Anesthetic Management of Pregnant Patient with Renal Disease

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9.1 Introduction

Changes in hormonal activity, increased metabolic requirements of the growing fetus and placenta, and mechanical obstruction of the growing uterus lead to reversible anatomic and physiological changes during pregnancy in the renal system [1]. A detailed awareness of renal physiology is of crucial importance in the perioperative evaluation of a kidney disease. There are basically two points to be considered:

1. Effect of pregnancy on maternal kidney disease
2. Maternal and fetal effects of kidney disease

Careful monitoring of both of these two key points in the preoperative and perioperative period will ensure proper planning and implementation of the anesthetic approach.

9.1.1 Changes Encountered in the Renal System During Pregnancy

During normal pregnancy, the size of the kidney grows up to 1 cm. Ureters and renal pelvis are initially dilated by progesterone-related atony followed by mechanical pressure exerted due to the growing uterus starting from the 12th week of pregnancy until the term. Prevention of urinary output from the kidneys and the bladder caused by that mechanical pressure effect increases the risk of urinary system infections which might further precipitate preterm birth.

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B. Gunaydin, S. Ismail (eds.), *Obstetric Anesthesia for Co-morbid Conditions*,
https://doi.org/10.1007/978-3-319-93163-0_9

In addition to these changes, there is a 20% decrease in systemic vascular resistance, while blood volume and cardiac output increase 40% and 50%, respectively [2]. Considering the important role of the kidney in maintaining homeostasis of fluid and blood pressure, the resulting cardiovascular changes have significant effects on renal function. During pregnancy, renal blood flow increases by 80%, while glomerular filtration rate (GFR) increases approximately by 50% [3]. Reabsorption of water and electrolytes from the tubes also increases, thus allowing liquid and electrolyte balance to be maintained. Blood urea nitrogen (BUN) and serum creatinine levels in healthy pregnancies are about 50% of a nonpregnant woman where normal reference range for BUN is 8–9 mg/dl and for serum creatinine is 0.4–0.6 mg/dl [3]. Therefore, the creatinine clearance is increased. Glomerular permeability is partially increased in pregnancy, and proteinuria (normal up to 300 mg/day) is encountered [3].

Maternal hyperventilation-related arterial carbon dioxide pressure decrease results in respiratory alkalosis. Subsequently compensatory changes characterized by a decrease in serum bicarbonate and basal negativity can be also encountered. Reduction in glucose reabsorption capacity and glycosuria may be observed secondary to the already-affected tubular functions during pregnancy. It is a physiological condition for the pregnant woman to gain weight up to 12 kg on average due to sodium and water retention. Plasma osmolality is also reduced by 10 mOsm/kg. These changes are related to the altered response of the antidiuretic hormone in the renal tubule. In addition, many vitamins that are not normally excreted in the urine are lost during pregnancy.

Evaluation of these changes during pregnancy is very important in the perioperative evaluation for proper planning of the perioperative anesthetic approach of the pregnant woman.

The values considered normal in a non-pregnant woman when occur in a pregnant woman indicates that her renal function is impaired. In pregnancy, serum creatinine levels of 0.8 mg/dl or BUN level ≥16 mg/dl or proteinuria more than 300 mg/day are considered as abnormal [2].

9.2 Anesthetic Approach to Pregnant Women with Kidney Disease

An anesthesiologist may come across with pregnant women with kidney diseases which have different diagnoses. Kidney diseases during pregnancy are listed below:

1. Acute renal failure (ARF)
2. Chronic renal failure (CRF)
3. Cases on dialysis treatment
4. Pregnancy after renal transplantation

The severity of kidney disease, biochemical test results, and accompanying comorbid diseases serve as a guideline in determining the anesthesia technique.

Fluid resuscitation to be performed perioperatively for the pregnant women with acute renal failure differs from the pregnant women with chronic renal failure [4]. For that reason, after overview of physiopathological conditions of the pregnant women, anesthesia choices for the pregnant women with acute or chronic renal failures and/or receiving hemodialysis treatment and pregnant women with kidney transplant will be addressed.

