REVIEW ARTICLE

Decision Making In Pregnancy Related Acute Kidney Injury

Kousalya Chakravarthy[1], Radha Ramana Murthy Konda[2]

ABSTRACT

Pregnancy Related Acute Kidney Injury (PRAKI) warrants more awareness as the condition can be reversible if recognized early. The deranged maternal renal parameters have a substantial effect on the foetal well being rendering both lives at risk. The most common causes of Pregnancy Related AKI are hypovolemia due to obstetric haemorrhage, preeclampsia and maternal sepsis. HELLP (Haemolysis, Elevated liver enzymes, Low platelet counts), AFLP (Acute Fatty Liver of Pregnancy), TTP (Thrombotic Thrombocytopaenic Purpura) and aHUS (atypical Haemol- ytic Uremic Syndrome) constitute the various causes of AKI in the third trimester of pregnancy. A decreased urine output of < 0.5 ml/kg/h for 6 hours should prompt the investigations for proper diagnosis of etiological factors and measures should be taken to avoid AKI. Intermittent haemodialysis is preferred to Peritoneal Dialysis especially in the third trimester. Anaesthetic management of PRAKI is more challenging due to intrinsic airway difficulty in Obstetrics compounded by electrolyte imbalances, altered drug metabolism, need for massive transfusions due to coagulopathy and risk of fluid overload and pulmonary oedema. A multidisciplinary approach in anticipation of the problem, maintaining the haemodynamics, preventing further damage to the kidneys, planning the mode of delivery and the optimizing the anaesthesia and neonatal care will bring better foeto maternal outcomes in PRAKI.

Keywords: Acute kidney Injury, Anaesthesia, Dialysis, Pregnancy.

How to cite this article: Kousalya Chakravarthy, Radha Ramana Murthy Konda. Decision Making In Pregnancy Related Acute Kidney Injury. International Journal of Contemporary Medical Research 2015;2(3):502-508

[1]Assistant Professor, [2]Professor, Department of Anaesthesia, Niloufer Hospital for Women & Children, Osmania Medical College, Hyderabad, India.

Corresponding author: Dr. Kousalya Chakravarthy DGO, MD (Anaes), Fellowship in Obstetric Anaesthesia, Assistant Professor, Department of Anaesthesia, Niloufer Hospital for Women and Children, Red Hills, Lakdikapul, Hyderabad, Telangana, India

Source of Support: Nil

Conflict of Interest: None

INTRODUCTION

The term Acute Renal Failure (ARF) has been replaced with the broader terminology Acute Kidney Injury (AKI). AKI-''Acute kidney injury/ impairment'' includes the entire spectrum of the syndrome from minor changes in markers of renal function to requirement for renal replacement therapy (RRT).[1] AKI is the abrupt deterioration in the renal parameters reflected by increased serum creatinine levels. Acute Kidney Injury in pregnancy warrants more awareness as the condition can be reversible if recognized early. The incidence of AKI in pregnancy is around 1 per 15,000 pregnancies and is more in the developing countries.[2] The deranged maternal renal parameters have a substantial effect on the foetal well being rendering both lives at risk. Mortality in established renal injury in pregnancy is as high as 20% to 30%. Awareness of the various causes of AKI in pregnancy, early recognition of the condition, prompt and appropriate treatment of the underlying cause are the key to decrease the severity of the insult and prevent the long term complications.

