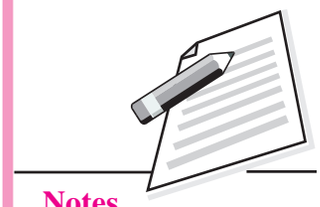

16

KIDNEY FUNCTION TEST

16.1 INTRODUCTION

The main function of the kidney is excretion of water soluble waste products from our body. The kidney has various filtration, excretion and secretary functions. Derangement of any of these function would result in either decreased excretion of waste products and hence their accumulation in the body or loss of some vital nutrient from the body. Based on the level of these excretory products and nutrients in the urine as well as in blood we can make an accurate calculation to decipher the efficieny of the kidney to undertake its various functions.

OBJECTIVES

After reading this lesson, you will be able to:

- explain the importance of kidney function test.
- describe the types of lesions detected by the renal function tests.
- describe the various components of the kidney function test.
- explain the importance of various components of the kidney function test.

16.2 THE FUNCTIONAL COMPONENTS OF A KIDNEY

The functional unit of the kidney is called a nephron. It consists of two main parts, the glomerulus and the tubular system.

The glomerulus is composed of a bowman's capsule and a tuft of leaky blood vessels encapsulated by the bowman's capsule. The primary purpose of the glomerulus is filtrations. The leaky vessels filter into the glomerulus almost all the water, electrolytes, small proteins, nutrients such as sugar etc and excretory

products such as urea etc. The filtrations is dependent on the size and charge of the particles. The average pore size is 8 nm hence particles of only smaller size will pass through. Also the basement membrane carries a negative charge hence preventing negatively charged particles from passing through.

The Tubular system is responsible for re absorption of most of the water, electrolytes, nutrients as well as excretion of the remaining nutrients by means of secretion into the tubules. These tubules are responsible for the concentration of urine.

