Renal Diseases in pregnancy

Renal changes in pregnancy:

1- Size: Both kidneys increase 1 to 1.5 cm in length during pregnancy. Kidney volume increases by up to 30%.

2- **Hemodynamic changes**: increased renal perfusion and glomerular filtration rate (GFR).

Changes in urinary tract:

Dilatation of the ureters and renal pelvis (hydroureter & hydronephrosis) is more prominent on the right than the left (up to 80 % of pregnant women) . These changes can be visualized on ultrasound examination by the second trimester, and may not resolve until 6 to 12 weeks postpartum.

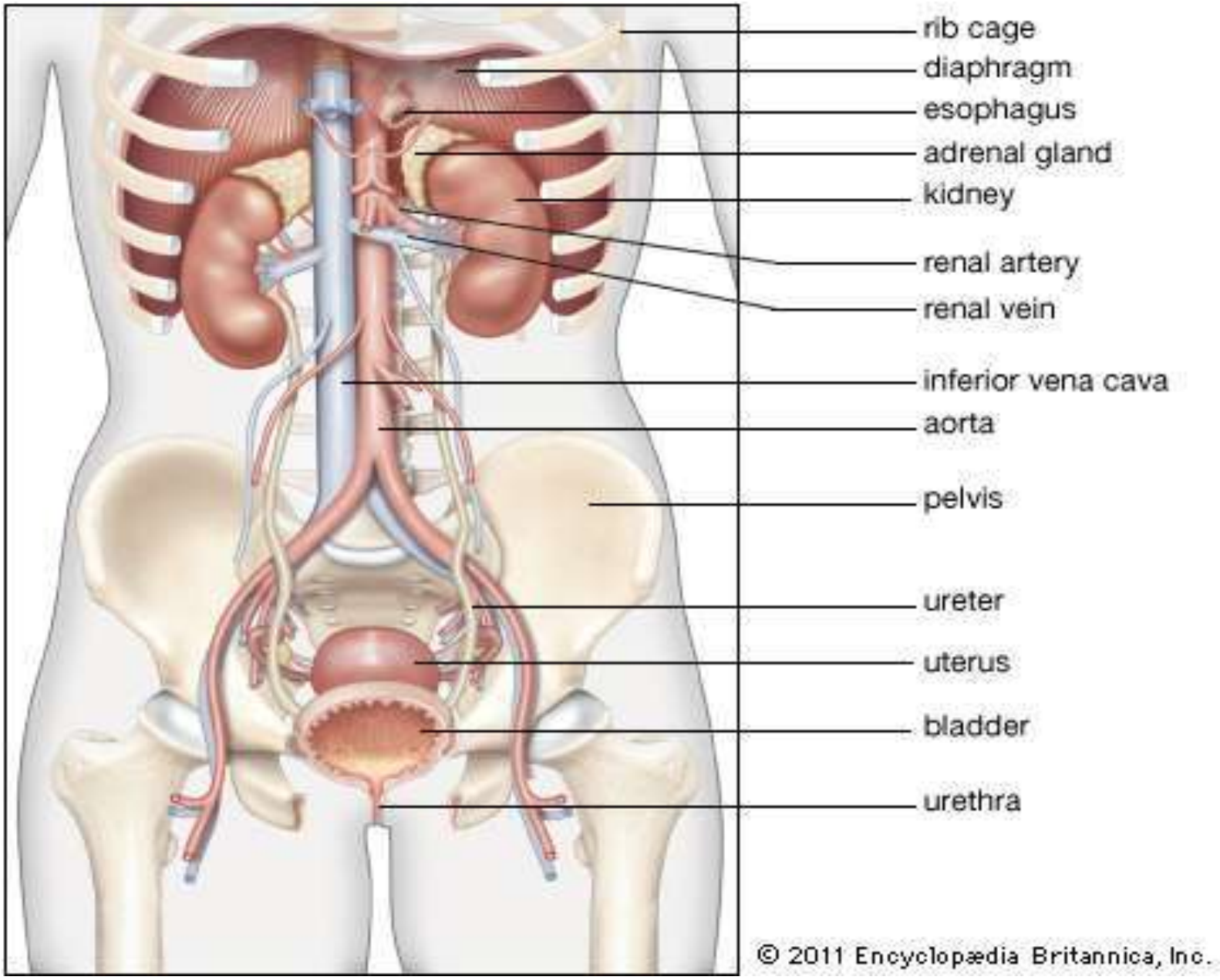
What factors are attributed to these changes?