Renal Changes in Pregnancy [3]

The various physiological changes of pregnancy redefine the laboratory parameters in haematological, renal, endocrinal, hepatic and acid-base parameters. Pregnancy causes progressive dilatation of the renal pelvis, calyces, and ureters along with decreased bladder tone, bladder hyperemia and edema. This potentiates the vesicoureteral reflux, urinary stasis, increasing the risk of asymptomatic bacteruria, urinary tract infections and, pyelonephritis. GFR (Glomerular filtration rate) and RPF (Renal Plasma Flow) increase by 50% during 1st trimester due to increased cardiac output. Due to increased GFR, urea and creatinine fall in pregnancy. Glycosuria is common due to increased GFR and slightly reduced proximal tubular reabsorption. Proteinuria is present in 20% may be due to increased renal venous pressure**.** Stimulation of anti-diuretic hormone (ADH) causes a lowered plasma osmolality. Plasma sodium concentration decreases by 4 to 5 mEq/L. Increased minute ventilation and CO_2 washout causes a mild chronic respiratory alkalosis in pregnancy, which is compensated for by renal excretion of bicarbonate.

Definition of AKI

To standardize the definition of AKI, Acute Dialysis Quality Initiative group in 2004, published the RIFLE (risk, injury, failure, loss of kidney function, and end-stage renal failure) criteria based on the level of serum creatinine (SCr) and urine output (UO). A patient can fulfil the criteria through changes in serum creatinine (SCreat) or changes in UO, or both. The criteria that lead to the worst possible classification should be used.[4] (Table 1)

The Acute Kidney Injury Network (AKIN) group in 2007, proposed a modified version of the RIFLE criteria. In AKIN classification, the AKI definition is considered after adequate hydration and after ruling out the obstructive uropathy. AKIN classification does not include GFR. AKIN Stage I is analogous to RIFLE-Risk, but requires at least two SCr determinations within 48hrs. Patients receiving renal replacement therapy were classified as AKIN stage-3 (RIFLE Failure). The loss and end-stage kidney disease categories were eliminated in the AKIN classification.

AKIN Staging and Grading of AKI: [5] (Table 2)

AKI is defined as any of the following:

1. Increase in SCr by ≥ 0.3 mg/dl (≥26.5 μmol/l) within 48 hours; or
2. Increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
3. Urine volume < 0.5 ml/kg/h for 6 hours.

Predictors of PRAKI (Pregnancy Related AKI)

There is no separate consensus on the definition for Pregnancy Related Acute Kidney Injury. Serum creatinine and GFR (Glomerular Filtration Rate) reflect the extent of damage in PRAKI. Both RIFLE and AKIN criteria have been correlated to the outcomes in patients with AKI. Hoste et al studied the clinical course of ICU patients with RIFLE criteria and concluded that the RIFLE classification is a very sensitive definition of acute kidney injury.[6] The RIFLE criteria have been applied to the Pregnancy Related Acute Kidney Injury with good prediction of maternal mortality. Silva et al studied 55 Obstetric patients with AKI under dialysis and found a positive association of RIFLE criteria with maternal mortality.[7] Incidence of oliguria was 65% in their study. The commonest cause of oliguria was HELLP syndrome. Kamal et al, in their recent 3 year prospective study concluded that the RIFLE classification system could predict the risk of mortality from AKI in obstetric ICU patients and that the mortality was positively associated with high RIFLE classes. [8]

1. Creatinine as the predictor of PRAKI:

The serum creatinine levels reflect the status of kidney function in pregnancy. The increase in the serum creatinine levels is taken as the hallmark of Acute Kidney Injury in pregnancy. The physiological increase in GFR, decreases serum creatinine to a range of 0.4 to 0.8mg/dl.[9] Hence a Serum creatinine level of ≥1 mg/dL over a period of 48hrs or a rapid rise of 0.5 mg/dL above baseline should prompt the investigations for AKI.

