1.1 Introduction

 Renal transplant is a surgical procedure performed to replace a diseased kidneys with a healthy kidney from another person . It is the organ transplant of kidney into a patient with end stage renal disease. Renal transplant is typically classified as deceased donor(formerly known as cadaveric) or living donor transplantation depending on the source of the donor organ. living donor renal transplants are further characterized as genetically related(living-related)or non related (living -un related) transplants depending on whether abiological relation ship exists between the donor and recipient. Exchanges and chains are anovel approach to expand the living donor pool (David petechuk,2006) .

  Renal transplantation first successfully carried out   between identical twins,is now the preferred treatment modality for chronic renal failure .I mprove immunosuppressive therapy now assumes a90%   survival of renal allograft at one year post-transplant,renal allograft rejection remains the commonest cause of graft failure, while other problems include technical difficulties harvesting the donor kidney and its re-anastomosis   in the recipient (Muirs ,2008) .

Renal Transplantation accounted for 28% of the total provided renal replacement therapies in sudan . The first renal transplant was in 1974 and till now . All the transplants have been from living donors .

Electrolytes are ions capable of carrying an electric charge classified as anions or cations based on the type of charge they carry . Most important function of electrolyte to maintain the acid -base balance of the body .Abnormalities in serum electrolytes serve as risk factors for graft dysfunction (Ahmadi F, Ali M ,2008) .

1.2 Rationale :

Increasing number of renal transplant people is great challenge for every society and become a big problem in sudan because renal transplant is very commissioned   and a serious . Although that renal transplant is constitute ideally therapy for end stage renal failure . Renal failure is dangerous problem which increase the morbidity and mortality rate . Renal transplant is effective therapy but some times can fail because many complications can occurs after transplant include : Transplant rejection , infections due to immuno suppressant drugs that require to decrease risk of rejection , and imbalances in electrolytes specially calcium and phosphate which can lead to bone problem . This study is conducted to assess the plasma electrolytes levels in renal transplant patient and correlate with age and duration of transplant to know whether there is disturbance in electrolytes among renal transplant to manages transplantation and avoid rejection .

1.3 Objectives :

1.3.1 General objectives :

To evaluate plasma electrolytes (sodium, potassium, calcium, phosphate) level among Sudanese renal transplant patients

1.3.2 Specific objectives:

-To estimate plasma electrolytes (sodium, potassium, calcium, phosphate)level in renal transplant patients in comparison with control group.

- To study the effect of sex on plasma electrolytes level in renal transplant patients

- To assess correlation between the age and duration of transplant and plasma level of electrolytes.

2. Literature Review

2.1 Renal Physiology and anatomy :

The Kidneys are paired,bean-shaped organ located retro-peritoneally on either side of the spinal column .

Macroscopically,each kidney is enclosed by a fibrous capsule of connective tissue, when dissected longitudinally ; two regions can be clearly discerned; an outer region called the cortex and an inner region called the medulla , the pelvis can be also seen, it is a basin-like cavity at the upper end of the ureters into which newly formed urine passes. The bilateral ureters are thick walled canals connecting the kidneys to the urinary bladder. urine is temporarily stored in the bladder until voided from the body by way of the urethra. The following five basic parts are The glomerulus , the proximal convoluted tubule, the loop of Henles, the distal convoluted tubule and the collecting duct . (Bishop et al 2000)

Each kidney contains about one million nephrons ,the nephron is the functional unit of the kidney .Each consisting of a glomerulus with a proximal convoluted tubule loop of Henle and a distal convoluted tubule which then drain into collecting ducts, the glomeruli,mostly suited in the cortex ,whereas the renal medulla contains loops of Henle ,blood vessels and collecting tubules ,Each glomerulus is surrounded by A Bowmans capsule consisting of epithelial cells which make contact with a basement membrane through cytoplasmic extensions.

The foot processes interdigitate regularly and maintains the structure of the glomerulus; their distortion by renal disease causes proteinuria . (Tietz,2001) .

