

بسم الله الفَتَّاح العليم

Kidney is a very important organ with many functions, which are :

- 1- **Electrolyte balance**; it controls k^+ , Na^+ , Ca^{++} , PO_4^{-2} , Mg^{++} , and others . if we have abnormality in any one of these electrolytes, then we'll have:

1st: symptoms of this abnormality, for example :

- Hyperkalemia → ECG changes , and sometimes arrhythmia.
- Hypokalemia → muscle weakness and ECG changes.
- Hypophosphatemia → muscle weakness.

2nd: the causes of this abnormality; why this happened ?!

Mostly, it's due to kidney problems or it's due to organs other than kidney, but sometimes , it's because of kidney and other organs. Most of the times, we can modify many of our abnormalities through the kidney when it's normal except if the abnormality is already in the kidney, then we need to repair the kidney in order to be able to handle it.

- 2- **Acid- base balance**

If a patient is suffering severe metabolic acidosis or metabolic alkalosis , then it's might be related to their kidneys.

- 3- **Kidney filters blood from waste products** ; the water we drink which have impurities , the food we eat , drugs and medications we take. All of them are metabolized by the kidney. Also, it removes excess substances even if regularly found in our bodies , like water, if you drink too much water, coffee, or tea, then you'll have more frequent urination and your urine will be very diluted. But if you drink only a little water , you'll have less frequent urination and a very concentrated urine.

So, kidney doesn't only excrete metabolic waste products , but also excess amounts of other normally found substances . if I have excess water in my body and I'm unable to remove it , I'd expect to have significant fluid overload and hyponatremia.

- 4- Producing hormones; erythropoietin, vitamin D , and renin.

If secretion reduces then we'll have problems;

- Erythropoietin reduction produces anemia .
- Vitamin D reduction produces bone diseases because it's associated with bone structure.
- Renin and PG reduction is associated with hypertension.

✂ Why we're studying functions of kidney?!

Because when there's an abnormality in one of these functions, I have to go back to kidney to see if it's working well or not. For example, a patient has fractures everywhere and severe bone abnormalities, why?! He might have a chronic kidney disease led to a decrease in secreted vitamin D. If a patient comes with an anemia and a chronic kidney disease, then there's a relation!

a patient with hyperkalemia eating much dates and fig, if he has renal impairment then he can't remove excess potassium, and he'll have significant hyperkalemia. He may end with cardiac arrest.

So, we need to know these details to be able to know and expect symptoms patient would have.

✂ spectrum of kidney diseases:

It's associated with extremes; from totally asymptomatic to life-threatening situations. Someone appearingly normal may come to your clinic to check up his body function, you discover he has renal abnormality. On the other hand, some patients come arrested at emergency room because they have life-threatening conditions.

Kidney diseases can be associated with other systemic diseases, which means symptoms are not primarily due to renal abnormality, but secondarily caused by a systemic disease affecting kidney.

- **SLE** patients come with many manifestations such as: joint pain, arthritis, redness in their faces "butterfly skin rash", mouth ulcers, abdominal pain and other manifestations. It's associated with renal impairment.
- **Sarcoidosis** which is associated with shortness in breath, fatigue and lack of energy, he can't move, lymph nodes enlargement in the neck. It also affects kidney.
- **Malignancies**; someone may have lung cancer and huge amounts of protein in urine "proteinuria".

So because it's a systemic disease, it's affecting the kidney.

✂ symptoms of kidney diseases

It might be: specific or not specific.

- **Specific** when Kidney can present itself, which means that if there's a problem in kidney, then the symptoms would be related to kidney itself as a result of impairment of kidney functions.
 - ➔ Increase in frequency of urination "frequent urination".
 - ➔ Nocturia; individual has to wake 3-4 times at night for voiding.

- ➔ Dysuria ; burning sensation during urination.
 - ➔ Hematuria ; blood with urine.
 - ➔ Lipiduria ; fat in urine.
 - ➔ Foamy urine.
 - ➔ Increase in blood pressure most of the times ; this might be either primary and associated with kidney disease, or secondary by causes affecting kidney ability to control blood pressure.
- All these symptoms indicate that there's a problem that can be associated with kidney disease.

- **Nonspecific** when it's associated with complications of kidney disease and not reflecting kidney disease. In acute kidney injury , patients doesn't come to you complaining of pain at their loins. They complain of:
 - ➔ Fluid overload.
 - ➔ nausea and vomiting.
 - ➔ Loss of appetite.
 - ➔ Decrease in level of consciousness.

They're very nonspecific, but it's a complication of accumulation of urea in the blood.

