1. Introduction and literature review

1.1Introduction:

Chronic renal failure (CRF) is a clinical syndrome that occurs when there is gradual decline of renal function over time. With renal failure there are many physiology derangement of homeostasis of water and minerals (sodium, potassium, chloride, calcium phosphate, magnesium, and sulphate). (Bishop, *et al.*, 2010).

Chronic kidney disease is a worldwide epidemic and escalating problem. Approximately 20 millions adults in the United States are in various stages of chronic kidney disease. (Coresh, 2003).

The gradual failure of kidney function is accompanied by metabolic abnormalities including disordered phosphorus and calcium metabolism. (Block, *et al.*, 2004)

Dialysis is used in cases of acute renal failure to improve the renal function, it may also used to prepare patient with chronic renal failure for transplantation, Dialysis to remove urea and other toxic substances from plasma and corrects electrolyte balance by dialyzing patient blood against fluid containing no urea and appropriate concentration of electrolytes, free ionized calcium and other plasma constituents (Mayne, *et al*., 2000).

1.2literature review

1.2.1Urinary system:

The paired kidneys lie on either side of the vertebral column below the diaphragm and liver, each adult kidney weighs about 160 g and about11cm long and 5to7cm

Wide about the size of first, urine produced in the kidneys is drained into a cavity known as renal pelvis and then it is channeled from kidney via long ducts the ureters to the urinary bladder (Ridge, 2006).

1.2.1.1Kidneys:

the right kidney is at a lower level compared to the left ,the is kidney covered by the renal fascia and per renal fat ,these coverings long with the renal vessels ,the helium of the kidney is in the Tran pyloric plane about 5cm from the midline ,its upper pole lies 2.5 cm and the lower pole 7.5 cm away from midline ,posterior the kidneys lie on the diaphragm the poses major the quadrates labarum and the transverses abdominals ,the cost diaphragm is an important posterior relation of the kidney (Jacob, 2002).

1.2.1.2 The ureters:

the ureter lies on the psoas major muscle behind the parietal peritoneum to which it is adherent on both sides the ureters cross the genitofemoral nerves and are crossed by the gonadal vessels, the right ureter lies behind the third part of the duodenum and as it descends is crossed by the ilecolic vessels and the root of the mesentery (Bishop, *et al.*, 1985).

1.2.1.3Urinary bladder:

The empty bladder has a superior surface; two infer lateral surfaces and abase the base faces posterior the lower part of the bladder which is continuous with the urethra is known as the bladder neck only the superior is covered by peritoneum (Bishop, *et al.*, 1985).

1.2.1.4Urethra:

female urethra which is about 4cm long lies on the anterior wall of the vagina and opens in the vestibule between the anterior ends of the labia minor and the clitoris, male urethra is about 20 cm long having three parts, it passes through the prostate deep perineal push and then through the corpus spongiosum of the penis (Bishop, *et al.*, 1985).

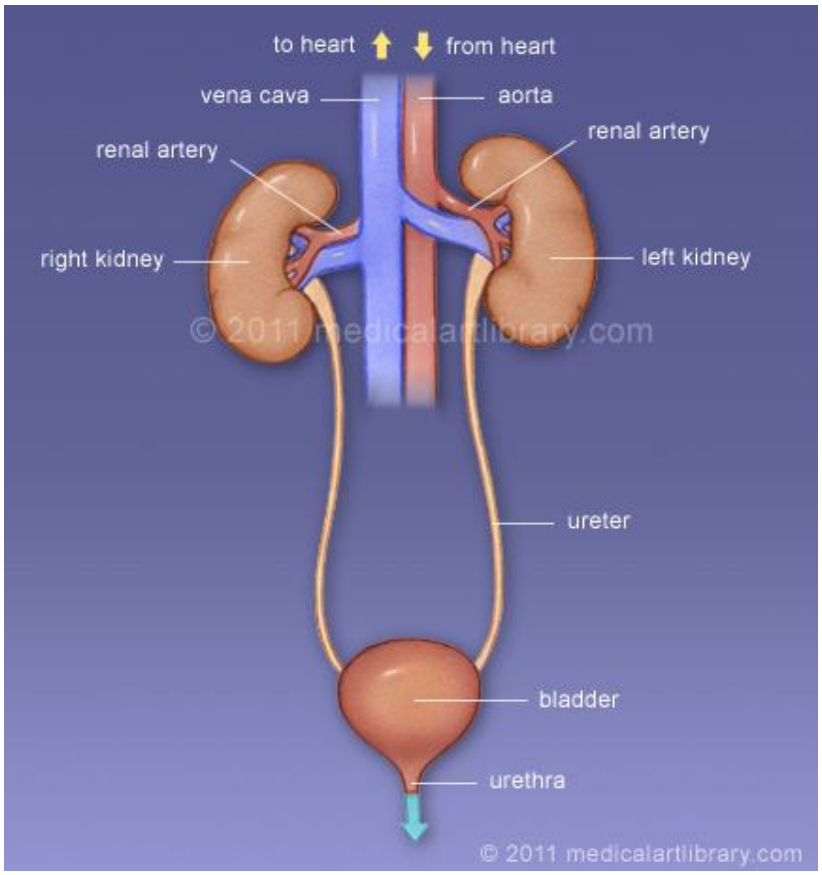

Figure (1.1): structure of Urinary System.

(medicallibrary.com,2011)

1.2.1.5Renal physiology:

There are three basic renal processes:

Glomerular filtration

Tubular reabsorption

Tubular secretion.