2.2 Renal function :

1. Glomerular function :

 The glomerulus is the first part of the nephron to receive incoming blood and functions to filter this blood .Every substance except cells and large molecules continues into further sections of the nephron .Several factors facilitate filtration ;One is the unusually high pressure in the glomerular capillaries ,which is due to their position between-two arterioles . This set 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 Daltons, about the molecular size of albumin . This means that water stopped .Another factor is that the basement membrane is negatively charged and this contributes to the filtration by repelling negatively el,electrolytes ,and small dissolved solutes such as glucose ,amino acids ,urea and creatinine pass freely through and enter the proximal convoluted tubules, however, albumin ,many plasma proteins ,cellular elements and protein bound substances ,such as lipid and bilirubin ,are charged molecules ,such as proteins ,Thus, of the 1200 ml to 1500 ml of blood that the kidneys receive each minute, the glomerulus filters out 125 ml to 130 ml of essential protein-free , cell-free fluid .The volume of blood filtered per minute is known as the glomerular filtration rate GFR   and its determination is essential for evaluating renal function .(Bishop ,2000)

2. Tubular function :

 (A) Proximal convoluted tubule :

The proximal convoluted tubule is the next part of the nephron to receive the now cell -and essentially protein -free blood .This filtration contains both waste products ,which are toxic to the body .One of the functions of the proximal tubule is to return the bulk of each valuable substance back

to the blood circulation .Thus ,three quarters of the water ,sodium, and chloride ,all of the glucose   up to the renal three shold ,almost all of the amino acids ,vitamins , proteins ,and varying amounts of ions such as magnesium ,calcium ,potassium , and bicarbonate are reabsorbed .when the movement of the substance is from the tubular lumen to the prei tubular 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 transport the substances across their plasma membrane to the blood .The plasma concentration above which the substance appears in urine is known as the renal three shold for that substance ,A renal three shold for water does not exist because it is always transported passively through diffusion down a concentration gradient .

A second function of the proximal tubule is to secrete products of kidneys tubular cell metabolism . such as hydrogen ions ,and drugs   such as penicillin   .The term tubular secretion is used in two ways ; it is used to describe the movement of substances from peritubular capillary plasma to tubular lumen .In addition tubule cells also secrete some products of their own cellular metabolism into the filtrate in the tubular lumen . (Bishop et al ,2000) .

 (B) Henle loop :

countercurrent Multiplier system .In this portion of the nephron ,the osmolality in the medulla, increasing steadily from the corticomedullary junction in ward ,facilitates the reabsorption of water ,and chloride .The hyper osmolality that develops is continuously maintained by the Henle loop .The Henle loop forms a hairpin-like loop between the proximal tubule and the distal convoluted tubule .Sodium and chloride are both actively and passively reabsorbed into the medullar interstitial fluid .Because the ascending limb is relatively impermeable to water, so the

medullar interstitial fluid becomes hyperosmotic compared to the fluid in the ascending limb .The interstitial hyperosmolality is maintained because the ascending limb continues to pump chloride and sodium ions into it.(Bishop et al ,2000) .

(C) Distal convoluted tubule :

The distal convoluted tubule is much shorter than the proximal tubule ,it is formed of two or three coils that connect to a collecting duct .The filtrate entering this section of the nephron is close to its final composition .About 95   of sodium and chloride ions and 90   of water have been already reabsorbed from the original glomerular filtrate .The function of the distal tubule is to effect small adjustments to achieve electrolyte and acid-base homeostasis . it s under the hormonal control of aldosterone .This hormone is produced by adrenal cortex and its secretion is triggered by decreased blood flow in the afferent renal arteriole , it s regulated by the rennin angiotensin mechanism and to a lesser extent by adreno corticotropic hormone   A CTH   .Aldosterone stimulates sodium reabsorption by the distal tubules and potassium and hydrogen ion secretion . Hydrogen ion secretion is linked to bicarbonate regeneration and ammonia secretion , in addition to these ;small amounts of chloride are reabsorbed .   (Roerick ,1992) .