9.2.1 Acute Renal Failure and Pregnancy

Acute renal failure (ARF) is rare during pregnancy. The prognosis is usually better than in non-obstetric cases [4]. Frequently hyperemesis gravidarum-induced hypovolemia and uterine hemorrhage cause prerenal failure. Sudden hypovolemia resulting in acute tubular necrosis results in azotemia [5].

One of the causes of acute renal failure in pregnancy is *renal cortical necrosis*. Septic abortion, amniotic fluid embolism, acute tubular necrosis, drug-induced acute interstitial nephritis, acute glomerulonephritis, acute pyelonephritis, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, acute fatty liver of pregnancy, and idiopathic postpartum renal failure may cause renal cortical necrosis which can occur in both early and late stages of pregnancy [4, 6]. Acute renal failure due to renal cortical necrosis is irreversible because there is bilateral, symmetric, and ischemic necrosis in the cortex of the kidneys. Patients may present a patchy necrosis despite the fact that the cortex involvement is often diffuse in the majority of the cases. Once diffuse cortical necrosis is developed, patients can survive by dialysis or have cure after transplantation. Renal functions still go on by decreasing in function in the patchy cortical necrosis, but these patients also require dialysis after a while. If prepregnancy azotemia is present, both maternal and fetal renal functions are negatively affected [7].

Rapid deterioration of renal function is observed in 35% of those with creatinine levels of ≥1.6 mg/dl [8]. Likewise, in those with reflux nephropathy, pregnancy accelerates the progression to end-stage renal failure [8, 9].

Acute renal failure may develop because of postrenal causes such as urolithiasis, pressure exerted by growing uterus to ureter, or tubo-ovarian masses [6].

9.2.1.1 Preeclampsia and Renal Failure

In preeclamptic pregnant women, renal blood flow and GFR are reduced by about 30–40%, as opposed to healthy pregnant women [9–11]. The serum creatinine and BUN levels are similar to those of healthy pregnancies. However, as the severity of preeclampsia increases, renal perfusion deteriorates, creatinine clearance decreases, and proteinuria increases. If the preeclampsia with acute renal failure is treated properly, renal function returns to normal after delivery.

The nephrotic syndrome rarely occurs in pregnancy and is usually caused by preeclampsia [12]. In the first trimester, intrinsic renal disease is present, and perinatal mortality is reported to be greater than 40% [12].

In addition to impaired renal function, risk of disseminated intravascular coagulation is of note in eclamptic pregnancies.

HELLP syndrome develops in 10–20% of parturients with severe preeclampsia and/or eclampsia. These cases are manifested with a clinical proteinuria (86–100%), hypertension (82–88%), right upper quadrant/epigastric pain (40–90%), nausea and/or vomiting (29–84%), headache (33–61%), or visual changes (10–20%) [12, 13].

9.2.1.2 The Approach to Pregnant Patients with Acute Renal Failure

In pregnancies with prerenal failure, to prevent renal damage and ensure renal perfusion, volume resuscitation at early stage should be considered to maintain adequate intravascular volume. Invasive arterial pressure monitoring may be needed to provide optimal intravascular volume for controlling the blood pressure. Diuretics should be used if heart failure is seen as a result of an increase in intravascular volume. If hypovolemia due to blood loss and subsequent acute renal failure develops, appropriate blood and blood product replacement should be performed.

Dialysis is started if serum creatinine level is >3.5 mg/dl or GFR <20 mL/min in pregnancies with renal disease [4]. Better fetal outcomes are observed after long-term and more frequent hemodialysis. The most important point is to avoid hypotension during hemodialysis because of its fetal negative effects resulting from uteroplacental failure. Although the prevalence of spontaneous abortus and preterm delivery during pregnancy is high, fetal survival in ongoing pregnancies is nearly 71% [7]. Intrauterine fetal growth retardation is a problem especially in developing countries [4].