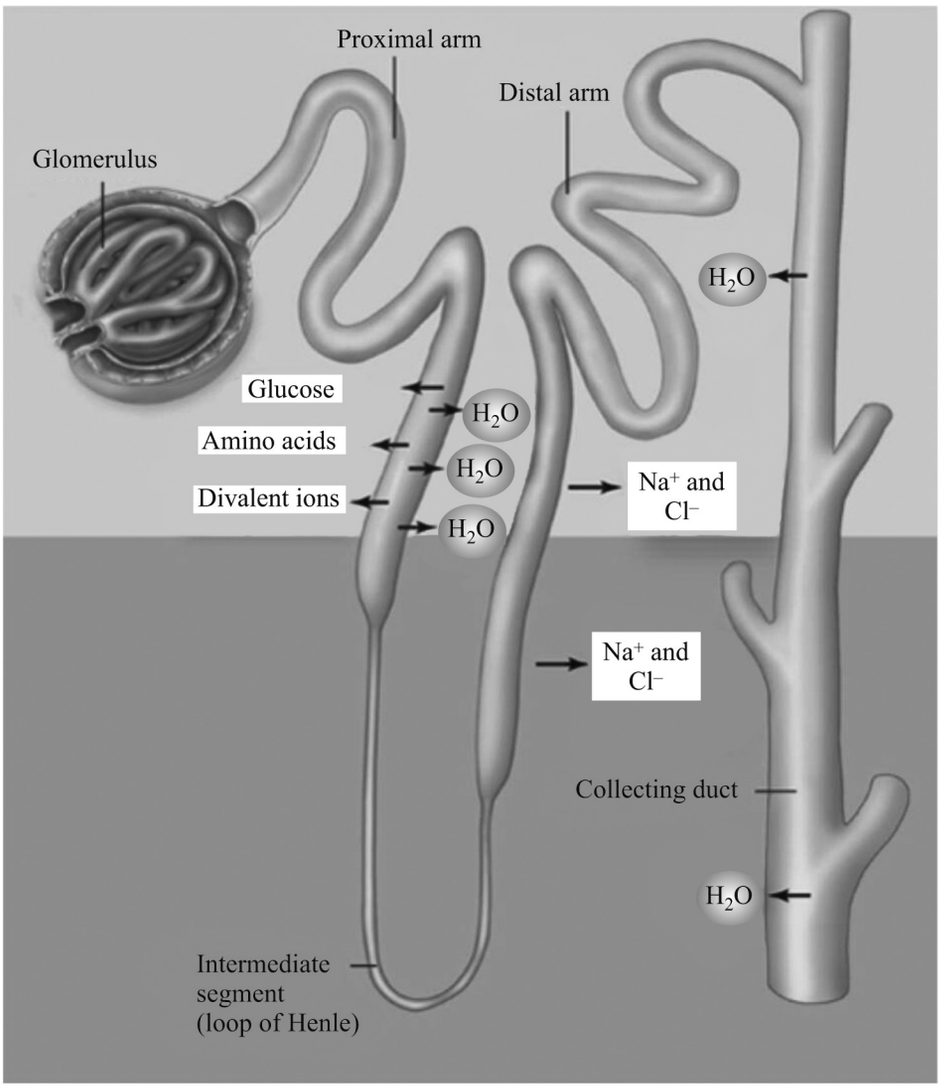

Fig. 16.1: A nephron showing the glomerulus as well as the tubules

16.3 COMPONENTS OF KIDNEY FUNCTION TEST

The components of the Kidney function test can be broadly divided into two categories.

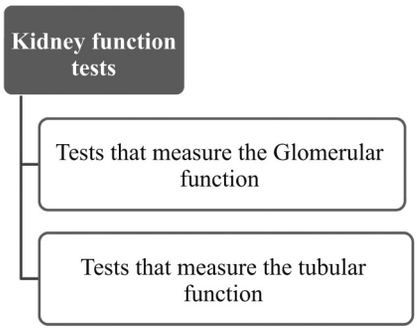

Fig. 16.2

The tests that are part of the Kidney Function test panel are:

(a) Urine examination
(b) Serum Urea
(c) Serum creatinine
(d) Blood urea nitrogen (BUN)
(e) Calcium
(f) Phosphorus
(g) Protein
(h) Albumin
(i) Creatinine clearance
(j) Urea clearance
(k) Inulin clearance
(l) Dilution and Concentration test
(l) Serum electrolyte levels

16.4 URINE EXAMINATION

Before we do a quantitative examination of urine a qualitative examination is necessary as it can provide excellent clues to the nature and location of the lesion in the renal system.

This examination consists of a physical examination where the colour, odour, quantity, specifc gravity etc of the urine is noted. Microscopic examination of urine is done to rule out any pus cells, Rbc casts, Crystals.

16.5 SERUM UREA

Urea is the end product of protein catabolism. The urea is produced from the amino group of the amino acids and is produced in the liver by means of the Urea cycle.

Notes

Urea undergoes filtrations at the glomerulus as well as secretion and re absorption at the tubular level. The rise in the level of serum urea is generally seen as a marker of renal dysfunction specially glomerular dysfunction. Urea level only rises when the glomerular function is reduced below 50%.

The normal serum urea level is between 20-45 mg/dl. But the level may also be affected by diet as well as certain non kidney related disorders. A high protein diet may increase the blood urea level. Similarly a low protein diet may decrease blood urea level. Other causes of protein catabolism such as any hyper metabolic conditions, starvation etc also cause increased blood urea levels. Similarly the level of urea may also be decreased in case of hepatic injury.

So even though blood urea is not an excellent marker of renal dysfunction as it rises quite late in the dysfunction and its rise is also not exclusive to kidney dysfunction, but for practical purposes serum urea level is still one of the most ordered test and forms an important part of the kidney function test.

Urea is measured in diagnostic labs either by UV kinetic method using á keto glutarate as an NH_3^+ acceptor in presence of enzyme glutamate dehydrogenase.

It is also measured calorimetrically by Berthelot's end point method and is read in visible range using a calorimeter.