2. Estimation of Glomerular Filtration Rate:

A decreased GFR (Glomerular Filtration Rate) may be an early marker of compromised renal function in pregnant patients, even in the presence of normal serum creatinine. Weight based Cockcroft-Gault formula may over estimate GFR in pregnancy because the increased body weight is not proportional to increased muscle mass or creatinine production. MDRD (Modification of Diet in Renal Disease) based on age, serum creatinine, and gender, underestimates GFR both in healthy and pre-eclamptic pregnancies and is less reliable as a screening test for kidney disease. Smith et al compared the performance of the modified MDRD formula with inulin clearance in three groups of women: healthy pregnant volunteers, women with preeclampsia, and pregnant women with CKD before pregnancy.[10] They concluded that, MDRD significantly underestimates GFR in both healthy and pre-eclamptic pregnancies. MDRD is less accurate than creatinine clearance and is not sensitive enough to be used as a screening test for renal disease in pregnant population. Creatinine clearance by 24-hour urine collection by far, is the gold standard method for estimating GFR in pregnancy. 24hr urine protein and urine protein to creatinine ratio can also give a good assessment of proteinuria in pre eclamptic patients.[11]

DEALING WITH RAISING SERUM CREATININE

The management of raising serum creatinine in pregnancy:

I. Recognizing the cause for raise in serum creatinine
II. Treatment of the underlying cause
III. Care of the pregnant patient with PRAKI:
   a) Measures to Optimize the renal function
   b) Raising serum creatinine - Indications for Dialysis

I. **Recognizing the cause for raising serum creatinine (**Table-3: The aetiology of AKI in pregnancy)

Hypovolemia of any aetiology, severe preeclampsia /

eclampsia /HELLP syndrome and sepsis are the common cases of acute kidney injury (AKI) in pregnancy. Siam et al from Egypt reported an incidence of 12.39% AKI, among 88 obstetric patients admitted to ICU. [12] The causes of AKI were obstetric hemorrhage in 34 (38.63%), pregnancy-related hypertension in 25 (28.4%), HELLP syndrome in 14 (15.9%), sepsis in 6 (6.81%), anaesthetic complications in 4 (4.54%), pulmonary embolism in 2 (2.27%) and acute fatty liver in 3 (3.3%) cases. A recent study at Morocco reported 37 cases of PRAKI over one year, with preeclampsia in 66.6%, hemorrhagic shock in 25% of the cases. [13]

Pregnancy is associated with progressive increase in the concentrations of procoagulant factors, decreased fibrinolytic activity, loss of endothelial cell thrombomodulin, and decrease in the activity of ADAMTS13, with the maximum abnormalities occurring at delivery and immediately postpartum. [14] All these factors can precipitate acute episodes of TTP-HUS in the later half of pregnancy. TTP – HUS may relapse during pregnancy and can recur in subsequent pregnancies. [15] Preeclampsia, HELLP, AFLP (Acute Fatty Liver of Pregnancy), TTP and HUS constitute the most common differential diagnosis of PRAKI in late pregnancy.

Investigations for diagnosing PRAKI:

