Clinical Queries: Nephrology 5 (2016) 8–15

Contents lists available at ScienceDirect

Clinical Queries: Nephrology

journal homepage: www.elsevier.com/locate/cqn

Review

Acute kidney injury in pregnancy

C. Praveen, Anupama Kaul, R.K. Sharma *

Department of Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

ARTICLE INFO

Article history:
Received 19 April 2016
Accepted 21 April 2016
Available online 12 May 2016

Keywords:
Pregnancy
Acute kidney injury
Pre-eclampsia
Acute fatty liver of pregnancy
Thrombotic microangiopathy

ABSTRACT

Pregnancy-related acute kidney injury (P-AKI) incidence has reduced over the recent years with better accessibility and advances in health care. It is still a concern in developing countries where septic abortions and puerperal sepsis persist due to lack of health facilities. Recent advances have helped in a better understanding of pathogenesis of disorders like pre-eclampsia, acute fatty liver of pregnancy, and thrombotic microangiopathy which has helped the physicians to solve the enigma in both diagnosis and management of these conditions. Diagnosis of P-AKI is challenging due to normal maternal physiological changes. Usual definitions of AKI are not very accurate in pregnancy and newer markers for diagnosis of AKI are not well studied in pregnancy. Early identification of the cause of P-AKI and its prompt treatment holds the key in the management of P-AKI. It is of utmost importance to maintain the hemodynamics and acid base balance for ensuring proper utero-placental blood flow and fetal well being in P-AKI. There is neither particular modality of RRT which is better than other nor a preset dialysis prescription for P-AKI, and renal replacement therapy should be individualized to provide optimal care.

1. Introduction

The physiological nature of pregnancy demands identification of any deviation from normalcy upfront. Moreover, many pre-existing diseases worsen during pregnancy and kidney diseases are no exception. Any P-AKI should raise an alarm, warranting immediate care and delay in treatment might lead to permanent kidney damage or dialysis dependency.

The incidence of P-AKI is declining in both developed and developing countries. Nevertheless, it is still a major problem in developing countries. In 1960, the incidence of AKI requiring dialysis was around 1 in 3000 which has reduced currently to 1 in 20,000 deliveries.[1] Mild to moderate renal failure not requiring any form of RRT can occur in 1 in 8000 deliveries.[2] P-AKI still comprises 25% of referrals to dialysis center in developing countries.[3] In India, its incidence ranges from 3.4% to 14.5%.[4,5] In developing countries, septic abortion is one of the leading causes of P-AKI.[2] The incidence of septic abortion has come down from 33.3% in 1960s to 6.3% in 1990s due to the improvement in medical care and better accessibility and also due to legalization of abortions. But it is still a major concern in the developing countries. A discrete feature of P-AKI is its higher risk for bilateral renal cortical necrosis leading to end stage renal disease. Renal cortical necrosis is otherwise uncommon and accounts for about 2% of all cases of AKI, but 50–70% cases of all acute cortical necrosis are due to obstetric complications.[6] Mortality due to P-AKI is reported with wide difference, ranging from 55% in former studies to 8% in a recent study from a single center.[7,8] Its incidence has reduced over the years even in developing countries like India (Table 1). A recent large series from China found P-AKI in only 22 out of 18,589 pregnancies studied (0.118%). The most common causes were hemorrhagic shock (31.8%) and severe pre-eclampsia (18.2%).[9]

2. Physiological changes during pregnancy

A woman undergoes both physical and physiological changes during pregnancy to accommodate the new guest within her. The kidneys change in both size and functions. The kidneys enlarge by 1–1.5 cm in length and 30% by volume. Hydronephrosis is common and seen in up to 90% of pregnant women due to dilatation of collecting system under the influence of estrogen, progesterone and prostaglandin E2.[15] These are usually asymptomatic, but due to urinary stasis it may predispose women to ascending urinary tract infections. Mechanical ureteral obstructions are rare which can happen due to ureteral compression between the gravid uterus and the linea terminalis. There is physiological decrease in BP which results from a profound reduction in systemic vascular

* Corresponding author at: Department of Nephrology, SGPGIMS, Raebareli Road, Lucknow 226014, India. Tel.: +91 9415026762.
E-mail address: rksharma@sgpgi.ac.in (R.K. Sharma).

http://dx.doi.org/10.1016/j.cqn.2016.04.003
2211-9477/

Table 1
Incidence of P-AKI in India.

Author	Year	Number of cases	Incidence of P-AKI (%)
Chugh[10]	1987	1862	38.6
Prakash et al.[6]	1996	59	14.5
Rani et al.[11]	2002	82	12.2
Kilari et al.[5]	2006	41	4.4
Goplani et al.[12]	2008	70	9.1
Najar et al.[13]	2008	569	7.0
Krishna et al.[4]	2011	98	3.4
Pahwa et al.[14]	2014	752	3.6
Gopalakrishnan et al.[8]	2015	1668	7.8

Table 2
Causes of P-AKI.