The Glomerular filtration:

The glomerulus is the first part of the nephron and functions to filter incoming blood Several factors facilitate filtration one factor is the unusually high pressure in the glomerular capillaries which is a result of their position between two arterioles. This sets up a steep pressure difference across the walls ,Another factor is the semi permeable glomerular basement membrane ,which has a molecular size cut off value of approximately 66,000 Dalton about the molecular size albumin .this means that water electrolytes and small dissolved solutes ,such as glucose ,amino acid ,low molecular weight proteins ,urea and creatnine pass freely through the basement membrane and enter the proximal convoluted tubule other blood convoluted tubule other blood constituents such as albumin many plasma proteins ,cellular elements and protein _bound substance such as lipids and bilirubin are too large to be filtered in addition ,because the basement membrane is negatively charged molecules such as proteins are repelled of the 1200_1500 ml of blood that kidneys receive each minute (approximately one quarter of the total cardiac out put)The glomerulus filters out 125_130 ml of an essentially protein free, cell free fluid per minute is the glomerular filtration rate (GFR) and it is determination is essential in evaluating renal function (Bishop, *et al.*, 1985).

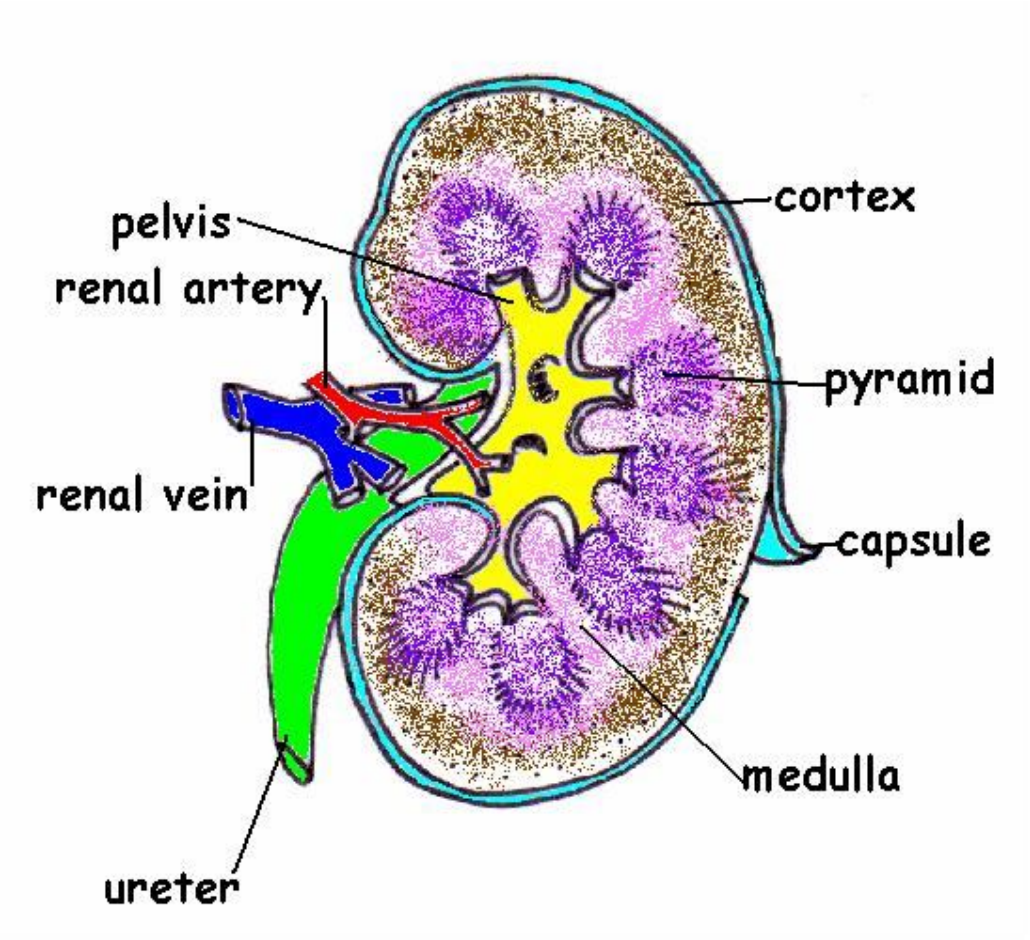

Figure (1.2) Structure of Kidney

(medicallibrary.com,2011)

Tubular Functions:

Proximal convoluted tubule:

The proximal tubule is the next part of nephron to receive the now cell free and essentially protein free food .this filtrate contains waste products which are toxic to the body above a certain concentration and substances that are valuable to the body .one function of the proximal tubule is to return the bulk of each valuable substance back to the blood circulation .thus 75%of the water ,sodium and chloride ,100% of glucose up to the renal threshold ,almost all of the amino acids vitamins and ions such as magnesium calcium, potassium and bicarbonate are reabsorbed .almost all (98% _ 100%) of uric acid a waste product is actively reabsorbed only to be secreted at the distal end of the proximal tubule ,when the substances move from the tubular lumen to the peritubular capillary plasma the process is called tubular reabsorption .with the exception of water and chloride ions ,the process is active that is the tubular epithelial cells use energy to bind and transport process that are involved normally have sufficient reserve for efficient reabsorption but they are saturable .when the concentration of filtered substance exceeds the capacity of the transport system ,the substance is then excreted in the urine the plasma concentration above which the substance appears in urine is known as the renal threshold and it is determination is useful in assessing both tubular function and non renal disease states (Bishop, *et al.*, 1985).

A renal threshold does not exist for water because it is always transported passively through diffusion down diffuse in the wake of sodium.

Asecond function of the proximal tubule to secrete products of kidney tubular cell metabolism such as penicillin the term **tubular secretion** is used in two ways:

1-tubular secretion describes the movement of substances from peritubular capillary plasma to the tubular lumen.

2. Tubular secretion describes when tubule cells secrete products of their own cellular metabolism into the filtrate in the tubular lumen .transport across the membrane of the cells in again either active or passive (Bishop, *et al.*, 1985).

1.2.1.5.1Loop of Henle:

Counter current multiplier system:

The osmolality in the medulla in the portion of the nephron increases steadily from the corticomedulary junction in ward and facilitates the reabsorption of water ,sodium and chloride the hyperosmolality that develops in the medulla is continuously mainted by the loop of Henle ,a hairpin _like loop between the proximal tubule and the distal convoluted tubule .the opposing flows in the loop,the down ward flow in the descending limb ,and the up ward flow in the ascending limb is termed a countercurrent flow .to under stand how the hyperosmolality is mainted in the medulla it is best to look first at what happens in the ascending limb ,sodium and chloride are actively and passively reabsorbed into the medulla interstitial fluid along the entire length of the ascending limb.