16.6 BLOOD UREA NITROGEN (BUN)

Sometimes the Serum urea level is expressed as blood urea nitrogen. BUN can be easily calculated from the serum urea level. The molecular weight of urea is 60 and it contains two nitrogen atoms of combined atomic weight of 28. Hence the contribution of nitrogen to the total weight of urea in serum is 28/60 that is equal to 0.47. Hence the serum urea levels can be easily converted to BUN by multiplying it by 0.47.

A rise in blood nitrogen level is known as azotemia.

16.7 CALCIUM

This test measures the amount of Calcium in your blood, not the calcium in your bones. The body needs it to build and fix bones and teeth, help nerves work, make muscles contraction, help blood clot, and help the heart to work. The Calcium test screens for problems with the parathyroid glands or kidneys, certain types of cancers and bone problems, inflammation of the pancreas (pancreatitis), and kidney stones.

Normal Results: 8.5 to 10.2 mg/dl

16.8 PHOSPHORUS

Phosphorus is a mineral that makes up 1% of a person's total body weight. The body needs phosphorus to build and repair bones and teeth, help nerves function, and make muscles contract. The Kidneys help control the amount of phosphate in the blood. Extra phosphate is filtered by the kidneys and passes out of the body in the urine. It plays an important role in the body's utilization of carbohydrates and fats and in the synthesis of protein for the growth, maintenance, and repair of cells and tissues.

High levels of phosphorus in blood only occur in people with severe kidney disease or severe dysfunction of their calcium regulation. Excessively high levels of phosphorus in the blood, although rare, can combine with calcium to form deposits in soft tissues such as muscle.

Normal Results: Standard range not available

16.9 PROTEIN

Protein in urine is noticeably increased in renal disease of any etiology, except obstruction, and is therefore a very sensitive, general screening test for renal disease, though not specific. The extent of proteinuria also provides useful information. The greatest degree of proteinuria is found in the nephrotic syndrome (> 3 - 4 g/day). In renal disease with the nephritic syndrome, the urinary protein excretion rate is usually about 1 - 2 g/day. In tubulo-interstitial disease, urine protein is generally less than 1 g/day. Only in the nephrotic syndrome is the urine protein loss sufficiently great to result in hypoproteinemia.

Protein in serum can generally be maintained at concentrations above the lower limit of normal by increased hepatic protein synthesis so long as protein loss is less than about 3 g/day

16.10 SERUM CREATININE LEVEL

Creatine is a small tripeptide found in the muscles. It stays in its phosphorylated form and releases energy for any burst of muscular activity. It is released from the muscles during regular wear and tear and is converted to creatinine (its internal anhydride). It is to be remembered that unlike urea, creatinine is not a toxic waste. It is simply used as a marker of renal function.

Creatinine is freely filtered at the glomerulus and is also to a very small extent secreted into the tubules. So any problem with gromerular filtrations has a significant effect on the excretion of creatinine resulting in a much substantial rise in serum creatinine level.

Notes

Normal serum creatinine level is 0.6 to 1.5 mg/dl. Serum creatinine is a better indicator of renal function and more specifically glomerular function than urea. For a particular individual the creatinine level is dependent on the muscle mass and muscle wear and tear. There may be significant difference in creatinine level of individuals with vastly differing muscle mass. For example a body builder or athlete will have higher creatinine levels than a sedentary desk worker. Similarly creatinine level will also increase in case of any muscle trauma or excessive wear and tear as seems in athletes and people involved in hard physical labor.

Creatinine is most commonly measured in laboratories calorimetrically by Jaffe's method.

16.11 UREA CLEARANCE

Urea clearance is the hypothetical amount of blood from which kidney clears urea in one minute. This is measured by measuring the concentration of urea in blood, concentration of urea in urine and amount of urine excreted over a one hour interval.

Urea clearance is less than its glomerular filtration as some of the urea that is filtered at the glomerulus is reabsorbed at the tubules.

To measure urea clearance first the patient is made to void urine and then the made to drink two glasses of water. Then the urine is collected after an hour and a blood specimen is also collected at the same time. Then the patients urine sample is collected after another hour. The urea level in the two urine samples and the blood sample is measured. The urine volume is calculated as urine output per minute.