Baseline investigations to rule out the various etiological causes of AKI

1. *Haemogram*
   a. Haematocrit – indicate anemia, haemconcetration
   b. Platelet count – thrombocytopaenia
   c. Leucocytosis or neutropania s/o sepsis
2. *Kidney function tests:*
   a. Serum creatinine levels
   b. Blood urea / BUN
   c. Serum electrolytes to detect dyselectrolytaemia
   d. Urine microscopy and culture sensitivity: to detect Proteinuria, Microscopic haematuria, Bacteruria
   e. 24hr Urine collection for Urinary proteins
   f. Protein creatinine ratio
   g. Creatinine clearance and GFR estimation
   h. Urine Biochemistry – Increase in FeNa may be noted even before oliguria. A FENa value <1% suggest prerenal and >2% indicates an intrinsic renal cause of AKI.
3. *LFT:* Bilirubin & liver enzymes – to rule out HELLP/AFLP/ Hepatoranal syndrome.
4. *LDH:* to detect microangiopathes (HELLP/ AFLP). Increased bilirubin levels, raised LDH and presence of schistocytes in peripheral smear suggest red cell fragmentation.
5. *Coagulation profile* - if platelet count is < 1.0 lakh/ mm^3 or Deranged LFT
6. Sepsis profile if the clinical features are suggestive of Sepsis with AKI
7. Acid base status as assessed by blood gases
8. ECG
9. *Ultrasound*: To identify parenchymal causes or obstructive uropathy
10. Indications for Renal Biopsy in PRAKI[16]
    a. In symptomatic women before 28 weeks gestation in the presence of sterile urine and kidneys >10 cm in size after excluding or correcting coagulopathy or thrombocytopenia and controlling the blood pressure.
    b. In such conditions where a knowledge of renal histology will have a major impact on the immediate therapeutic interventions ensuring materno foetal safety.
    c. Sudden deterioration of renal function before 32 weeks where prerenal and postrenal causes of acute kidney injury have been excluded and intrinsic renal injury is suspected.
    d. Symptomatic nephrotic syndrome before 32 weeks
    e. In patients with oliguria who have rapidly worsening acute kidney injury, hematuria, and red blood cell casts
11. Other Biomarkers: [17] are not routinely used in PRAKI
    a. Cystatin-C is an endogenous cysteine proteinase inhibitor. It is neither secreted nor reabsorbed but completely metabolized, by proximal renal tubular cells. It is unaffected by sex, age, height, weight, and muscle mass and identifies AKI 24-48 hours earlier than serum creatinine.
    b. Kidney Injury Molecule-1(KIM-1) KIM-1 is a type 1 trans-membrane marker of severity of AKI.
    c. Neutrophil gelatinase-associated lipocalin (NGAL): NGAL may be a sensitive urinary biomarker of sepsis- related, ischemic and nephrotoxic (contrast induced) AKI.

II: Treatment of the underlying cause

The earliest manifestation of PRAKI is a decrease in urine output. A decreased urine output of < 0.5 ml/kg/h for 6 hours should prompt the investigations for proper diagnosis of etiological factors. A detailed history and clinical examination should precede the investigations. Early identification of at risk patients

	Serum creatinine (SCr)	Urine output (UO)
Risk	Increased creatinine x 1.5 or GFR decreases >25% from the base line	Urine output < 0.5ml/Kg/hrx6hrs
Injury	Increased creatinine x 2 or GFR decreases >50% from the base line	Urine output < 0.5ml/Kg/hrx12hrs
Failure	Increased creatinine x 3 or or GFR decreases >75% or S.Creat ≥4mg/dl	UO <0.3ml/kg/h x 24h or anuria x 12h
Loss of Function	Persistent ARF complete loss of renal function >4 weeks	
End Stage Renal Disease	End-stage renal disease (>3 months)	

Table-1: The RIFLE criteria for Acute Kidney Injury[4]

RIFLE	AKIN Stage	Serum creatinine	Urine output
Risk	1	1.5–1.9 times baseline OR ≥ 0.3 mg/dl (≥26.5 mmol/l) increase with in 48hrs	< 0.5 ml/kg/h for 6–12 hrs
Injury	2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 hrs
Failure **Loss** **ESRD**	3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 mmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to < 35 ml/min per 1.73 m^2	< 0.3 ml/kg/h for ≥ 24 hrs OR Anuria for ≥ 12 hours

Table-2: Staging of AKI: The AKIN & RIFLE criteria [4, 5]

AKI in early pregnancy	AKI in late pregnancy	Postpartum AKI
1. Hyperemesis gravidarum **2.** Septic abortion **3.** Hypovolemia – ruptured ectopic **4.** Urosepsis- bilateral pyelonephritis **5.** Anticardiolipin/ antiphospholipid antibodies / TTP **6.** CKD with pregnancy **7.** SLE with flare	1. HDP / Preeclampsia 2. HELLP Syndrome 3. Hypovolemia –APH and PPH - shock 4. Maternal sepsis – septic shock 5. HUS 6. AFLP 7. Amniotic Fluid emb – DIC - Shock	1. Puerperal sepsis – septic shock 2. Consequences of Hypovolemia due to APH/ PPH/ AFE/ Septic shock/ DIC causing ATN or cortical necrosis 3. Intrinsic renal causes 4. CKD with AKI