Daily intake of protein, potassium, and phosphate should be limited in pregnancies with ARF. In eclamptic pregnant women for seizure prophylaxis, intravenous loading dose of 4 g of $MgSO_4$ in 10–15 min followed by an infusion of 1 g/h.

Besides the general treatment for pregnant women with acute renal failure, it is also important to terminate the pregnancy at the best available fetal maturity by evaluating severity of preeclampsia and maternal and fetal well-being.

9.2.1.3 Anesthesia Management

Changes in intravascular volume status, electrolyte imbalance, coagulopathy, thrombocytopenia, platelet dysfunction, and altered drug clearance should be considered in determining the anesthesia type. Platelet dysfunction may occur in patients with preeclampsia particularly receiving low-dose aspirin therapy. Although corticosteroid use is controversial, there are some reports that corticosteroids increase platelet count and fetal lung maturation in pregnancies with HELLP syndrome [14, 15]. If there is no coagulopathy, thrombocytopenia, or platelet dysfunction, regional anesthesia could be preferred after obtaining the patient's consent.

In cases where hemodynamics is not stable, invasive pressure monitoring may be necessary. The GFR should be monitored when administering intravenous anesthetics, inhalation agents, opioids, muscle relaxants, and perioperative antibiotics. Drugs with short duration of action and nontoxic to the kidney or having less metabolism (such as desflurane, propofol, atracurium/cisatracurium, remifentanil) should

be preferred [12]. Neuromuscular monitoring is recommended. Follow-up in postoperative intensive care unit in pregnancies with acute renal failure reduces morbidity and mortality.

9.2.2 Chronic Renal Failure and Pregnancy

Chronic renal failure (CRF) is seen in 0.03–0.12% of all pregnancies [4]. In pregnancies with CRF, the live birth rate varies depending on the severity of renal failure and the presence of hypertension [16]. Nephrologists do not recommend pregnancy to women with severe renal failure (if serum creatinine ≥2.5 mg/dL); these cases are usually infertile.

It has been found that approximately 20% of the pregnant women who developed early preeclampsia had most probably previously unknown chronic renal disease [4, 17]. The risk of developing preeclampsia in chronic renal failure cases increases according to the degree of impairment in renal function. It is 20% in patients with mild renal impairment, 60–80% in severe renal failure, and approximately 5% in the general population and is often associated with hypertension and proteinuria present before the pregnancy [18]. Gestational course and results are usually good in women who have mild renal failure with a serum creatinine level of <1.4 mg/dl.

Women with diabetic nephropathy and normal serum creatinine levels do not experience deterioration in kidney functions during pregnancy, but the risk of preeclampsia and preterm labor is increased. For that reason, the metabolic status before and during pregnancy should be well monitored, and antihypertensive treatment with low-dose aspirin is required starting from the 12th week of pregnancy [19].

Systemic lupus erythematosus (SLE) is often seen in women of childbearing age and leads to lupus nephritis. Women with SLE are advised to conceive before their renal functions worsen (at least after 6 months of remission phase). Presence of an active disease, impaired renal function, hypertension, and antiphospholipid antibodies has increased maternal and fetal morbidity and mortality [20].

Pregnant women with chronic renal failure cannot maintain the required GFR increase in normal pregnancy in addition to vitamin D3, erythropoietin, and renin production increases. This leads to normochromic normocytic anemia, a decreased plasma volume, and vitamin D deficiency. In preeclampsia due to reduced plasma volume, resulting prerenal failure and this cause more renal damage. Venous thromboembolism risk is increased in the pregnancies with severe proteinuria (3 g/day), and it requires prophylaxis with low molecular weight heparin [12]. Mild kidney dysfunction is observed in the majority of chronic renal failure pregnancies. In these cases, kidney function is not affected negatively from pregnancy. However, a rapid deterioration of renal function may be seen in the presence of proteinuria and hypertension prior to pregnancy. Maternal and fetal morbidity and mortality are increased in pregnancies with severe renal failure. Therefore, these cases should be evaluated before pregnancy, and they should be informed about the possible risks and warned about their medications. Thus, it has been reported that both maternal and fetal risks

such as spontaneous abortion, prematurity, and intrauterine growth retardation (IUGR) can be minimized [4, 21]. Anemia, hypertension, and proteinuria presenting with CRF should be treated.