Because the ascending limb is relatively impermeable to water, little water follows and medulla interstitial fluid become hyper osmotic compared with the fluid in the ascending Limb (Bishop, *et al.*, 1985).

1.2.1.5.2Distal convoluted tubule:

The distal convoluted tubule is much shorter than the proximal tubule ,with two or three coils that connect to a collecting duct the filtrate entering this section of the nephron is close to it is final compostion .about 95% of the sodium and chloride ions and 90% of water have already been reabsorbed from the original glomerular filtrate .the function of the distal tubule is to effect small adjustments to achieve electrolyte and acid _base homestasis ,these adjustments occur under the hormonal control of both anti diuretic hormone (ADH) and aldosterone (Bishop, *et al*., 1985).

1.2.1.5.3Collecting Duct:

The collecting ducts are the final site for either concentrating or diluting urine ,the hormones ADH and aldosterone act on this segment of the nephron to control reabsorption of water and sodium .chloride and urea are also reabsorbed here .urea plays an important role in maintaing the hyperosmolality of the renal medulla .Because the collecting ducts in the medulla are highly permeable to urea ,urea diffuse down its concentration gradient out of the tubule and into the medulla interstitum,increasing its osmolality (Bishop, *et al.*, 1985).

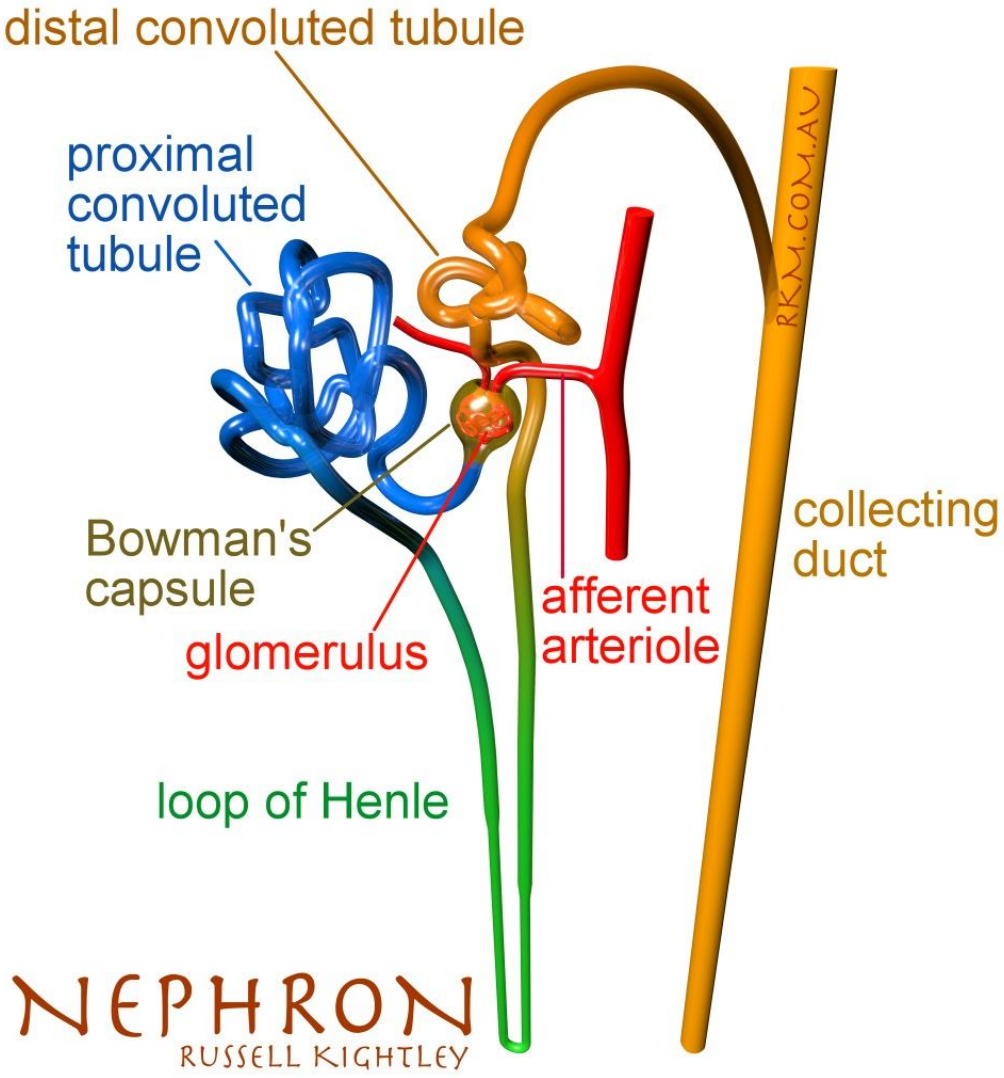

Figure (1.3): Structure of Nephron

(medicallibrary.com,2011)

1.2.2 Functions of the urinary system:

Urine formation,fluid and electrolyte balance,regulation of acid _base balance excretionOf the waste products of protein metabolism,excretion of drugs and toxins Secretion of hormones (Bishop, *et al.*, 1985).

1.2.3 Normal Functions of the Kidneys depend on:

the integrity of the glomeruli and the tubular cells

Abnormal blood supply under normal circumstances about20percent of the cardiac output flows through the kidney

Normal secretion and feed back control of hormones acting on kidney (Mayn, 1994).

1.2.4 chronic RenalFailure:

Chronic kidney disease (CKD) is a clinical syndrome that occurs when there is gradual decline in renal function over time , according to the 2007 US ,Renal Data System (USRDS) Annual Data report one in nine US adults has CKD and 20 million more are at risk, early detection and treatment are needed to prevent progression to ESRD and complications such as coronary vascular disease .the national kidney foundation has formulated guidelines for earlier diagnosis ,treatment and prevention of further disease progression .GFR and evidence of kidney damage based on measurement of proteinuria or other markers form the basis of the classification The conditions that can precipitate acute renal failure also may lead to chronic renal failure (Bishop, *et al*., 1985).