- If I have a patient with a chronic renal disease , I have symptoms related to kidney. According to wiki: "CKD is initially without specific symptoms and is generally only detected as an increase in serum creatinine or protein in the urine" , but as the kidney function decreases, symptoms start to appear.
 - ➔ Anemia.
 - ➔ Fatigue.
 - ➔ Muscle pain.
 - ➔ Fractures.

⚕ diagnosis

There's two points you should take care of when you're diagnosing your patient abnormality

- 1- Family history ; which is very important, because there's many inherited diseases can be associated with kidney diseases.
- 2- Drug history, because many of the drugs we take can make injury to our kidneys, like ; antibiotics, stomach medications, pain medications "NSAIDS, high doses of acetaminophens" , they are very dangerous to the kidney and patient can end with a kidney disease.

So, we need to know if the patient has affected kidney functions to make proper diagnosis.

Now let's move to scenarios of some clinical cases to make a differential diagnosis according to what's written above.

☞ cases associated with hematuria

- 1- A male aged 24 years came to emergency with severe left loin pain, associated with gross hematuria. He has no significant past medical history, he never complained any symptoms before.

These symptoms suggest more than one differential diagnosis :

- He might have renal stone causing obstruction to his ureter, severe pain, and bleeding. I should ask the patient if he noticed sand in his urine.
- It might be caused by an infection, unilateral pyelonephritis, ask the patient if he has fever, chills, or burning sensation when voiding "especially last part of voiding".
- Drugs usually don't cause unilateral kidney injury, in this case, the patient has a local cause in his left kidney not a systemic cause.
- Malignancy, though it's not the age of malignancy except if there's a family history of malignancies then he could have an inherited type of cancers. If this is true, then it's a complicating malignancy which might cause this kidney injury. When the mass enlarges, blood supply becomes insufficient, which causes infarction inside leading to severe pain. bleeding inside malignancy causes stretching of the capsule and severe pain.
Note that malignancy is something chronic but patients come with an acute situation if there's **infarction** or **bleeding** inside it, which is considered as an event in malignancy.
- Vascular event; renal artery stenosis for example. Patients would have significant bleeding and hematuria, but he's 24 years old, he's young to have a vascular event.
- Direct trauma to his kidney or trauma with vascular event

Don't forget to ask for family history of renal stones or problems and malignancies.

These are all possible situations, but at the top of the list we have :

Renal stone → trauma → pyelonephritis

- 2- A male aged 40 years complaining of painless intermittent hematuria, he's hypertensive for the last 2 years and taking medications for that. He has strong family history for end stage renal diseases. Some of his brothers are on dialysis.

3 important points to notice:

- ➔ he has no localized pain, so it's associated with a systemic disease.
- ➔ It's something inherited
- ➔ It can be associated with something serious, and can end with a chronic kidney disease.

The possible causes of this case:

- Hematological disease :
✗ blood hemolysis diseases such as; PNH or most commonly G6PD or others.

✗ bleeding tendency like hemophilia or platelet abnormalities.

- One of the possible causes is a hereditary kidney diseases called polycystic kidney disease , patients usually end with dialysis. By ultrasound, we can see cysts everywhere in the kidney, these cysts might be infected leading to intermittent bleeding. They also cause increase in blood pressure.
- SLE is also a systemic inherited disease but it's more in females (9:1) , so we exclude it.
- Hypertension he's suffering from is not a common cause of hematuria.
- Not all chronic kidney diseases cause hematuria.

There's other congenital diseases can cause intermittent or microscopic hematuria such as: Alport syndrome " primarily affects the glomeruli", and thin basement membrane. We'll talk about them more later.

Most of kidney diseases is painless except if you have tension , or increase of pressure in urinary tract.

- 3- A male aged 70 years come with hematuria for the last 4 months. He's hypertensive and a heavy smoker for 20 years. He already had difficulties in urination; he has nocturea and goes frequently for voiding but with a minimal urine output.

Having blood in urine is alarming, the patient might have many difficulties in urination but when he sees blood in his urine he's panicked.

The possible differential diagnosis :

- Prostate abnormality; he might have benign prostatic hyperplasia. Huge prostate obstructing urinary tract flow, bleeding happens because their venous system becomes congested and can leak blood.
- He's hypertensive, hypertension can cause chronic kidney disease, but it doesn't cause significant bleeding and my patient has gross hematuria, which means there's a local cause.
- Malignancy in:
 - ➔ urinary bladder; he's a heavy smoker and has gross hematuria then he's at high risk to develop urinary bladder carcinoma.
 - ➔ Prostatic cancer.
 - ➔ Problems in kidney ,Renal cell carcinoma.
 - ➔ Urethral carcinoma.
 - ➔ Ureter carcinoma.
- Bleeding tendency; he might be taking warfarin because of his heart disease, or taking high doses of aspirin or Plavix "antiplatelet agent". Also, if he has bone marrow malignancy then he would have severe thrombocytopenia.

