Renal Function Tests

TUTORIAL 4TH YEAR

DR MUHAMMAD RIAZ

CLINICAL PATHOLOGY SECTION, PATHOLOGY

Department PGMI/AMC

- Urea, commonly referred to as blood urea nitrogen (BUN) when measured in the blood, is a product of protein metabolism. BUN is considered a non-protein nitrogenous (NPN) waste product. Amino acids derived from the breakdown of protein are deaminated to produce ammonia. Ammonia is then converted to urea via liver enzymes. Therefore, the concentration of urea is dependent on protein intake, the body's capacity to catabolize protein, and adequate excretion of urea by the renal system.

- Creatinine, also a waste product, is produced from the breakdown of creatine and phosphocreatine and serve as an indicator of renal function. Creatine is synthesized in the liver, pancreas, and kidneys from the transamination of the amino acids arginine, glycine, and methionine. Creatine then circulates throughout the body and is converted to phosphocreatine by the process of phosphorylation in the skeletal muscle and brain. The majority of the creatinine is produced in the muscle. As a result, the concentration of plasma creatinine is influenced by the patient's muscle mass. Compared to BUN, creatinine is less affected by diet and more suitable as an indicator of renal function.

- Although not as specific as creatinine, BUN can also be used as an indicator of renal function. BUN is not the preferred marker for clearance because it is influenced by factors such as a high protein diet, variables in protein synthesis, and patient hydration status. Alone BUN is not the ideal marker for GFR. Combined with plasma creatinine as a creatinine/BUN ratio, BUN can be a useful analyte in differentiating pre or post renal increase .

- Creatinine may be measured using serum, plasma, or urine specimens. Measuring creatinine clearance requires the collection of a 24-hour timed urine specimen and a plasma sample collecting within the 24-hour urine collection period.
- Serum or plasma may be tested for BUN.

Principal

Creatinine may be measured either chemically or enzymatically. The chemical method known as the Jaffe reaction involves creatinine reacting with picric acid in an alkaline environment to produce an orange-red colored compound. Other sources in the patient sample such as ascorbic acid, acetone, or cephalosporins may produce an orange-red color as they react with the picric acid.

- Multiple enzymatic methods utilizing creatiniase have been used to measure creatinine. These enzymatic methods employ the use of a spectrophotometer to measure NADH to NAD^+ or H_2O_2 to H_2O.

Principal

- BUN is most frequently measured using enzymatic methods. The first step involves the enzyme urease to hydrolyze urea, thereby producing ammonium. The second step involves the quantitative measurement of ammonium using a variety of methods to determine the amount of urea in the sample. The various methods include the glutamate dehydrogenase (GLDH) method which measures NADH to NAD_{+}, measurement of ammonium ion conductivity, or an indicator dye that reacts with ammonium ions.

Acute Kidney Injury

- An abrupt (within 48 hours) reduction in kidney function i.e. an absolute increase in serum creatinine of ≥ 26.4 μmol/L (or 0.3 mg/dL); a percentage increase in serum creatinine of 50% or more (1.5-fold from baseline); or a reduction in urine output (documented oliguria of less than 0.5 mL/kg per hour for more than 6 hours).

Chronic Kidney Disease

- Latest definition of Chronic Kidney Disease (CKD) includes presence of kidney damage or decreased kidney function for three or more months.
- The definition is based on 3 components:

a. An anatomical or structural component (markers of kidney damage, including albuminuria,
b. A functional component (based on GFR)
c. A temporal component at least 3 months' duration of structural and/or functional alterations.

Causes of CKD

- **Cause of disease** e.g.:
  - Diabetes Mellitus
  - Drug toxicity
  - Auto-immune diseases
  - Urinary tract obstruction,
  - Kidney transplantation

Clearance of a Substance

- Glomerular filtration rate(GFR describes the flow rate of filtered fluid through the kidney).
- GFR is a measure of the efficiency with which the kidneys remove waste products from the blood stream.
- Normal GFR is 80-120ml/min.
- GFR can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys.