Table-3: The aetiology of AKI in pregnancy

AFLP = acute fatty liver of pregnancy; AKI = Acute Kidney Injury; APH= Antepartum Haemorrhage; AFE = Amniotic Fluid Embolism; ATN = Acute tubular necrosis; CKD = Chronic Kidney Disease; DIC= Disseminated intravascular coagulation; HUS = Hemolytic uremic syndrome; HELLP = hemolysis, elevated liver enzymes and low platelet count; PPH = Post partum haemorrhage; TTP = thrombotic thrombocytopenic purpura; SLE= Systemic Lupus Erythematosis

and institution of appropriate measures are highly recommended for prevention and management of Pregnancy Related AKI. Massive transfusion protocols in Obstetric haemorrhage and adequate resuscitation can prevent the onset and also decrease the magnitude of AKI. Aggressive management of hypovolemia, correction of coagulation derangements with blood and blood products, judicious use of oxytocics is necessary to prevent AKI in obstetric haemorrhage.[18]

Maternal sepsis and APLA syndrome can present as deranged renal parameters any time in pregnancy. Severe Preeclampsia is one of the common causes of AKI in third trimester. HELLP and AFLP may constitute the far end of the spectrum of Hypertensive disorders of pregnancy. Termination of pregnancy will prevent further renal damage in Severe Preeclampsia, HELLP and AFLP. The differential diagnosis of Low platelet counts with AKI includes TTP and aHUS where plasma exchange is the first-line treatment (Table-4).

	Severe preeclampsia	HELLP	AFLP	TTP	aHUS
Frequency of hypertension	100%	80%	25%-50%	Occasional	+
Neurologic symptoms	No	No	No	Yes	No
AKI	Mild	Mild/ moderate	Moderate	Mild / moderate	Severe
Hemolytic anemia	0	+	0/+	++	+
Thrombocytopenia	0/+	+	+	++	++
↑Liver transaminase	0/+	+	+ ++	0	0
↑aPTT	0/+	0+	+	0	0
ADAMTS-13 activity	<10%	0	0	0	+++
Gestational Age	3rd Trimester	3rd Trimester	3rd Trimester	2/3rd Trimester	Postpartum
Treatment	Delivery; Support measures			Plasma infusion /exchange	

Table-4: Differential diagnosis Severe preeclampsia, HELLP, AFLP, TTP & HUS[15]
AFLP = acute fatty liver of pregnancy; aPTT = Activated partial thromboplastin time; aHUS = atypical hemolytic uremic syndrome; HELLP =hemolysis, elevated liver enzymes and low platelet count, TTP = thrombotic thrombocytopenic purpura.

Obstetric aetiologies account for approximately 50-70% of cases of renal cortical necrosis.[19] Patients present with the abrupt onset of oliguria or anuria, gross hematuria, flank pain and hypotension. The diagnosis can be made by ultrasonography or post partum CT scan.

Other causes of decrease urine output like Congestive cardiac failure should be managed with diuretics and afterload reduction.

PREEXISTING RENAL DISEASE

Approximately 3% of women of child bearing age will have pre-existing CKD. [20] Pregnant patients with CKD may develop Preeclampsia, aggravation of hypertension and renal function deterioration during pregnancy. The rate of complications are higher in mothers with Severe CKD (Scr >1.9 mg/dl or GFR 15-29 mL/ min/1.73m^2), than in those with Moderate CKD (Scr 1.3-1.9 mg/dl or GFR 30-59 mL/min/1.73 m^2) or Mild CKD (Scr < 1.3mg%, GFR 60-89 ml/min/ 1.73m^2).[21]

CARE OF THE PREGNANT PATIENT WITH AKI

a. Measures to Optimize the renal function
b. Raising serum creatinine - Indications for Dialysis