Let's now make our priorities :

- ❖ We should insert a Foley catheter in his bladder.
- ❖ We should do cystoscopy to see prostate, urethra, urinary bladder.. and make sure he doesn't have malignancy

- ❖ Make sure he has no bleeding tendency causes and test for platelet count, if low number of platelets then it's a problem.
- ❖ CT-scan to make sure he doesn't have renal mass causing this significant bleeding.

Remember that You should put the main differential diagnosis depending on basic knowledge of anatomy and physiology and start from urinary system, then think of those related to other organs and systemic diseases.

We should know that dark urine isn't always caused by blood in it "hematuria", it may be caused by :

- ➔ Some kinds of drinks of food ; Turmeric "الكرّم", Roselle "الكرّديه".
- ➔ Drugs ; rifampicin taken by whom having TB or liver diseases.
- ➔ Having muscle edema
- ➔ When having very concentrated urine, it appears dark in color. Concentrated urine means low kidney perfusion, so kidney increases water reabsorption in order to reserve as much fluids as it can, this leads to minimal dark-colored urine output.
- ➔ Having RBCs in urine.
- ➔ Myoglobin or hemoglobin in urine.

In G6PD patients hematuria happens when severe hemolysis of RBCs so that they'll have overflow in their kidneys to a degree allows blood in urine.

- 4- A male aged 26 years came to emergency complaining of minimal output of very dark urine, severe pain, and significant tenderness in his muscles. He has been doing heavy lifting exercises and working very hard.

- By analyzing the case we find that:

1st the minimal urine output means he has kidney problem.

2nd dark urine means kidney injury causing leaking of blood or something else. When we come to the part describing his muscle tenderness then dark urine is mostly caused by lysis or significant injury in muscles.

According to this , we should think of: a systemic disease that is related to muscles and causing renal impairment. Rhabdomyolysis is the one, it causes dark urine due to myoglobinurea. When this patient did a renal function test, we found he has very high creatinine level equal to 7, normal creatinine levels are <1 ! this means he has acute kidney injury, muscle involvement suggests it's related to muscle injury . Urine test shows +2 blood. Centrifusion "centrifugation" shows no RBCs, but he has very dark urine so it's mostly myoglobin not hemoglobin. In rhabdomyolysis, patient also has hyperkalemia, hypercalcemia, hyperphosphatemia.

We should put other possible differential diagnoses , here are some :

- Maybe he didn't drink water during the whole time in the gym, so he became dehydrated and the situation exaggerated by heavy exercising and he developed problem in the kidney.

- If he has sickle cell anemia , by heavy exercises he would become dehydrated and have sickle cell crisis even if the last crisis was before 5-6 years. You should ask him if he had blood transfusion and order for CBC.
- If he took carbohydrates and he's a G6PD patient, then maybe significant hemolysis happens causing acute kidney injury associated with dark urine.
- It might be a vascular event; While he was exercising, a dissection in renal artery happened causing bleeding and severe muscle pain everywhere.

Though we thought of all possible causes, but rhabdomyolysis is on top of the list because we should have other differential diagnoses and order tests. Why ?! to assure there's no any other problems :

- ➔ Assure there's no coagulopathies by making PT or PT-INR tests.
- ➔ No platelet abnormalities by ordering a platelet test.
- ➔ Order ultrasound with a sample of urine.
- ➔ Kidney function test
- ➔ Order CBC if he has sickle cell anemia as we said before.

☞ cases associated with proteinuria

It means leaking proteins to urine, so basement membrane is not well enough to prevent proteins from leaking through. By testing using dipsticks "measurement devices" we'll find protein in urine which can be caused primarily by a kidney disease and secondarily by a systemic disease.