1.2.4.1 Increasing Incidence of chronic kidney disease:

There is an increasing incidence of CKD in the US due to the increase in diabetes mellitus can have profound effects on the renal system patients with type 1 diabetes have an insulin deficit approximately 45% of patients with type 1 diabetes will develop progressive deterioration of kidney function (Diabetic nephropathy)within 15_20years after diagnosis ,a smaller percentage of persons with type 2 diabetes will also develop this condition .the effects are primarily glomerular but they may affect all kidney structures as well and are theorized to be caused by the abnormally hyperglycemic environment that constantly bathes the vascular system (Bishop, *et al.*, 1985).

1.2.4.2Therapy of the chronic renal disease

For patients with irreversible renal failure, dialysis and transplantation are the only two therapeutic options, initiation of either treatment occurs when the GFR falls to 5ml\min (10_15ml/min) in patients with diabetic nephropathy (Bishop, *et al*., 1985).

1.2.4.2.1Dialysis:

traditional hem dialysis or it its more recent high efficiency form as well as peritoneal dialysis are the available methods the clinical laboratory used in conjunction with ahemodialysis facility must be able to adequately monitor procedural efficiency a wide variety of areas, renal dialysis has basic goals and specific laboratory tests should be performed to evaluate the achievement of each goal (Bishop, *et al*., 1985).

1.2.4.4.2.2 Transplantation:

The most efficient hemodialysis techniques provide only 10%_12% of the small solute removal of two normal kidneys and considerably less removal of larger solutes even patients who are well dialyzed have physical disabilities and decreased quality of life.

Kidney transplantation offers the greatest chance for full return to healthy productive life however this option is limited by the significant shortage of donor organs for ESRD patients waiting for an organ donation can vary from several months to several years (Bishop, *et al*., 1985).

1.2.5Blood Definition:

Specialized vital connective tissue, opaque, alkaline in pH , and consists of two portions; fluid called plasma and solid which called cells. It is temperature is 38C, blood viscosity is 4.5-5.5; and it is equal about (8%) from the body weight (Harland Themal2002).

1.2.6 Blood Composition:

Blood composed of pale yellow fluid called plasma in which are suspended red cells (erythrocytes), white cells (leucocytes), and platelets (thrombocytes) (Harland Themal2002).

1.2.6.1 Plasma:

Forms about 55% of blood volume and contains water 90% and many solutes including proteins, minerals, irons, organic molecules, hormones, enzymes, products of digestion, and waste products for execration(Harland Themal2002).

1.2.6.2 Blood Cells:

There are three types of blood cells that are suspended in plasma which are;

1- Red blood cells (erythrocytes). 2- platelets (thrombocytes). And

3- white blood cells (leucocytes) (Harland Themal2002).

1.2.6.2.1 Red blood cells (Erythrocytes);

RBCs are biconcave disk shaped a nucleated cells produced from bone marrow under the influence of erythropoietin hormone. RBCs contain hemoglobin which is responsible for gaseous exchange (CO_2 and O_2), RBCs express CR1 on their membrane which help in immunologic removal of tissue depress from the Circulation. Normally RBCs count in the Peripheral blood is ($4.5\text{-}5.0xl0^{12}$/l) in adult males and ($4.0\text{-}4.5x\ 10^{12}$/1) in adult females(Harland Thernal2002).

1.2.6.2.2 Platelets (Thrombocytes):

Thrombocytes are 2-4 um in size and anuclear, their light blue stained cytoplasm and their process give them astar like shape, reddish blue granules near the centre. Young thrombocytes are more spread out; older ones look like pyknotic dotes. Thrombocytes are produced in bone marrow from amature megakaruocyte (150-450 $x10^9$/l), and have and important role in prevention of blood loss by making primary haemostatic plug (Harlard Themal 2002).

1.2.6.2.3 White blood cells (Leucocytes):

One of blood cells that are characterized by it's color less ness (absence of Hemoglobin) so they are referred to as white cells. Their main function is body defense and found in the peripheral blood within the range of (4-11x109!l). Asecondary granules' which materials that help them to fight pathogens. There are three cells which are granulocytes(Harland Themal2002).

1.2.6.2.3.1 Granulocytes:

They are known as granulocytes because of their cytoplasmic granulation "primary and secondary granules" which contain hydrolytic enzymes, nitrogenoxide, hydrogen peroxide and other materials that help them to fight pathogens. There are three cells which are granulocytes. Harlard Themal(2002)

1.2.6.2.3.1.1 Neutrophilic Granulocyte "Neutrophil":

Band cells "Band neutrophil" ; Present the further development of meta myelocyte which characterized by unsegmented band shape nucleus and represent about 2% in the peripheral blood. Segmented Neutrophil; it's the final cells in the lineage started with myeloblaste characterized by segmented nucleus 10-20 % have two segments ,40-50% have three segments, 10-20 % have four segments, and 0-5% have five segments, fine blue cytoplasm

granules. Neutrophils are phagocytic cell against bacteria and represent about 50-70% in peripheral blood(Harland Themal2002).

1.2.6.2.3.1.2 Eosinophilic Granulocyte (Eosinophil):

Eosinophil arise from same stem cell population as neutrophil, and mature in parallel with them, generally eosinophil characterized by bilobed nucleus, rough red orange granules. Normally represent about 1-6% from the peripheral WBCs count, active aganist parasitic infections(Harland Themal 2002).

1.2.6.2.3.1.3 Basophilic Granulocytes "Basophil":

Like eosinophil, basophil mature in parallel with cells of neutrophil lineage the earliest stage at which they can by identified is the myelocyte stage at which large black violet stained granules is present. Basophil have bibbed nucleus which covered by large dark violet cytoplasm granules, normally they represent about 0- 1% from the peripheral leucocyte count. Basophil like tissue mast cells are responsible for allergic and hyper sensitivity reactions(Harlard Themal2002)

1.2.6.2.3.2 Agranulocytes:

Because of absence of cytoplasmic granulation there for they are known as agranulocyte, and include: 1- Monocyte. 2- lymphocyte(Harland Themal2002).