A. Measures to optimize renal function (KIDGO Recommendations): [22]

1. Correction of hypovolemia: For patients with or at risk of AKI, in the absence of haemorrhage, isotonic crystalloids are preferred to colloids (albumin or starches) as initial expansion of intravascular volume.[23]
2. EGDT (Early Goal Directed Therapy) should be followed in Maternal Sepsis /septic shock. Vasopressors (Noradrenaline) should be used along with fluids whreindicated.
   Avoid Nephrotoxic drugs: Avoid NSAIDs and aminoglycosides. If necessary aminoglycosides shoud be given as a single daily dose.
3. Correction of Hyperkalaemia and other electrolyte disturbances.
4. Regular monitoring of serum creatinine and urine output.
5. Restriction of diuretic use only to patients with AKI with Fluid Overload.
6. Glycaemic control targeting plasma glucose 110 – 149 mg/dl (6.1 – 8.3mmol/L).
7. Early enteral nutritional supplementation in patients with any stage of AKI. Restrictions of protein intake will not prevent or delay initiation of RRT.

In patients with HELLP/ AFLP/ Rapid progress of AKI with worsening of renal parameters termination of pregnancy should be planned.

AKI may be associated with multiple organ dysfunctions and hence care should be extended towards monitoring for, prevention and management of other organs dysfunction.[24]

B. Raising serum creatinine – Decision making- Indications for dialysis

Acute indications for dialysis are the same for pregnant patients as for non-pregnant patients in terms of fluids and electrolytes, and complications of uraemia. Early dialysis is necessary in pregnant women with renal failure. The increased cardiac output, increased renal perfusion and lesser muscle mass may spuriously reflect higher GFR and lesser serum creatinine levels. The changing trend in the laboratory parameters should be considered instead of a single value.[25]

The indications for dialysis can be summarized as

1. Glomerular filtration rate (GFR) less than 20 mL/min per 1.73 m^2
2. Blood urea nitrogen more than 100mg/dl
3. Uremic symptoms : encephalopathy, pericarditis or neuropathy
4. Metabolic acidosis (pH < 7.15) unresponsive to initial medical treatment
5. Hyperkalemia >6mEq/L
6. Diuretic resistant Volume overload

There is some controversy over the optimal point of initiation of prophylactic dialysis. [26] The need for early intervention depends upon the cause and reversibility of AKI and the gestational age. In conditions of raising serum creatinine and azotemia with reversible causes like pyelonephritis, aggressive control of azotemia results in better fetal and maternal outcomes.

Mode of dialysis: Any dialysis modality can be used in pregnancy. In most cases, the choice is intermittent hemodialysis.[27] Peritoneal dialysis with smaller volumes and frequent exchanges is another option. Peritoneal dialysis may be difficult in the third trimester due to increased uterine size. A daily dialysis program with longer low volume high frequency HD (20h/week) improves and minimizes hemodynamic fluctuations.[28] BUN levels < 60mg% and prevention of metabolic acidosis are better achieved with longer HD compared to shorter dialysis. Intense dialysis management improved the care of the pregnant patients with CKD with ESRD on dialysis. Meticulous care during dialysis including nutritional support, control of anaemia, blood pressure and electrolyte imbalance, has increased fetal survival from 23% in 1980 to 90% in the recent years.[29]

Anaesthetic management of operative deliveries in pregnant patients with AKI.[30]

Anaesthetic management of PRAKI is challenging because of increased peri operative risks with both regional and general anaesthesia techniques. The need for massive transfusion due to coagulopathy and the risk of fluid overload due to AKI needs to be balanced. Regional anaesthetic techniques such as spinal / epidural anaesthesia are considered safe and effective provided, the coagulation profile and intravascular volume status are normal. General anaesthesia when required is challenging. The intrinsic difficulty in Obstetric airway management is compounded by the associated pre eclampsia and AKI.