- 1- A male aged 20 years with no past medical history, he looks very healthy and he came to check up his body health. After doing tests, we found he has +1 protein in urine and +2 RBCs. There's no macroscopic but microscopic hematuria, he don't see dark urine. When ordered to do 24 hour urine collection in a closed bucket we already gave to him -it's better to make it in the weekend, he can't carry the bucket wherever he goes!- we found 500mg/day of proteins, this means he has significant proteinuria and hematuria, his kidney leaks blood and urine, though he looks healthy. I should solve this, if I told him: " you look healthy, go home!" then he will end up having kidney dialysis. Because tests shows he has protein and blood in urine , it indicates he has a glomerular disease which is something progressive, it's not something subside by itself usually, you should follow up your patient and his adherence to medications in order to prolong his kidney life. Asymptomatic kidney diseases can progress to end stage kidney diseases.
- 2- A female aged 24 years has generalized edema especially in her face, foot , and periorbital region so she wakes up in the morning with her eyes closed and can't see, after a while her eyes open up and things get better. She has morning stiffness, significant arthritis, when she goes out in a sunny day her face becomes red with a butterfly "malar" rash. She also has multiple mouth ulcers and a chest pain when breathing. In urine analysis it's found she has +3 protein with no

blood. After doing 24 hour urine accumulation, significant proteinuria appeared; 4gm/day of proteins in urine which is of nephrotic range of proteinuria (>3gm/day).

The whole situation indicates significant serious kidney disease, and these are manifestations of a systemic disease. Arthritis, mouth ulcers, chest pain and skin rash are not associated with kidney itself but to an autoimmune disease. Symptoms suggest SLE which is one of important diseases in females in this age, and it's associated with kidney manifestations so I should target kidney in my treatment; they can end with kidney dialysis if it's not controlled.

SLE patients have psychological issues, psychosis associated with SLE and social problems. Also this is the age of pregnancy; if she's pregnant, then with this proteinuria she'll die and her baby will die because kidney can't tolerate a baby in the mother's body, kidney can't take significant amounts of blood leading her to end up with preeclampsia, babies born early and with seizures and they die.

It's very important to know that the age of this patient is in the spectrum of autoimmune diseases, the manifestations are related to a systemic disease which can affect kidney itself. 24 hour urine accumulation shows if it's serious. It might be associated with autoimmune diseases other than SLE like : seronegative arthritis, rheumatoid arthritis, or vasculitis, so I need to put them in my differential diagnosis.

- 3- A male aged 70 years came with lower limb edema, proteinuria, generalized weakness and fatigue. He was very pale and he doesn't eat or drink well. After doing tests, we found he is anemic, he has very high ESR, +1 RBCs which is a minimal amount of blood, and negative for protein in urine. 24 hour urine collection showed 2gm/day of proteins. Normally proteinuria is specific for albumin, if it's not then I need to look for something else. Doctor found he has multiple myeloma so there's overproduction of immunoglobulins and kidney is overwhelmed with this large amount of immunoglobulins , which results in filtering much proteins outside. Here, it's not the kidney which is abnormal but the amount of proteins delivered to the kidneys is large making a **significant outflow proteinuria**. It's associated with multiple myeloma and other malignancies.

☞ cases of renal failure

- 1- An elderly patient came to your clinic saying he has not been urinating since 3-4 days. He already has difficulties in urination but lately he hasn't been urinating at all. When you put your hand on his abdomen to palpate his urinary bladder, you found it reaches mid abdomen and has severe tenderness. His creatinine level is very high reaching 7,8 ,or even 10 sometimes. You put a Foley catheter to relieve obstruction to find a huge amount of urine came out.

This means renal failure is related to volume of urine output , we have obstruction of the outlet called **post obstruction cause of renal impairment**.

- 2- A patient has nausea and vomiting many times a day, he's not eating or drinking the whole day. He has concentrated urine. If this happens frequently then the patient would have hypointravascular fluid, he becomes hypovolemic leading to low kidney perfusion causing acute renal injury called **prerenal azotemia**. I should give him fluids in emergency room and things back to normal, because we have a normal kidney but low it reserves fluids to the max, so of you restore normal intravascular volume you'll restore normal kidney functions.
- 3- A patient taking medications such as NSAIDs which are an important cause of renal impairment ; interstitial nephritis and acute tubular necrosis leading to an acute kidney injury.

Kidney is a very important organ, if there's dysregulation of renal kidney functions (BP, electrolytes balance...) you should look to the kidney and causes of the kidney disease.

"د عنيآتقدّم بصلاتي

لأأكوني منجسنا لأخطار

ولكن لأقابلها وأجهأ لأوجه دون وجل

لأأسأ لألتفر رجعأ ألمي

ولكن ليكون ليأ الجأء علتحملها

لأأأوسأ لفير عبشديد، بغية النجاة

ولكن لأأعأبأ بالصبر حتأأظفر بحر يتي

هي علي، يارب، أأأكون جبأنا لأأستشعر بنعمتك إأأينأصيبأ النجأح

بلد عنيأظفر بضمة يدك فيأخذ لاني"

طأغور