1.2.6.2.3.2.1 Monocyt:

Monocyte development line is branches off at avery early stage from that of granulocytic series but does not contain any distinct, specific precursor that can be surly identified

1.2.6.2.3.2.2 Lymphocytes;

with diagnostic significance in every day morphological studies.

Monocyte is alargest cell in the peripheral blood "20-40um" and has an ovoid nucleus usually irregular and ling with ivagination and often pseudopodia like cytoplasmic process, their cytoplasm stained light gray blue. Monocyte is the main phagocytic cell and gives arise to tissue macrophage, they represent about 2-10% from the total leucocyte count(Harland Themal2002).

Lymhpocytes are produced every where, particularl in the lymphnode, bone marrow, and lyrnphatic islands of intestinal mucosa under the influence of thymus gland "T-lymphocytes 80%" or bone marrow "B-lymphocyte 20%" afew fraction of lymphocytes are natural killer cells (NK). Morphologicall lymphocytes are classified into small and large lymphocyte. Lymphocyte represent about (20-40%) of peripheral

WBCs count, and active against viral infections, and they are the most important immune cells(Harland Themal2002)

1.2.7 Blood Function:

Blood has three main functions; 1-Transport. 2- productive, and 3 Regulation(Harland Themal2002).

1.2.7.1 Transport:

Transport of the following substances;

- Gases, namely oxygen (O2) and carbon dioxide (CO2) between
• the Lungs and rest of the body.
- Nutrients from the digestive tract and storage sites to the rest of the body.
- Waste products to be detoxified or removed by the liver and kidney.
- Hormones from the glands in which they are produced to their target cells.
- Hormones from the glands in which they are produced o their target cells.
- Heat to the skin so as to help regulate body temperature.

(Saladinks2004).

1.2.7.2 Productive:

Blood has several roles in inflammation;

- Leukocytes, or white blood cells, destroy invading micro organism and cancer cells.
- Antibodies and other proteins which destroy pathogenic substances.
- Platelet factors initiate blood clotting and help minimize blood loss(Saladinks2004).

1.2.7.3 Regulation:

- by PH interacting with acids and bases.
-Water balance by transferring water t and from tissues.

1.3 Blood Formation "Haemopoiesis":

1.3.1 Definition:

Haem: latin word means blood poiesis latin word means production. Is the production of the formed elements of blood. Haemopoietic tissues refer to the tissues that produce blood. The earliest haemopoietic tissue to develops the yolk sac, which also functions in the transfer of yolk nutrients of the embryo. In the fetus, blood cells are produced by the bone marrow, liver, spleen and thymus. This changes during and after birth. The liver stops producing blood cells around the time of birth, while the spleen

stops producing them soon after birth but continues to produce lymphocytes for life. From infancy on wards, all formed elements are produced in the red bone marrow.

Lymphocytes are additional produced in lymphoid tissues and organs widely distributed in the body, including the thymus, tonsils, lymphonodes, spleen and patches of lymphoid tissues in the intestine(Saladinks2004)

1.3.2 Sites of haematopoiesis:

The sites of haematopoiesis depend on the presence of disease and on the developmental state of the individual.

-Normal Conditions;

Under normal conditions, all cellular components originate in the bone marrow Some components (e.g., erythrocytes and platelets) complete their development at medullary (i.e. bone marrow) sites, whereas other components (e.g. T and B cells) complete their development at extra medullary sites(Emmanuel C . Besa1992).

Fetal sites of hematopoiesis:

In utero, hematopoiesis proceeds as follows;

1- hematopoiesis can be detected first in the blood islands, groups of mesenchymal cells in the yolk sac, at 3-12 weeks gestation.

2- The liver is active in hematopoiesis from 5-6 weeks up to 6 months gestatin and even as long as 2 weeks after birth.

3- The spleen is active at 4-8 months gestation.

4- Bone marrow becomes active at about 5 months gestation and becomes the primary site by 7 months. The bone marrow remains the principal site of hematopoiesis after birth(Emmanuel C.Besa 1992).

- Postnatal changes in the sites of hematopoiesis:

At birth , all bone marrow cavities are hematopoietic. At the individual ages, the loci of hematopoiesis shift;

- The marrow cavities of peripheral bones stop producing cells.
- The marrow cavities of the axial skeleton becomes more prominent until, after 20 years of age, blood production has become limited to the vertebrae, sternum, iliac bones, skull, and proximal ends of the long bones of the extremities.

-Gross morphologic changes accompany the physiologic changes in marrow. Such as;

1- Red marrow. 2- Yellow marrow(Emmanuel C Besa1992).

1.3.3 Haemopoiesis growth factors:

Include s; GM-C SF (Granulocytes. monocyt, colony, stimulating, factor), G-CSF (Granulocytes, colony, stimulating, Factor-i), IL-3 (Ititer, leukine-3), 1L5 (Inter, leukine-5). Erytheropoiteine (Epo) and Thrombopoietin(Hoffbrand2006).

1.3.4 Erythropoiesis:

Formation of red boold cell. Red cells are produced by proliferation and differentiation of precursors whose dominant representatives in the bone marrow are the erytherocytes. Erythroblasts referred to as normoblasts when their morphological features are within normal limits. During the course of differentiation, the size of the erythroblasts progressively decreases and the character of the nucleus and cytoplasm changes the cells proceed toward the point where proliferative capacity is lost and (hemoglobin becomes the predominant protein the cytoplasm D.Penington1989).

-Pro erythroblast (Pronormoblast):

is the least maturation of the morphologically identifiable members of the erythroid series. It has a diameter of 14-20µm, and abasically round outline with minor peripheral protuberances. There are several nucleoli in the nucleus, the chromatin in the nucleus consists of a net work of fine red purple strands (Penington1989).