If the urine output is more than 2 ml/minute then urea clearance (in ml/ minute) is measured as:

$$\frac{(\text{Urine urea conc.} \times \text{Urine volume per minute})}{\text{Urea conc. in serum}}$$

If urine output is less than 2 ml/minute then urea clearance (in ml/min) is measured as:

$$\frac{(\text{Urine urea conc.} \times \sqrt{\text{urine volume}}\ \text{ml/min})}{\text{Urea conc. in serum}}$$

Maximum urea clearance of an average individual or body surface area of 1.73 sq m is 75 ml/ min and a standard urea clearance is 54 ml/min. A urea clearance below 60% of standard is considered impaired.

16.12 CREATININE CLEARANCE RATE

Creatinine is filtered at the glomerulus and its reabsorption at the tubular level is insignificant. Because of this creatinine clearance can be used to measure Glomerular Filtration Rate (GFR).

It is measured over a period of 24 hrs. For this urine is collected over a 24 hour period and blood sample is also collected. The concentration of creatinine is measured both in the urine as well as the serum sample.

Creatinine clearance is measured by the following method:

$$\frac{(\text{Conc. of creatinine in urine} \times \text{volume of urine})}{\text{Conc. of creatinine in serum}} \times 1440$$

The normal range of creatinine clearance is:

Males : 100 – 120 ml/ min

Females : 95 – 105 ml/min

This is very close to the glomerular filtration rate.

16.13 INULIN CLEARANCE

Inulin is a small polysaccharide of low molecular weight made up of fructose.

To measure glomerular filtrate the substance used should have the following qualities:

(a) It should be non toxic.

(b) Should not be metabolized in the body.

(c) Should be completely filtered at the glomerulus.

(d) Should neither be secreted or reabsorbed at the tubules.

Inulin meets all these criteria and hence makes for a suitable candidate to measure GFR. Inulin clearance hence equals to GFR. GFR is the amount of blood that passes though and is filtered through the glomerulus in a minute.

To measure Inulin clearance first Inulin is introduced in the blood by means of a slow continuous infusion to maintain a steady conc. of Inulin in the blood. This is done by first infusing 30 ml of 10% inulin in 250 ml of normal saline infused at a rate of 20 ml/ min to achieve desired concentration.

Then 70 ml of 10% inulin in 500 ml saline in infused at a rate of 4 ml/ min to maintain the desired concentration.

Notes

The patient is asked to micturate 20 minutes after the second infusion and the urine in discarded and the time noted. After exactly 60 minutes, take another sample of urine and blood is collected. Measure the volume of urine and the conc. of inulin in both the serum and urine.

Thereafter the inulin clearance is measured by the formulae:

$$\frac{\text{(Conc. of Inulin in urine} \times \text{volume of Inulin)}}{\text{Conc. of Inulin in serum}}$$

Normal inulin clearance is 120 to 130 ml/minute for an average person with a body surface area of 1.73 sq m. This is a close approximation of the GFR.

A below normal inulin clearance shows an impaired glomerular function.

16.14 CONCENTRATION TEST

In case of water shortage in the body the kidney is able to concentrate urine and conserve water. This is done by increasing the reabsoption of water from the glomerular filtrate at the tubular level. So in effect the measure of the ability of the kidney to conserve water and concentrate urine is a measure of tubular function.

For this test the patient is not allowed to take any food or water after the evening meal. The first three urine samples passed in the morning are collected and their specific gravity measured. In a normal person the specific gravity of atleast one of the samples should be above 1.025 or above. If the specific gravity remains below 1.025 then it is a sign of tubular dysfunction.

16.15 DILUTION TEST

Like the concentration test the dilution test is also a measure of functioning of the tubules. In cases of fluid overload of our body the tubules reabsorb lesser amounts of water resulting in excretion of diluted urine.

For this test the subject is put on overnight fast and then in the morning the subject is made to drink 1200 ml of water over a time period of 30 minutes. Then the urine samples are collected every hour for 4 hours. The specific gravity of the samples is measured and atleast one of the samples should have a specific gravity of 1.003 or less. If none of the samples have the specific gravity of 1.003 or less this is a sign of tubular dysfunction.