Low-dose aspirin (50–150 mg/day) in the early period of gestation (12th week) reduces the risk of preeclampsia and the subsequent renal damage observed [4]. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers should not be used as an antihypertensive due to their teratogenic effects. If the diastolic blood pressure is above 90 mmHg, it causes renovascular injury and low blood pressure values also limiting fetal growth and causes IUGR [11].

Another important finding of chronic renal failure is anemia. Therefore ferritin levels should be assessed; iron and erythropoietin therapy should be initiated to maintain hemoglobin level between 10 and 11 g/dl [4]. Until 30th week of gestation every 2–3 weeks and after weekly, hemoglobin levels should be checked. Antenatal tests showing fetal growth should be initiated at week 28 and should be closely monitored against the risk of IUGR.

9.2.2.1 Anesthesia Management

Pregnant patients with CRF should be carefully evaluated before anesthesia. These patients should be evaluated in terms of the accompanying medical conditions or diseases (such as anemia, hypertension) and the drugs they use. The physiological anemia of the pregnancy becomes even more prominent due to such reasons as erythropoietin deficiency in CRF and shortened erythrocyte life.

A multidisciplinary team approach including nephrologists, anesthesiologists, and obstetricians is a must. Monitoring of changes in plasma volume and electrolyte balance in pregnant patients with CRF is of critical importance in determining the appropriate need for any replacement and to choose the most proper anesthesia modality.

Presence of left ventricular hypertrophy and decreased left ventricular ejection fraction as a consequence of uremic cardiomyopathy will negatively affect hemodynamics in the perioperative period [22]. *Fluctuations* in hemodynamic may threaten both maternal and fetal life because of the sympathetic block caused by regional anesthesia in these pregnancies. Central blocks should be avoided in cases with cardiomyopathy.

Gastric emptying is further reduced in pregnant patients with CRF compared to nonpregnants. Therefore, aspiration prophylaxis using H_2 receptor blocker must routinely be performed [4]. Metoclopramide is best avoided because of the reduced clearance and the prolonged elimination half-life.

Invasive arterial blood pressure monitoring is required for anticipated hemodynamic fluctuations. Central venous pressure should also be monitored in pregnancies with cardiomyopathy.

Due to the hypoalbuminemia, free fractions of drugs are increased leading to reduced dose requirements of drugs that are bound to albumin, e.g., benzodiazepine and thiopental sodium. The pharmacokinetics of propofol does not change [4, 23]. Alfentanil can be a safe option because it has short duration of action and its metabolism does not change. Remifentanil is a better choice because of its rapid metabolism by plasma esterases. Meperidine hydrochloride is avoided

because it has an active metabolite (normeperidine) which is neurotoxic that may cause convulsions [4]. Atracurium and cisatracurium are the preferred safe non-depolarizing muscle relaxants because they are metabolized by Hoffman elimination independently from the liver or kidney [1]. Succynilcholine should be avoided in pregnancies with hyperpotassemia. Hypermagnesemia and metabolic acidosis may prolong the duration of action of all non-depolarizing neuromuscular blockers. Neuromuscular monitoring is necessary in these cases [12, 22]. The duration of action of rocuronium is prolonged in these cases. Sugammadex (4 mg kg^{-1}) rapidly and safely reverses profound rocuronium induced neuromuscular blockade [24].

Although inhalation agents lead to reversible renal dysfunction by reducing renal blood flow, GFR, and urinary output, the uptake and distribution of these drugs remain almost unchanged in cases with CRF [4]. Sevoflurane is not preferred in case of using low-flow anesthesia. Desflurane is a good choice in the pregnancies with CRF. Normovolemia should be preserved by replacing with appropriate fluids (0.9% NaCl). Potassium-containing fluids should be avoided [11].

Of note, thrombocytopenia, platelet function, and coagulation abnormalities are taken into account when selecting anesthesia method.