-Basophilic erythroblast (Early normoblast):

Is around cell with diameter of 12-16µm, and more basophilic cytoplasm than the pro erythroblast(D.Penington1989).

-Polychromatophilic erythroblast (intermediate normoblast):

Is around cell between 12-l4µm in diameter the characteristic polychromatic appearance of the of the cytoplasm derived from the mixture of the basophilic ribonucleic acid (RNA), and acidophlic haemoglobin. Nuclear chromatin is coarse , deeply basophil clumps(Penington1989).

-Orthochromatophilic erythroblast (Late normoblast):

Constitute the next final stage of maturation of the nucleated red cell series. They are smaller than their predecessors, and have a diameter between 8 and l2µm.

Nucleus small and pyknotic, with ahomogeneous blue-black appearance(Penington 1989).

- Reticulocyte:

Have the same biconcave discoid shape as mature red cells, although they have aslightly greater volume and diameter than the latter (Penington1989).

-Erythrocyte (Mature RBCs):

Biconcave discoid shape, with diameter 7.2µm , a nuclear cell, with centeral pale area (Penington1989).

Erythropoietin (EPO):

Erythropoietin is specific erythroid growth factor. it was originally purified from the urine of anemic subjects, and is a highly glycosylated protein with amolecular weight of about 34KDa, with about 35% being glycosyl residues. Erythropoietin is encoded by a gene of chromosome 7 in a 5.4kb region of genomic DNA with 4 introns and 5 exons. In the fetus and during the neonatal period, EPO is produced in the liver as well as in the kideny' s but there after more that 90% of EPO production occurs in the kidneys. A small amount of EPO is still produced by the liver in adult life(Hoffbrand 2006)

1.3.5 Leucopoiesis:

The prosses of production white blood cell, include;

1.3.5.1 Granulopoiesis:

The predominant white blood cell, or leucocyte, in the circulation is mature granulocyte. The granulocyte series, such as,

-The myeloblas:

Large cell, 1 5-20µm in diameter, with around to oval nucleus, no typical granules in the moderately basophilic cytoplasm. Nuclear chromation red-purple strands, nucleoli are two or three is usual number (Penington1989).

-Promyelocyte:

It is similar to those of the myeloblast, except for the development of some cytoplasmic granules, and aslightly more coarse appearance of the chromatin. Nucleoli are still present(Penington l989).

-Myelocyte:

it has prominent cytoplasmic granules, less basophilic, nucleoli no longer present, and the chromation appears more aggregated than in the promyelocyte(Penington1989).

-Metamyelocyte:

The nucleus becomes indented and as same a kidney shaped appearance, granules are prominent in the cytoplasm. When the degree of indentation of the nucleus is greater than 50% of the nuclear diameter, the precursor has reached the band or stab, form stage. Cytoplasmic granules are identical to those in the mature segmented form (Penington 1989).

-Segmented or polymorphonuclear granulocytes:

With diameter 12-l4um, characterized by alobulated nucleus with two to five lobes of clumped chrornation, each linded by a thin chromation strand . Approxirnally 1-3% of segmented neutrophils in females have clearly defined drum stick (Penington1989).

-Polymorpho nuclear eosinophils:

Are slightly larger than segmented neutrophils and have a diameter of up to l6µm. The number of nuclear lobes is usually two. The cytoplasm has apale blue similar to that of neutrophil, and contains many granules, large, stained bright orange with Romanowsky stains(Penington1989).

-Polymorhponuclear basophils;

Are similar to the mature eosinophil, with the characteristic distinction that the granules are intensely basophilic, and tend to over lie and obscure the nucleus (Penington1989).

1.3.5.2 Formation of monocytes:

The series of it;

-Monoblasts

Are the least mature of the morphologicall recognizable members of the monocyte. Very similar in appearance to myeloblasts. Located predominantly in the bone marrow, which is the major site of monocyte production (Peningtonl989).

-Promonocyte;

Is next stage in the differentiation pathway. It is similar in size to the promyelocyte, but has amore irregulary shaped, and often deeply cleft, nucleus containing nucleoli. The cytoplasm contain large granules and more basophilic than in the mature monocyte(D.Penington1989).

-The mature monocyte:

Is slightly larger than the segmented granulocyte. It has an irregularly shaped nucleus from around to sufficiently idented to produce alobulated appearance.

Cytoplasm is abundant, and of aple grey to blue tine. It contains some small neutrophile or basophilic granules. Monocytes are motile cells and are thus capable of migrating into the blood passing through bone marrow sinusoids (Penington1 989).

1.3.5.3 Lymphopoiesis:

Production of the lymphocyte, the lymphoid series

-Lymphoblasts;

Are slightly smaller than the myeloblasts which they resemble, except that the ratio of the diameter of the nucleus to that of the cell tends to be greater, and the number of nucleoli to be fewer than in myeloblasts(Penington1989).

-The large lymphocyte;

Is between 12 and 14µm in diameter, the nucleus is round or idented, chromation more clumped than in the lymphoblast. Cytoplasm abundant, and usually pale blue. (Penington l989)

-The small lymphocyte;

Is between 9 and 12µm in diameter, and smaller than Segmented granulocytes, cytoplasm is scanty(Penington1 989)

1.3.6Thrombopoiesis:

Thrombopoiesis refers to the production of platelets in the blood, because of this platelets called thrombocytes. This starts when ahaemocytoblast develops receptors for the hormone thrombopoietin which is produced by the liver and kidneys. When these receptors are in place, the haemocytoblast becomes acommitted cell called amegakaryoblast. This replicates its DNA

(Beker1976).