16.16 ELECTROLYTES

The purpose of the kidney is not just water balance and excretion but also to maintain the electrolyte balance of our body. Kidneys actively reabsorb or

excrete electrolytes to maintain the electrolyte balance of the body. Owing to their small size almost all electrolytes are filtered at the glomerulus. After filtration most of the electrolytes are absorbed back at the tubular level but any problem at the tubular level will result in non absorption and excessive loss of electrolytes in urine.

Serum electrolytes that are measured for this purpose are:

Serum Sodium levels (Na^+) : 135 to 145 mmols/liter

Serum Pottasium level (K^+) : 3.5 to 5 mmols/liter

Serum Chloride level (Cl^-) : 95 to 105 mmols/liter

INTEXT QUESTIONS 16.1

1. The functional unit of kidney is .....
2. Kidney functional test measure ..... & ..... function
3. Urea level rises when the flomerular function is reduced below .....
4. Normal serum urea level is .....
5. A rise in blood nitrogen level is known as .....
6. Normal serum creatinine level is .....
7. Creatinine is commonly measured in laboratories calorimetrically by ..... method
8. ..... rate can be used to measure Glomerular Filteration rate

WHAT HAVE YOU LEARNT

- The main function of the kidney is excretion of water soluble waste products from our body. The kidney has various filtration, excretion and secretary functions.
- Derangement of any of these function would result in either decreased excretion of waste products and hence their accumulation in the body or loss of some vital nutrient from the body.
- The functional unit of the kidney is nephron. It consists of two main parts, the glomerulus and the tubular system.
- Components of Kidney function test are tests that measure the Glomerular function and tubular function.

Notes

The tests that are part of the Kidney Function test panel are:

(a) Urine examination
(b) Serum Urea
(c) Serum creatinine
(d) Blood urea nitrogen (BUN)
(e) Urea clearance
(f) Creatinine clearance
(g) Inulin clearance
(h) Dilution and concentration test
(i) Serum electrolyte levels

- Urine examination consists of a physical examination where the colour, odour, quantity, specifc gravity etc of the urine is noted.
- Microscopic examination of urine is done to rule out any pus cells, Rbcs, casts, Crystals.
- Urea is the end product of protein catabolism and Urea undergoes filtrations at the glomerulus as well as secretion and re absorption at the tubular level.
- The normal serum urea level is between 20-45 mg/dl. But the level may also be affected by diet as well as certain non kidney related disorders.
- Blood Urea Nitrogen can be easily calculated from the serum urea level and the serum urea levels can be easily converted to BUN by multiplying it by 0.47.
- Creatine is a small tripeptide found in the muscles and is simply used as a marker of renal function.
- Normal serum creatinine level is 0.6 to 1.5 mg/dl. Serum creatinine is a better indicator of renal function and more specifically glomerular function than urea.
- Creatinine is filtered at the glomerulus and its reabsorption at the tubular level is insignificant. Because of this creatinine clearance can be used to measure Glomerular Filtration Rate (GFR).
- The purpose of the kidney is not just water balance and excretion but also to maintain the electrolyte balance of our body.

TERMINAL QUESTIONS

1. What is the functional unit of the kidney? Draw a diagram showing its various components.

2. What is the purpose of a Kidney Function Test?
3. What is urea? How is it excreted by the kidney?
4. What is urea clearance? How is it measured?
5. What is Creatinine? How is its clearance measured?
6. On what conditions other than renal function does the level of creatinine in blood depend upon?
7. What is GFR (Glomerular filtration rate)? How is it measured?
8. What are the ideal characteristics of a substance used to measure the GFR?

ANSWERS TO INTEXT QUESTIONS

16.1

1. Kidney
2. Glomerular & Tubular
3. 50%
4. 20-45 mg/dl
5. Azotemia
6. 0.6 - 1.5 mg/dl
7. Jaffe's
8. Creatinine Clearance