1- Progesterone: Reduces ureteral tone, peristalsis, and contraction pressure.

2- More on the right ureter: Dextrorotation of the uterus by the sigmoid colon, kinking of the ureter as it crosses the right iliac artery, and/or proximity to the right ovarian vein.

3- The vessels in the suspensory ligament of the ovary enlarge and may compress the ureter at the brim of the bony pelvis.

4- Pathologic obstruction (by nephrolithiasis or stricture) will also lead to ureteral dilatation. It frequently results in flank pain, and can often be distinguished from physiologic hydronephrosis by radiographically or sonographically visualizing the cause of the obstruction.



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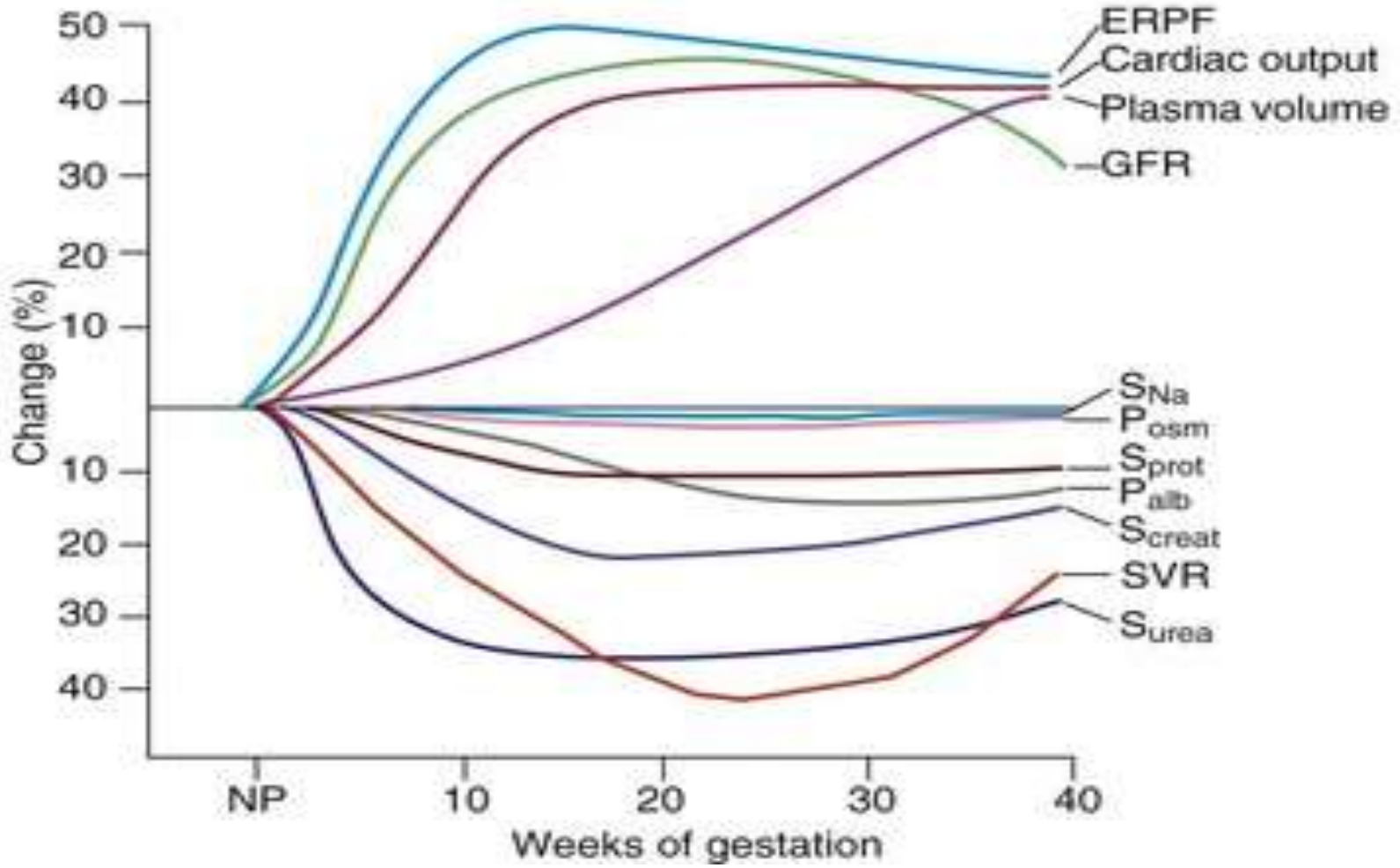
Bladder:

**The bladder mucosa is edematous and hyperemic in pregnancy.

** Although progesterone-induced bladder wall relaxation may lead to increased capacity, the enlarging uterus displaces the bladder superiorly and anteriorly, and flattens it, which can decrease capacity.

Hemodynamic and Biochemical Changes in Normal Pregnancy



Mechanisms of increased GFR in pregnancy:

**Reduced vascular responsiveness to vasopressors such as angiotensin 2, norepinephrine, and antidiuretic hormone (ADH) is well documented. This may be mediated, in part, by altered vascular receptor expression.

**Nitric oxide synthesis increases during normal pregnancy and may contribute to the systemic and renal vasodilation and the fall in blood pressure.

Relaxin: It increases endothelin and nitric oxide production in the renal circulation, leading to generalized renal vasodilation, decreased renal afferent and efferent arteriolar resistance, and a subsequent increase in renal blood flow and GFR.

Lab Tests:

Hyponatremia:

The fall in the plasma sodium concentration during pregnancy correlates closely with increased production of hCG that can induce a similar resetting of the thresholds for ADH release and thirst .

Also, hCG appears to produce these changes via the release of relaxin.

Proteinuria:

Urinary protein excretion rises in normal pregnancy, from the non-pregnant level of about 100 mg/day to about 150 - 200 mg/day in 3rd trimester

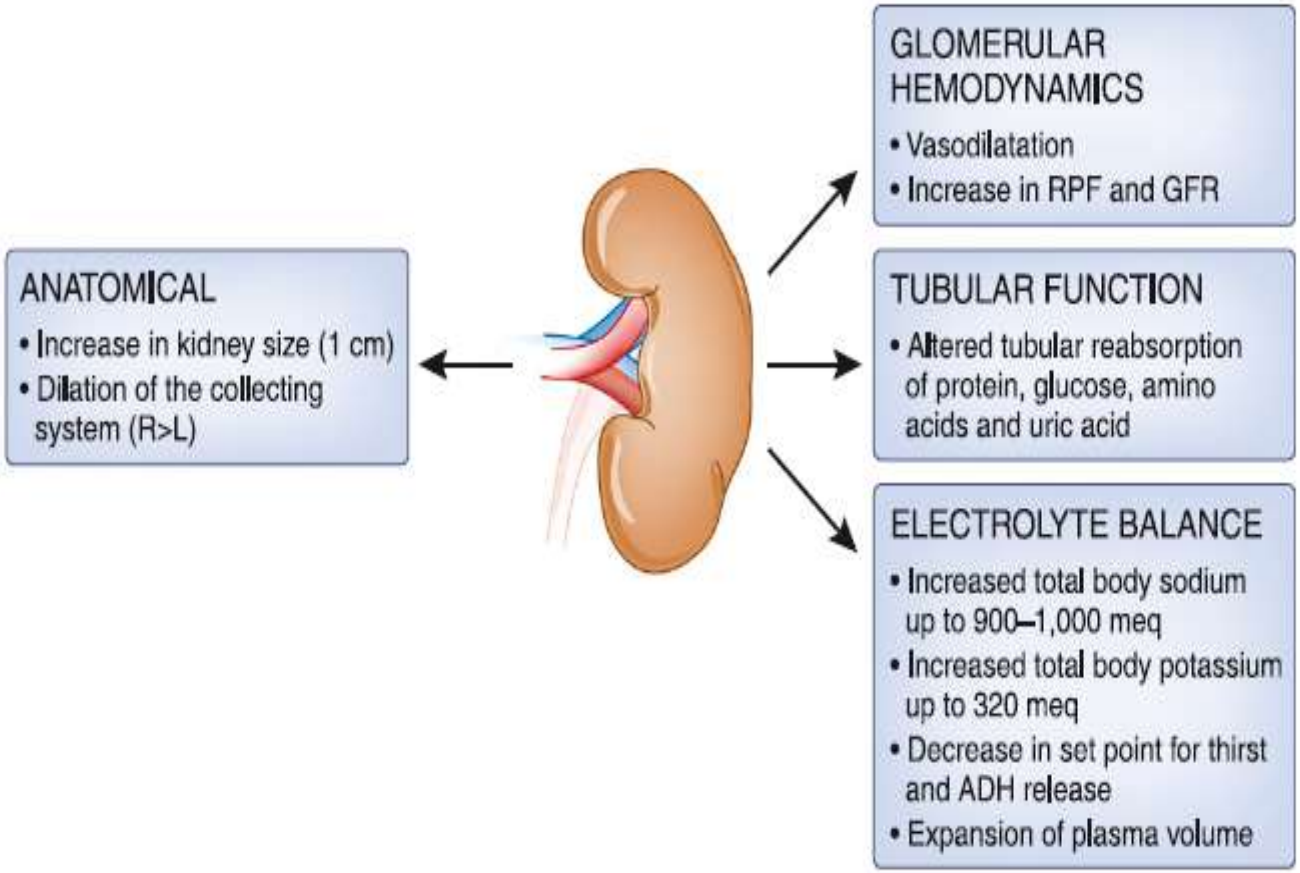
Glucosuria:

Seen in 50% of pregnant women

Variable	Change in pregnancy
Kidney size	The kidney length increases by 1 cm to 1.5 cm, and kidney volume increases by up to 30%
Hydronephrosis	Physiological dilation of the urinary collecting system with hydronephrosis in up to 80% of women (Rt > Lt)
Renal blood flow	Increased by 80% above baseline
GFR	150–200 mL/min (rises 40–50% above baseline)
S. creatinine	Falls to 0.4 to 0.5 mg/dL ($n = 0.8$)*
Uric acid	Falls to 2.0 to 3.0 mg/dL ($n = 4–5$)
BUN	Falls to 8 to 10 mg/dL ($n = 13$)*
Sodium	Mild hyponatremia (Fall of 4–5 mol/L)
Osmolality	Falls to a new osmotic set point of about 270 mosm/kg

*Considered normal in a non-pregnant individual, reflects renal impairment in a pregnant woman.

Summary of renal hemodynamic and metabolic adaptations to normal human pregnancy.



Urinary tract symptoms:

Frequency and nocturia : (among the commonest & earliest symptoms in pregnancy)
**80 -95% of pregnant women.
**Multifactorial (Changes in bladder function & in part to a small increase in urine output)

Urgency & incontinence (85% of pregnant):
Due to Uterine pressure on the bladder, hormonal effects on the suspensory ligaments of the urethra, and/or altered neuromuscular function of the urethral striated sphincter. Treatment includes pelvic floor muscle exercises.

Urine retention:

POSTPARTUM:
4-6 weeks after delivery for the pregnancy-induced physiologic changes to return to the non-pregnant state. Urinary incontinence during pregnancy may persist, and there is a risk of persistent incontinence six months postpartum.

Urinary Tract Infections:

Asymptomatic bacteriuria occurs in **2-7%** of pregnant women & typically occurs during early pregnancy, with approximately 25% identified in the second and third trimesters.

Without treatment, as many as 30-40% of pregnant women with asymptomatic bacteriuria will develop a symptomatic UTI, including pyelonephritis. This risk is reduced by 70- 80% if bacteriuria is eradicated.

Acute cystitis occurs in **1-2%** of pregnant women, with 0.5-2% develop acute pyelonephritis during pregnancy. Most cases of pyelonephritis occur during the 2nd & 3rd trimesters.