1.3.7 Haemoglobin:

Haemoglobin is alarge complex molecule (molecular weight 6800). It is synthesized in the developing red cells and consists of four ploypeptide chains closely linked together (goblin). An iron containing complex called haem is attached to each polypeptide chain and it is this part of the molecule which is responsible for its oxygen carrying properties. If the ferrous iron of haem is oxidized the oxygen carrying capacity of the haemoglobin is lost. Haemoglobin has the property of combining reversibly with oxygen. Oxygen is taken up by the red cell in the lungs and given up to the tissue while circulating through the body. The oxygen is bound to the iron component of haemoglobin, forming oxyhaemoglobin. When the oxygen has been given up to the tissues reduced haemogloobin is formed. Haemoglobin also plays apart in the transport of carbon dioxide to the lungs, where it is exhale. Carbon dioxide is not bound to the haemoglobin in the same way as oxygen, but is carried in the red cell in the form of bicarbonat . About 90% of the carbon dioxide is removed from the tissue in this way, the remainder being carried away as bicarbonate in the plasma. The haemoglobin value is usually recorded in g per 100 ml of blood

(Baker1976)

-Types of Haemoglobin:

The types of haemoglobin is determined by the globin chains that comprise it. The types of globin chains available for haemoglobin synthesis depend on the developmental stage of the individual.

1- Embryonic haemoglobin; include;

- Gower 1
- Gower 11
- Portland

2- Fetal Haemoglobin.

3- Adult Haemoglobin. (C.Besa 1992).

1.4 CompLete Blood Count (CBC):

1.4.1 Definition:

Acomplete blood count (CBC) is a series of tests used to evaluate the composition and concenteration of the cellular components of blood(Chernecky2001).

1.4.2 Tests included in CBC:

1.4.2.1 Red blood cell (RBC) Count & HGB level:

The red blood cell (RBC) count determines the total number of red cells in sample of blood, also can measure the level of Hb in the sample(Shernecky2001)

1.4.2.2 Hematocrit (HCT):

The hematocrit is a test that measures the volume of blood in precent is comprised of the red blood cells. Automated cell counters calculate the hematocrit bymultiplying the RBC by the mean red cell volume(Shernecky2001).

1.4.2.3 Mean Corpuscular Volume (MCV):

The average size of the red cells expressed in femtoliters. MCV is calculated by dividing the hematocrit (as percent) by the RBC count in millions per microliter of blood, then multiplying by 10 (Shernecky 2001).

1.4.2.4 Mean Corpuscular Hemoglobin (MCH):

The average amount of hemoglobin inside an RBC expressed in pictograms. The MCH is calculated by dividing the hemoglobin concentration in grams per deciliter by the RBC count in millions per microliter, then multiplying by 10(Shernecky 2001).

1.4.2.5 Mean Corpuscar Hemoglobin Concentration (MCHC):

The average concentration of hemoglobin in the RBC expressed in percent. Calculated by dividing the hemoglobin in grams per deciliter by the hematocrit, then multiplying by 100(Shernecky2001).

1.4.2.6 White Blood Cell (WBC) Count:

The majority of CBC include both a WBC count and an automated differential. A differential determines the percentage of each of the five types of mature blood cells (Shernecky2001).

1.4.2.7 Platelet(PLT) count:

The platelet count is most often measured by impedance counting but is performed manually when the platelet count is very low, platelet clumping is observed, or abnormally large (giant) platelets are present(Shernecky2001).

1.5 Rationale :

Chronic kidney disease (CKD) is a clinical syndrome that occurs when there is gradual decline in renal function over time It effects the haemopoietic system .this require different type of therapy such as blood transfusion and erythropoietin . so this study is carried out to evaluated the status of erythropoietin in patient on dialysis .

1.6 Objectives:

1.6.1 General objective:

To determine of blood parameters in Sudanese chronic renal failure under hemodialysis

1.6.2 Specific objectives:

-To determine the avaribles values of haemoglobin , hematocrit, white blood cell count, red blood cell count, and platelets count and red cell indices in Sudanese chronic renal failure in Khartoum state.

2. Materials and Methods:

2.1 study Design:

Analytical case-control to determine complete blood count in patient with chronic renal failure in EL-Ribat national hospital in June 2014.

2.2 study population:

The study conduct in hemodialysis unit of EL-Ribat national hospital.

2.3 study area:

Khartoum state.

2.4 study duration:

The study was carried out at the period between (march-June /2014).

2.4.1 Sampling;

5 ml EDTA blood was collected.

2.4.2 Sample Size:

200 samples,100 from patient 100 control.

2.5 Study Variables:

The variables include quantitative data such as different blood parameters, and semi qualitative data such as living place. Economis state.

2.6 plan of data Collection:

The data was collected by direct interview through designed questionnaire for each patient .

2.7 Data analysis:

Data was analyzed by statistical package social program (SPSS 2011).

2.8 Methodology:

2.8.1 sample collection:

5m1 of venous blood in EDTA containers was collected.

2.9 complete Haemgram:

EDTA blood samples were analysed for CBC by sysmex automated hematological analyzer.

2.9.1 Equipment:

Sysmex laboratory diagnosis of blood haemogramin,

• Hb g/dl

• HCT%

• RBCs count

• Red cells indices:• Mean Corpuscular Volume (MCV fl)

• Mean Corpuscular Hemoglobin (MCH pg).

• Mean Corpuscular Hemoglobin Concentration (MCH g/dl).

• Platelets count x109/1.

• WBCS count x109/l.

2.9.2 method of diagnosis:

Automated method by (sysmex).

2.9.2.1 definition:

The TOA sysmex series instrument(TOA. Medical electronic Co. LTD) analysis the blood specimen and report at complete blood count HB, RBCs count , red cells indices, platelets count, WBCs count and WBCs percentage.

2.9.2.2 principle of Sysmex:

Sysmex instruments, manufactured by TOA. Medical electronics company , included a full line of hematology analyzers from the smallest. Which performed complete blood count, and five parts of differential (white blood cells red blood cells haemglobin packed cell volume , and platelets count) are considered to be measured directly three hydraulic sub systems are used to determine the hemogram : the white blood cells channel , red cell, Platelets channel , and aseparate hemoglobin channel. In white cells transducer chambers, the diluted white blood cells and red cells samples are separated through the different apertures and are Counted by using the electronic resistance (impedance) detection method for counting and sizing cells. Two unique features enhance the impedance technology.