Considerations during General Anaesthesia in PRAKI:

1. Acid aspiration prophylaxis
2. Mandatory preoxygenation with 100% Oxygen
3. Modified RSI (Rapid Sequence Induction). The use of succinylcholine is limited by the presence of Hyperkalaemia. Atracurium is the intermediate muscle relaxant of choice as the renal metabolism of anaesthetic drugs is decreased in AKI.
4. NSAIDs should be avoided. Dexmedetomidine can be used safely in the perioperative period for the attenuation of stress response during laryngoscopy and intubation. It decreases the intra operative awareness and can be used to enhance the post operative pain relief.
5. Short acting Opioids can be used for postoperative pain relief.
6. Antihypertensive should be continued in cases of severe pre eclampsia and HELLP syndrome. The dose of $MgSO_4$ if started for seizure prophylaxis should be halved and determined by serum magnesium levels.

Care during post partum period: The post operative/post partum care includes optimization of nutritional requirement, correction of anaemia and electrolyte imbalance. Strict Intake /output chart has to be maintained to avoid Fluid overload and positive balance. Pharmacological or mechanical VTE Prophylaxis should be started. In the postpartum period, the need for dialysis is reflected by etiological factor and the Stage of AKI. Obstetric causes and early stages of AKI tend to resolve after delivery. Renal protection strategies should be followed till the normalization of renal parameters. All the patients should be followed up for 3months after delivery for resolution of AKI or development of CKD.

CONCLUSION

Pregnancy Related Acute Kidney Injury needs more awareness, preventive measures in high risk pregnant patients, early evaluation and management. The etiological factor of PRAKI and the staging of AKI reflect the possible extension of the renal injury and also the reversibility of the condition. A multidisciplinary approach in anticipation of the problem, maintaining the hemodynamics, preventing further damage, planning the mode of delivery and the optimizing the anaesthesia and neonatal care will bring better foeto maternal outcomes in PRAKI.

REFERENCES

1. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
2. Lafayette R. AKI in pregnant patient: two lives at stake. Nephrology Times. 2010;3:9-10.
3. Yaakov Beilin, Robert W. Reid. Renal Disease. In: David H. Chestnut, editor. Obstetric Anesthesia: Principles and Practice, 5th edition. Philadelphia, PA : Elsevier/Saunders; 2014. p.1165 -1178.
4. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P and the ADQI workgroup. Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis

Quality Initiative (ADQI) Group. Critical Care 2004, 8:R204-R212.
5. José António Lopes and Sofia Jorge. The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review. Clin Kidney J 2013; 6: 8–14.
6. Hoste E AJ, Clermont G, Kersten A, Venkataraman R, Angus DC, Bacquer DD et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Critical Care 2006; 10:R73.
7. Silva GB, Monteiro FA, Mota RM, Paiva JG, Correia JW, Bezerra Filho JG et al. Acute kidney injury requiring dialysis in obstetric patients: a series of 55 cases in Brazil. Arch Gynecol Obstet. 2009;279: 131-7.
8. Kamal EM Behery MM, Sayed GA, Abdulatif HK. RIFLE classification and mortality in obstetric patients admitted to the intensive care unit with acute kidney injury: a 3-year prospective study. Reprod sci. 2014;21:1281-7.
9. Sharon E. Maynard and Ravi Thadhani. Pregnancy and the Kidney. J Am Soc Nephrol. 2009; 20:14–22.
10. Smith M, Moran P, Ward M, Davison J. Assessment of glomerular filtration rate during pregnancy using the MDRD formula. BJOG 2008;115:109–112.
11. Price CP, Newall RG, Boyd JC. Use of Protein:Creatinine Ratio Measurements on Random Urine Samples for Prediction of Significant Proteinuria: A Systematic Review. Clinical Chemistry 2005; 51:1577-1586.
12. Siam S, Hameed AA, Heba Matar. Evaluation of Acute Kidney Injury Defined by Rifle Criteria and its Association with Mortality in Critically Ill Obstetric Patients: A Retrospective Study. Med. J. Cairo Univ. 2011;79: 589-593.
13. Mohamed Arrayhani, Randa El Youbi, and Tarik Sqalli, Pregnancy-Related Acute Kidney Injury: Experience of the Nephrology Unit at the University Hospital of Fez, Morocco," ISRN Nephrology, vol. 2013, Article ID 109034, 5 pages,.
14. James N. George. The association of pregnancy with thrombotic thrombocytop- enic purpura–hemolytic uremic syndrome. Curr Opin Hematol 2003; 10:339–344.
15. Machado S, Nuno Figueiredo 1, Andreia Borges 1, Maria São José Pais 2, Luís Freitas 1, Paulo Moura 2, Mário Campos 1 Acute kidney injury in pregnancy: a clinical challenge J Nephrol. 2012;25*:*19-30.
16. Day C, Hewins P, Hildebrand S, Sheikh L, Taylor G, Kilby M et al. The role of renal biopsy in women with kidney disease identified in pregnancy. Nephrol Dial Transpla-nt. 2008;23:201-6.
17. Vaidya VS, Ferguson MA, Bonventre JV. Biomarkers of Acute Kidney Injury.Annual review of pharmacology and toxicology. 2008; 48:463-493.
18. Rajashree Chavan and M Y Latoo. Recent advances in the management of massive obstetric haemorrhage. BJMP 2013;6:a604.
19. Prakash J, Vohra R, Wani I A, Murthy A S, Srivastva P K, Tripathi K et al. Decreasing incidence of renal cortical necrosis in patients with acute renal failure in developing countries: a single-centre experience of 22 years from Eastern India. Nephrol. Dial. Transplant 2007; 22:1213-1217.
20. David Williams, John Davison. Chronic kidney disease in pregnancy. BMJ 2008; 336:211-5.
21. Bili E, Tsolakidis D, Stangou S, Tarlatzis B. Pregnancy management and outcome in women with chronic kidney disease. Hippokratia 2013; 17*(2):* 163–168.
22. KDIGO Clinical Practice Guideline for Acute Kidney Injury. 2012;2 http://www.kidney-international.org
23. Phillips DP, Kaynar AM, Kellum JA, Gomez H. Crystalloids vs. colloids: KO at the twelfth round? Crit Care. 2013;17:319.
24. S. C. Yap and H. T. Lee. Acute Kidney Injury and Extrarenal Organ Dysfunction New Concepts and Experimental Evidence. Anesthesiology 2012;116:1139-*48*.
25. Gibney N, Hoste E, Burdmann EA, Bunchman T, Kher V, Viswanathan R et al. Timing of Initiation and Discontinuation of Renal Replacement Therapy in AKI: Unanswered Key Questions. Clin J Am Soc Nephrol. 2008;3*:876-*80.
26. Tattersall J, Dekker F, Heimbu¨rger O, Jager KJ, Lameire N,Lindley E. When to start dialysis: updated guidance following publication of the Initiating Dialysis Early and Late (IDEAL) study. Nephrol Dial Transplant. 2011 ;26:2082-6.
27. N. Kevin Krane. Peritoneal Dialysis and Hemodialysis in Pregnancy. Hemodial Int. 2001; 5:97–101.
28. Manisha Sahay (2012). Acute Kidney Injury in Pregnancy, Basic Nephrology and Acute Kidney Injury, Prof. Manisha Sahay (Ed.), ISBN: 978-953-51-0139-0, InTech, DOI: 10.5772/25962. Available from: http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/acute-kidney-injury-in-pregnancy
29. Manisco G, Potì M, Maggiulli G, Tullio MD, Losappio V, Vernaglione L. Pregnancy in end-stage renal disease patients on dialysis: how to achieve a successful delivery. Clin Kidney J 2015;8: 293-299.
30. Bajwa SJ, Kwatra IS, Bajwa SK, Kaur M. Renal diseases during pregnancy: Critical and current perspectives. J Obstet Anaesth Crit Care 2013;3:7-15.