In addition to prior untreated bacteriuria, other clinical characteristics that have been associated with acute pyelonephritis during pregnancy include age <20 years, nulliparity, smoking, late presentation to care, sickle cell trait, and pre-existing (not gestational) diabetes

Pregnancy outcomes:

** Untreated bacteriuria: Increased risk of

1- Preterm birth

2- Low birth weight

3- Perinatal mortality

**Pyelonephritis: Increased rate of:

1- Preterm birth, primarily between weeks 33 and 36 (10.3 versus 7.9 percent among those who did not). No differences in stillbirth or neonatal death.

2- Anemia, sepsis, and respiratory distress.

** Maternal morbidity and obstetric outcomes with pyelonephritis do not appear to differ by trimester

Pathogenesis & Microbiology:

E. coli is the predominant uropathogen (70%) found in both asymptomatic bacteriuria and UTI in pregnant women.

Other organisms responsible for infection:
Klebsiella and ***Enterobacter*** species (3% each), ***Proteus*** (2%), & gram+ve organisms (group B Streptococcus (10%)).

Asymptomatic bacteriuria:

**Screening:

- It is recommended to screen all pregnant women for asymptomatic bacteriuria at least once in early pregnancy. Screening is performed at 12 to 16 weeks gestation.
- Rescreening among those who did not have bacteriuria on the initial test is generally not performed in low-risk women. It is reasonable to rescreen women at high risk for infection (history of UTI or presence of urinary tract anomalies, diabetes mellitus, hemoglobin S, or preterm labor).

**Diagnostic criteria:

For asymptomatic women, bacteriuria is defined as two consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of $\geq 10^5$ colony forming units (cfu)/mL or a single catheterized urine specimen with one bacterial species isolated in a quantitative count of $\geq 10^2$ cfu/mL.

**Management:

UTIs in pregnancy

Table 3.5: Treatment regimens for asymptomatic bacteriuria and cystitis in pregnancy (44)

Antibiotics	Duration of therapy	Comments
Nitrofurantoin (Macrobid®) 100 mg	q12 h, 3-5 days	Avoid in G6PD deficiency
Amoxicillin 500 mg	q8 h, 3-5 days	Increasing resistance
Co-amoxicillin/clavulanate 500 mg	q12 h, 3-5 days	
Cephalexin (Keflex®) 500 mg	q8 h, 3-5 days	Increasing resistance
Fosfomycin 3 g	Single dose	
Trimethoprim-sulfamethoxazole	q12 h, 3-5 days	Avoid trimethoprim in first trimester/term and sulfamethoxazole in third trimester/term

G6PD = glucose-6-phosphate dehydrogenase

Acute Cystitis:

Clinical manifestations:

**Sudden onset of dysuria, urgency and frequency.
**Hematuria and pyuria are also frequently seen on urinalysis.
**Systemic symptoms, such as fever and chills, are generally absent in isolated cystitis.

Diagnosis:

A quantitative count ≥10^3 cfu/mL in a symptomatic pregnant woman as an indicator of symptomatic UTI. If bacteria that are not typical uropathogens (such as lactobacillus) are isolated, the diagnosis of cystitis is typically made only if they are isolated in high bacterial counts (≥10^5 cfu/mL).

Differential Diagnosis:

1- Dysuria in pregnant women can be seen with **vaginitis** or **urethritis**.

2- Urinary frequency and urgency may be symptoms of normal pregnancy in the absence of urinary tract infection.

3- If not already performed, testing for sexually transmitted infections (chlamydia and gonorrhea) is warranted for pregnant women with dysuria without bacteriuria or women who have persistent dysuria despite successful treatment of bacteriuria.

Management:

- Prior to confirming the diagnosis, empiric treament is typically initiated in a patient with consistent symptoms & pyuria on urine analysis.

- Treatment is by the same drugs used in treatment of asymptomatic bacteriruia.

Acute Pyelonephritis:

Clinical Manifestations:

The typical symptoms in pregnant woman are the same as in non-pregnant women & include

1- Fever (>38ºC or 100.4ºF),

2- Flank pain.

3- Nausea & vomiting.

4- Costovertebral angle tenderness.

5- Symptoms of cystitis (eg, dysuria) are not always present.