Hydration before neuraxial blockade should be done in order not to decrease the renal perfusion pressure. During neurological blockade, sensory block starts more quickly and reaches higher levels. Excessive hemodynamic fluctuations associated with autonomic neuropathy or neuraxial blockade are not rare [4]. Epidural anesthesia should be preferred to spinal anesthesia. Invasive hemodynamic monitoring is recommended to avoid hypotension and to maintain renal perfusion with available vasopressors (phenylephrine or ephedrine).

9.2.3 Dialysis and Pregnancy

Successful pregnancies can be observed in patients undergoing peritoneal dialysis. After peritoneal dialysis, uremia is reduced, and rapid fluid balance changes are prevented. As pregnancy progresses, the growing uterus may reduce peritoneal blood flow and prevent adequate fluid to make effective peritoneal dialysis.

Pregnancy is not uncommon in women under hemodialysis. The live infant rate in hemodialysis-dependent pregnancies is around 60% [25]. Investigations have reported a positive correlation between more frequent and intense hemodialysis and better neonatal outcome [4, 26].

It is necessary to immediately initiate continuous renal replacement therapy (CRRT) in the presence of refractory hyperkalemia/metabolic acidosis and encephalopathy or severe uremia that could result in pericarditis [18]. Since it does not lead to hemodynamic fluctuations, it is applied safely both in terms of maternal and fetal well-being.

Hypokalemia/hypophosphatemia should be avoided in pregnant women dependent to hemodialysis. As in other pregnancies, hypotension may cause fetal distress by reducing uteroplacental perfusion. Therefore, hypotension should be avoided at all times, and fetal monitoring should be performed during hemodialysis [4]. The

time elapsed since last dialysis is crucial because severe hypotension may occur during anesthesia induction or in the perioperative period in the cases of patients who underwent hemodialysis. In addition, heparin use during hemodialysis may trigger clotting disorders. Hemoglobin, biochemistry, and coagulation tests should be repeated after hemodialysis in these cases.

If coagulation parameters are observed to be normal and platelet dysfunction is absent, peripheral nerve blocks can be safely used.

9.2.4 Pregnancy After Renal Transplantation

In reproductive age renal transplant patients, pregnancy rate is 2% [4, 27]. Pregnancies following renal transplantation, the risk of preterm delivery, premature rupture of membranes, spontaneous abortion, low birth weight, and IUGR are high.

Preoperative anesthetic evaluation is important in these cases. Due to the immunosuppressive drugs (prednisolone, azathioprine, cyclosporine) affecting the kidney and liver function, biochemical parameters should be evaluated carefully [18]. Asepsis is extreme in these immunosuppressed patients.

Additional corticosteroids should be administered to these pregnant women who are currently receiving corticosteroid therapy in the perioperative period.

As with other pregnancies, perioperative hypovolemia/hypotension should be avoided.

Nonsteroidal anti-inflammatory drugs should not be used for postoperative analgesia; instead, non-nephrotoxic simple analgesics such as paracetamol can be administered [12].

Key Learning Points

- Pregnancy leads to anatomical and physiological changes in the renal system most of which are reversible.
- During pregnancy, renal blood flow and GFR increase by approximately 50%. Serum creatinine and BUN levels are nearly 50% of a nonpregnant woman.
- If the serum creatinine level in the pregnancy is 0.8 mg/dl or BUN level is ≥16 mg/dl, or proteinuria is more than 300 mg/day, it is considered as abnormal.
- The management of anesthesia for the pregnancies with ARF is different from the pregnancies with CRF.
- Anesthetics drugs with short duration of action and metabolized independently from the kidney (atracurium/cisatracurium, remifentanil, etc.) should be preferred.
- Aspiration prophylaxis using H2 receptor blocker should be performed in patients with CRF.
- Neuraxial anesthesia is preferred if there is no coagulopathy, thrombocytopenia, and platelet dysfunction.
- Central blocks should be avoided in patients with uremic cardiomyopathy.

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