- Measuring serum creatinine is a simple test and it is the most commonly used indicator of renal function.
- Lower in women, elderly, malnutrition, muscle paralysis and smaller persons.
- Higher in high intake of meat , exercise, coricosteroids, ketoacidosis.
- A better estimation of kidney function is given by the creatinine clearance test. A 24 hour urine collection is performed but shorter collection periods are acceptable.
- A blood sample is drawn during the urine collection period
- Height ,Weight.

Clearance calculation

- Creatinine clearance(ml/min)=UCrV/PCr
- U is concentration of creatinine in urine,
- P is conc. of creatinine in plasma,
- V is volume of urine.
- A urinalysis screens for the presence of protein and blood in the urine. There are many possible reasons for protein in urine. Infection increases urine protein, but so does a heavy physical workout. On the day that you start the test, urinate into the toilet as you normally would when you wake up.
- For the rest of the day and night, urinate into a special container provided by your doctor. Keep the container capped and refrigerated during the collection process. Make sure to label the container clearly and to tell other family members why it's in the refrigerator. On the morning of the second day, urinate into the container when you get up. This completes the 24-hour collection process.

Improving Global Outcomes (KDIGO) stages of chronic kidney disease (CKD):

- Stage 1 GFR greater than 90 ml/min/1.73 m
- Stage 2 GFR-between 60 to 89 ml/min/1.73 m
- Stage 3a GFR 45 to 59 ml/min/1.73 m
- Stage 3b GFR 30 to 44 ml/min/1.73 m
- Stage 4 GFR of 15 to 29 ml/min/1.73 m
- Stage 5-GFR less than 15 ml/min/1.73 m (end-stage renal disease).

Albuminuria

- Albuminuria refers to the presence of urine albumin 30 to 300 mg per day. Microalbumin, considered an obsolete term as there is no such biochemical molecule, is now referred to simply as urine albumin. Albuminuria is used as a marker for detection of incipient nephropathy in diabetics; it is an independent marker for the cardiovascular disease . Urine albumin may be measured in 24-hour urine collections or early morning/random specimens as an albumin/creatinine ratio. Presence of albuminuria on two occasions with the exclusion of a urinary infection indicates glomerular dysfunction. The presence of albuminuria for 3 or more months is indicative of chronic kidney disease. Frank proteinuria is defined as greater than 300 mg per day of protein. Normal urine protein up to 150 mg per day (30% albumin; 30% globulins; 40% Tamm Horsfall protein). Increased amounts of protein in urine may be due to…….

- Glomerular proteinuria: Caused by defects in perm selectivity of the glomerular filtration barrier to plasma proteins (for example, glomerulonephritis or nephrotic syndrome)
- Tubular proteinuria: Caused by incomplete tubular reabsorption of proteins (for example, interstitial nephritis)
- Overflow proteinuria: Caused by increased plasma concentration of proteins (for example, multiple myeloma-Bence Jones protein, myoglobinuria)
- Urinary tract inflammation or tumor
- A1: Less than 30 mg/g creatinine
- A2: 30 to 300 mg/g creatinine
- A3: Greater than 300 mg/g creatinine

Acute Kidney Injury

- Causes that result in decreased blood flow to the kidneys (pre-renal causes), for example, hypotensive and cardiogenic shock, dehydration, and blood loss from major trauma
- Causes that result in direct damage to the kidneys (renal /intrinsic causes) such as damage to kidneys by nephrotoxic medication , sepsis, cancers such as myeloma, autoimmune diseases or conditions that cause inflammation, or damage to the kidney tubules
- Causes that result in blockage of the urinary tract such as bladder, prostate, or cervical cancer, large kidney stones, and blood clots in the urinary tract. Urine output is a good tool for evaluating kidney function and is used in guidelines to define (AKI). Patients with AKI present with oliguria (less than 400 ml per day). The RIFLE classification of (risk, injury, failure, loss of kidney function, and end-stage kidney disease) is based on serum creatinine, GFR changes, and urine output.

- Normal levels of creatinine in the blood are approximately 0.6 to 1.2 milligrams per deciliter in adult males and 0.5 to 1.1 milligrams per deciliter in adult females.
- Results of the blood urea nitrogen test are measured in milligrams per deciliter (mg/dL) and in millimoles per liter (mmol/L) internationally. In general, around 7 to 20 mg/dL (2.5 to 7.1 mmol/L) is considered normal.
-