6- Pyuria is a typical finding. (its absence suggests an alternative diagnosis or complete obstruction)

**Most cases of pyelonephritis occur during the 2nd & 3rd trimesters.

Diagnosis:

- Clinical Symptoms + urine analysis & culture.
- Pyuria is present in the majority of women.
- Low threshold for suspicion.
- In patients who are severely ill or who have symptoms of renal colic or history of renal stones, diabetes, history of prior urologic surgery, immunosuppression, repeated episodes of pyelonephritis, or urosepsis, imaging of the kidneys can be helpful to evaluate for complications.

  In pregnant women, *renal ultrasound* is the preferred imaging modality in order to avoid contrast or radiation exposure.

Treatment:

- Hospital admission for parenteral antibiotics. Antibiotic therapy can be converted to an oral regimen tailored to the susceptibility profile of the isolated organism following clinical improvement.
- Parenteral, broad spectrum beta-lactams are the preferred antibiotics for initial empiric therapy of pyelonephritis .
- Following the treatment course, suppressive antibiotics are typically used for the remainder of the pregnancy to prevent recurrence.

Obstetric Management:

- Pyelonephritis is not itself an indication for delivery.
- If induction of labor or cesarean delivery for standard obstetrical indications is planned in a patient on treatment for pyelonephritis (wait until the patient is afebrile, as long as delaying the delivery is relatively safe for the mother and fetus.

Acute Kidney Injury (AKI)

- Defined by the abrupt loss of kidney function.

- It is uncommon in the developed world with an incidence of 1 in 20,000 pregnancies are affected by AKI severe enough to require renal replacement therapy (RRT).

- Causes can be divided according to the trimester:

1- Early pregnancy: *hyperemesis gravidarum*, septic abortion, viral (influenza) or bacterial infection and/or sepsis & OHSS.

2- Late Pregnancy: Severe preeclampsia & HELLP syndrome, TTP or HUS, Acute fatty liver of pregnancy, hemorrhage (placenta previa, placenta abruption, prolonged intrauterine fetal death, or amniotic fluid embolism)

3- **Postpartum:**

** **Pre-Renal AKI:**

It is generally a hemodynamic disturbance that starts with reversible reduction in GFR, leading to ischemic acute tubular damage and resulting in irreversible cortical necrosis in the most extreme cases.

**** Intra-Renal AKI:**

Conditions that potentially are precipitated and worsened by pregnancy

**** Post-Renal AKI:**

Causes of AKI in Pregnancy

Pre-renal • Hypereremesis gravidarum • Hemorrhage • Heart Failure
Intra-renal • Acute tubular necrosis • Acute cortical necrosis • Acute fatty liver of pregnancy • Preeclampsia/HELLP • Thrombotic thrombocytopenic purpura/ atypical hemolytic uremic syndrome • Pyelonephritis • Amniotic fluid embolism • Pulmonary embolism • Lupus nephritis • Acute Interstitial Nephritis
Post-renal • Hydronephrosis due to uterine compression • Injury to ureters or bladder during C-section • Ureteral obstruction from stones or tumor • Obstruction at bladder outlet

HELLP, hemolysis, elevated liver function tests, low platelet count;

Preeclampsia with or without HELLP

- The most common cause of AKI during pregnancy, & is more common when preeclampsia is accompanied by features of the HELLP syndrome (From 1% to 7-15%).
- In most women with preeclampsia, GFR decreases on average by only 30 to 40%, which results in only minor increases in the serum creatinine.

TTP & HUS

- It is more common among patients with HUS.
- Plasma exchange is an important component of treatment of AKI due to either pregnancy-associated TTP or HUS

Renal cortical necrosis

- only 1-2% of all cases of AKI

- Presents with abrupt onset of oliguria or anuria following an obstetric catastrophe, that is frequently accompanied by gross hematuria, flank pain, and hypotension. The triad of oliguria/anuria, gross hematuria, and flank pain is unusual in the other causes of renal failure in pregnancy.

- The diagnosis can usually be established by ultrasonography or CT scanning, which demonstrates hypoechoic or hypodense areas in the renal cortex.

- No specific therapy has been shown to be effective in this disorder. Many patients require dialysis, but 20 to 40% have partial recovery.

Treatment of AKI is supportive:

1- Identification of the underlying source of injury

2- Volume resuscitation and prevention of further injury,

3- Timely initiation of renal replacement therapy (RRT) and prompt delivery of fetus, if necessary