Pre-renal
Hyperemesis gravidarum
Ante-partum or post-partum hemorrhage
Vomiting due to other pregnancy related disorders (preeclampsia/HELLP, AFLP)
Renal
ATN/ACN-hemorrhage, sepstic abortion, postpartum sepsis, pre-eclampsia, HELLP, AFLP
TMA-HUS/TTP, malignant HTN due to pre-eclampsia
Acute pyelonephritis
Post-renal
Ureteral injury during cesarean section
B/L HDUN due to gravid uterus (rare)

resistance due to unknown cause and is maximal in late second trimester. This may be contributed by the loss of responsiveness to vasoconstrictor agents like angiotensin II, arginine vasopressin, etc.[16]

Rise in glomerular filtration rate (GFR) is an early change in pregnancy, GFR increases by 25% at 4 weeks after last menstrual period and up to 50% by mid pregnancy and this is partly contributed by the increase in blood flow to kidneys by about 80% during pregnancy. The interstitial compliance of the kidneys is also increased which may also play a role in elevation of GFR. The increase in renal plasma flow (RPF) of about 60% which is a little more than the GFR leads to a decrease in filtration fraction (FF) due to filtration pressure disequilibrium. At the end of pregnancy, the RPF decreases proportionally more than the GFR, so that FF returns to the non-pregnant value.[17,18]

There is volume expansion in pregnancy due to activation of the renin-aldosterone-angiotensin system and results in a sodium retention of up to 950 mmol and water retention of 6–8 L (4–6 L of which are extracellular).[18] This accounts for the physiological edema of pregnancy. The volume expansion causes a reduction in serum concentration of sodium by 5 mEq/L and other associated anions resulting in a decrease of plasma osmolality by 10 mOsm/kg below the non-pregnant state. In a normal person, a reduction in plasma osmolality of this magnitude will cause release of the antidiuretic hormone, which does not occur in pregnancy as the osmotic thresholds are reset to this new level. The placental hormone human chorionic gonadotropin may have a role in this reduction in the osmotic threshold for AVP release.[19]

The corpus luteum when stimulated by human chorionic gonadotropin produces a potent vasodilatory peptide hormone called relaxin. Relaxin decreases the tone of both afferent and efferent arterioles in kidneys causing increased renal blood flow as well as GFR. Another hormone vasopressinase is secreted by the placenta which inactivates the antidiuretic hormone in the body and may result in a state of nephrogenic diabetes insipidus.[20] However, it seldom causes volume depletion severe enough to cause AKI.

As the renal blood flow and GFR increase, the solute clearance also naturally increases during pregnancy, thus leading to a decrease in serum urea, uric acid, and creatinine. The serum creatinine (SCr) during pregnancy is around 0.5–0.6 mg/dL which is lower than the normal and hence a lower cut-off of SCr of around 1.0 mg/dL may be reflective of renal impairment. Blood urea nitrogen decreases to approximately 8–10 mg/dL.[21] The secretion of uric acid is increased along with a decrease in net tubular reabsorption in normal pregnancy. This results in a decrease of serum uric acid concentration by about 25% in early pregnancy and nadirs around 2–3 mg%. As pregnancy advances, fractional excretion of uric acid decreases, and serum uric acid level rises nearly to the non-pregnant mean.[17]

Like other solutes, proteins are also filtered in excess. The net tubular re-absorption of protein is also reduced causing an increase in protein excretion from 60–90 mg/24 h to 180–250 mg/24 h around third trimester.[22] Total protein excretion greater than 260 mg/24 h or 1+ protienuria in dipstick is considered abnormal.[23] Any pre-existing kidney disease and especially protienuric kidney disease worsen during pregnancy as the level of protienuria increases, especially in the latter half of pregnancy. Any hematuria is pathological in pregnancy. Macroscopic hematuria may be associated with acute cortical necrosis.

It should be remembered that there is a mild respiratory alkalosis during pregnancy due to hyperventilation as an effect of progesterone which leads to cause compensatory metabolic acidosis.[24] This causes kidneys to secrete bicarbonate ions leading to a reduction in serum bicarbonate levels up to 4 mEq/L, which is normal in pregnancy. This should always be considered during the correction of acid base balance during treatment of P-AKI. All these physiologic changes revert back to pre-pregnancy state within few weeks postpartum.

3. Etiology

P-AKI can be broadly classified as pre-renal, renal, and post-renal causes like in general population. The causes may be either related directly to pregnancy or those seen in normal population such as drug induced acute interstitial nephritis. In Table 2, the causes of AKI mentioned are related directly to pregnancy. Some of the disorders can cause AKI by multiple mechanisms.

Incidence of P-AKI is more common in first trimester and peri-partal period showing a bimodal distribution. In the first trimester, the cause is mainly infectious, especially those related to septic abortions or pre-renal due to hyperemesis gravidarum. In the third trimester, AKI is caused mainly by pre-eclampsia, ante-partal hemorrhages and rarely by thrombotic thrombocytopenic purpura (TTP), and acute fatty liver of pregnancy (AFLP). Post-partal AKI is usually associated with puerperal sepsis, post-partal hemorrhage hemolytic uremic syndrome (HUS).

4. Pathophysiology

4.1. Sepsis/septic abortions

The common causes of sepsis in pregnancy are pyelonephritis, septic abortions, puerperal sepsis, and chorioamnionitis. The incidence of asymptomatic bacteruria is similar in pregnancy to that of non-pregnant women of similar age; however, there is an increased likelihood of pyelonephritis in pregnancy as well as higher risk of sepsis.[25] Hence, asymptomatic bacteruria must be treated during pregnancy. This elevated risk is due to the physiological changes in the urinary collecting system like ureteral dilatation and bladder wall flaccidity due to effect of relaxin. There is also increased susceptibility to bacterial endotoxin induced tissue damage known as Shwartzman phenomenon. Around 25% of pregnant women with pyelonephritis show significant decrease in