrease in maternal-fetal mortality and morbidity.
10. Each additional week added to gestational age was associated with a 14% reduction in the risk of an unfavorable maternal and fetal prognosis.
11. The association of urinary tract infections in pregnancy with acute kidney injury is described by a higher mean serum creatinine value than in its absence (2.02 +/- 1 mg/dL vs. 1.51 +/-0.68 mg/dL), but no adverse maternal-fetal prognosis.
12. The association of genital infections in pregnancy with chronic kidney disease results in prolonged hospitalization (31.25 +/- 43.85 days compared to 15.28 +/- 9.93 days).
13. The absence of other types of infections (bronchopneumonia, enterocolitis) is associated with a maternal-fetal prognosis 4 times more favorable.
14. The highest risk of prematurity in the CKD group was in patients with lupus nephritis (100%), with a mean gestational age of 30 +/- 3.74 weeks.
15. The risk of developing eclampsia is much higher in patients with AKI than in pregnant women with serum creatinine below 1.1 mg/dL (7.78% vs. 1.12%).
16. Preeclampsia in patients with AKI does not associate a higher risk of prematurity compared to patients who developed AKI from other causes (35.31 +/- 3.48 vs. 33.51 +/- 5.19 weeks of gestation). Moreover, in these patients, considering only singleton pregnancies, fetal birth weight was higher than in singleton pregnancies with AKI from other causes (2542.74 +/- 849.45 grams vs. 2134.26 +/- 1015.61 grams).
17. Caesarean delivery in patients with acute kidney injury was not associated with prolonged hospitalization. However cesarean delivery patients had a decrease in mean serum creatinine during hospitalization with a mean of 0.53 +/- 0.87 mg/dL vs. 0.06 +/- 0.66 mg/dL in those who delivered naturally. As for the mean urea value, it showed a much higher increase during hospitalization in patients who delivered vaginally (17.7 +/- 31.78 mg/dL vs. 0.51 +/- 26.68 mg/dL).

18. Regarding hematologic parameters, a mean hemoglobin <9 mg/L and a hematocrit <25% are associated with a 7-fold and 4-fold increase in the risk of a poor prognosis, respectively. A leukocyte count above 17000/μL, is associated with a 3.46-fold increase in the risk of maternal-fetal complications.
19. In terms of coagulogram parameters, an APTT >32.60 sec is associated with a 3.89-fold increase in unfavorable prognosis, while an INR >1.09 increases the risk by 9.12-fold. Hospitalization times are significantly higher in patients with renal injury and coagulopathy compared to controls.

In terms of inflammatory parameters, a CRP value >7 mg/L is associated with a 7.22-fold increased risk of unfavorable prognosis. Also, an increased CRP value is associated with a low fetal birth weight compared to the control group.

21. In terms of biochemical parameters, the cut-off value of serum creatinine was recorded as 1.15 mg/dL. A serum urea value above 48 mg/dL is associated with a 2.41-fold increase in the risk of developing complications, while a glomerular filtration rate above 58 is associated with a 6-fold decrease in maternal and fetal mortality and morbidity.
22. A blood glucose value greater than 90 mg/dL is associated with a 6.2-fold increase in the risk of maternal-fetal complications.
23. Proteinuria above 200 mg/L is associated with a 4.14-fold increased risk of maternal-fetal complications.
24. Renal injury was associated overall with lower fetal birth weight compared to controls (2893 +/- 770 grams vs. 2184 +/- 923 grams, $p<0.001$).
25. The Apgar index at 1 minute is lower in patients with renal injury than in patients with serum creatinine below 1.1 mg/dL/ (8.43 +/- 1.53 vs. 6.68 +/- 2.60, $p < 0.001$).
26. Renal injury associated an increased risk of intrauterine growth restriction (59%).
27. Patients with renal injury benefit more frequently from albumin and diuretic administration ($p<0.001$). In these situations, the majority of patients associate a prolonged hospitalization period and a higher need for renal replacement therapy.
28. Dialyzed patients maintaining a serum urea value above 60 mg/dL have a higher death rate.

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