In the red blood cells, Platelets channel, asheathed stream with hydrodynamic focusing is used to direct the cells in single file through the aperture, there by reducing coincident passage and pulse height irregularities, and in both the white blood cells and red blood cells, platelets channels (floating thresholds) are used to discriminate each cell population.

As the cells pass through the apertures the signals are transmitted in sequence to the analog circuit and then to the particle size distribution analysis circuits for conversion to cumulative cell size distribution data. Particle size distribution curves are constructed, and the optimal position of the auto discrimination level is then set by the micro processor for each cells population for example, the lower platelets threshold may be set between 26 fl and the upper threshold any where from 12-30 fl based on the particle size distribution, likewise, the red blood cells lower and upper thresholds may be set between 25-75 fl, and 2000-250 fl, respectively. This floating threshold circuitry allows for discrimination of cells population on sample. By sample basis, the cells count include the pulses between the lower and upper auto discrimination levels , with dilution ratio , volume counted , and coincidence error accounted for in the final computer generated counts.

In the red blood cells channel , the floating discriminator is particularly useful in separating platelets from small red blood cells. The hematocrit is also determined from red blood cells/ platelets channel, based on the principle that pulse height of the red blood cells in proportional to cell volume. The hematocrit is then the cumulative pulse height and is considered atrue relative percentage volume of red cell (erythrocyte).

ln the hemoglobin flow cell, the concentration of cyanme the molobin is measure as absorbance at 540 nm for the hemoglobin concentration.

The following indices are calculated in the microprocessor using the directly measured or derived parameters:

Mean cell volume (MCV) , mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC) red cell width standard deviation (RDW.SD) RDW. CV, MPV, platelet distribution width (PDW), and platelet large cell ration(P.LCR). the redw. Sd is the red blood cell ratio(P.LCR).the RDW.SD is the is red blood cell arithmetic distribution width measured at 20% of the height of the red blood cell curve , reported in fimto liters with reference interval of 37-54 tI.RDW.CV is the red blood cell distribution width reported as aco efficient of variation. (Rodak. 1995).

3. Results

One hundred patients with chronic renal failure (47 males and 53 females) minimum age 27 years maximum age 82 years and mean of age 50 years from EL.Ribat Hospital were enrolled in the study as a test group and 100 all adult people apparently healthy as control.

1- Table (3.1): Show Sex frequency for patients with chronic renal failure.

2- Table (3.2): Show mean of Age, minimum and maximum.

3- Table (3.3): Show Age group.

4- Table (3-4) compare between the mean of hematological parameters in study and control.

Table 3-1 Distribution of study population according to gender

	Frequency	Percentage
Male	47	47.0
Female	53	53.0
Total	100	100.0

Table (3.2): Show mean of Age, minimum and maximum.

	Mean ±SD	Minimum	Maximum
Age	50	27	82

Table 3-2 Distribution of study population according to age:

Age group	Percentage
20-30	11.0
31-40	14.0
41-50	29.0
51-60	24.0
61-70	8.0
71-80	13.0
81-90	1.0
Total	100.0

Table 3-3 compare between the mean of hematological parameters in study and control

Parameters	**population**	**Mean**	**Std.Deviation**	**P value**
HBg/d	patient	8.95	1.87	.000
	control	12.59	1.51	
RBCS×10^{12}/l	patient	3.38	0.70	.000
	control	4.81	0.61	
HCT%	patient	29.02	6.24	.000
	control	39.13	5.25	
MCV fl	patient	81.58	6.24	.000
	control	86.05	6.54	
MCH pg	patient	27.86	1.58	.002
	control	29.23	2.02	
MCHC %	patient	30.17	2.23	.000
	Control	32.12	1.53	
TWBCS×10^{9}/l	patient	5.67	1.61	.003
	control	6.60	3.60	
Platelets×10^{9}/l	patient	202.98	64.07	.000
	control	268.04	72.08	

4.1Discussion:

The most common causes of CKD are high blood pressure and diabetes (Bishop, *et al.*, 1985)..

The peak age in the study group is between (41-50).

High blood pressure can also damage the blood vessels of the kidneys, heart, and brain. This is key, because, in general, blood vessel diseases are dangerous to the kidney. The kidneys are very vascular—meaning they contain lots of blood vessels.

Autoimmune diseases such as lupus can damage blood vessels and can make antibodies against kidney tissue.

Other causes of CKD are varied. polycystic kidney disease is a hereditary cause of CKD. Glomerulonephritis can be caused by lupus. It can also appear after a streptococcal infection (http://www.healthline.com).

The results showed:

That the hemoglobin concentration is low Because chronic renal disease can cause low levels of iron in the body.

Hematochrit and RBCS count are extremely decrease as result of chronic renal failure low levels of erythropoietin.

MCV and MCH and MCHC lower than control but still in normal range because erythropoietin deficiency .

there is no effect of platelets and white blood cell count.

This simller to result agree with study carry out by Ali etal(2008) and Alghythan (2012) and Asmaa etal (2014) they are found the mean of (Hemoglobin and Red Cell Count and hematochrit)is decrease and White blood cell and Platelets no effected.

As shown in table 3-1the study population comprise of 100 patients ,53% female and remaining 47% male that means females are more exposed for chronic renal failure than male ,our finding agree with study in Bangladesh.

4-2 conclusion:

The study conclude that :

1-the majority patient suffer from chronic renal failure were female and the peak age between 41-50 years

2-the majority of patient were anemic (low Hemoglobin , Hematochrit ,Red blood cell)were decrease in compare with control group.

3-the Mean cell volume , Mean cell hemoglobin, Mean cell hemoglobin concentration were unaffected by chronic renal failure and there were normal compared to the control group.

4-White blood cell and platelet count were unaffected by chronic renal failure.

4-3Recommendation:

1-in order to get more informative data ,the sample size should be increased in related subsequent researches.

2-continous monitoring of red cells parameters should be included as routine test in chronic renal failure .

3- the erythropoietin should be regulated as life saving drugs especially in the end stage renal failure and should be given freely and regulary for anemic patient according to the HB level.

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