(D) Collecting duct :

The collecting ducts are the final site for either concentrating urine or diluting it .The upper portions are under the influence of aldosterone ,which acts to stimulate sodium reabsorption .Chloride and urea are also reabsorbed in the collecting duct . In addition the collecting duct is under control of antiduratic hormone ADH   , this peptide hormone is secreted by the posterior pituitary in response to neutral impulses triggered mainly by increased blood osmolality or decreased intravascular volume . ADH

stimulates water reabsorption .The walls of the collecting duct are normally impermeable to water like the ascending Henle loop ,but in the presence of ADH ,they become permeable to water ,which diffuses passively from the lumen of the collecting duct to the medulla resulting in a more concentrated urine .   (Bishop et al 2000)

2.2.3 Endocrine function :

In addition to its numerous excretory and regulatory functions ,the kidney has endocrine responsibilities as well ,it s both aprimary endocine site (producer of its own hormones) and secondary site (target locus for hormones) manufactured by other endocrine organs .

(a) Primary endocrine function :

The kidneys synthesize rennin ,the prostaglandins and erythropoietin

1.Renin : Renin is the initial component member of the renin angiotensin- aldosterone feed back system .It serves to catalyze the synthesis of angiotensin by means of cleavage of the circulating plasma precursor angiotensinogen .Renin is produced by the juxta glomerular cells of the renal medulla wherever extracellular fluid volume decreases .It also serves as a vasoconstrictor to increase blood pressure and is responsive to changes in both the sodium and potassium levels in the blood .

2.Prostaglandins : The prostaglandins are a group of potent cyclic fatty acids formed from essential (dietary) fatty acids ,primarily the unsaturated arachidonic acid .They are formed in almost all tissues and their actions are diverse .They behave like hormones but differ in that they are synthesized at the same site of action .Once formed prostaglandins exert a very short lived effect and are rapidly catabolized .Prostaglandins can be either PG1 or PG2 .The PG2 type is more

common . The prostaglandins produced by the kidneys such as PGA2 ,PGE2 ,PG1 ,and PG2 increase renal blood flow .Sodium and water excretion ,and rennin release .They act to oppose renal vasoconstriction due to angiotensin and nor epinephrine.An angiotensin is believed to stimulate PGE2 .

3.Erythropoietin : It s asingle -chain poly peptide produced by cells close to the proximal tubules and its production is regulated by blood oxygen levels . Thus hypoxia produces increased serum concentrations within 2 hours . Erythropoietin acts on the erythroid progenitor cells in the bone marrow ,causing their maturation and increasing the number of red cells . In chronic renal insufficiency erythropoietin production is significantly reduced .Erythropoietin concentration in blood can be measured by an enzyme -linked immunoassay . (Roger ,2001) .

(b) secondary endocrine function :
The kidneys are the target locus for the action of aldosterone ,antiduratic hormone (ADH) and parathyroid hormone (PTH) ,for the catabolism of insulin , glucagon ,and aldosterone ,and as the point of activation for vitamin D metabolism .Vitamin D is one of the three major hormones ,that determine phosphate and calcium balance and bone calcification in the human body .Chronic renal insufficiency is there fore often associated with osteomalacia (inadequate bone calcification , the adult form of rickets),owing to the continual distortion of normal vitamin D metabolism . (Roger,2001) .

2.3 Renal failure :
Renal failure is the cessation of kidney functions (Gaw et al,2008) . Renal failure is classified as either acute or chronic renal failure (Muirs ,2008).

2.3.1 Acute renal failure :

Acute renal failure is the failure of renal function over aperiod of hours or days identified by arising serum urea and creatinine .It is a common condition in the general population , with an annual incidence of approximately 200 cases per million population per year . The incidence rate is higher in hospitalized patients 5% of whom may require the intensive care units . (Bruce,2005) .

2.3.1.1 classification of acute renal failure:

Acute renal failure may be classified as pre-renal ,or renal ,or post renal (Gaw et al,2008) .

(A) pre- renal acute renal failure :

This is caused by circulatory insufficiency , as may occur with sever heamorrhage , burns , fluid loss, cardiac failure or hypotension and leads to renal hypoperfusion and a decrease in GFR (Marshal,2008) .

(B) Intra renal acute renal failure :

This is resulting from the abnormalities within the kidney it self ,including : B lood vessels , Glomeruli , Tubules .(whitby et al ,1987)

(C) post renal acute renal failure:

It meaning obstruction of the urinary collecting system any where from the calices to the out flow from the bladder .The most important causes of obstruction of the urinary tract out side the kidney are :(a) kidney stone ,caused by precipitation of calcium , urate or cystine , (b) kidney tumors . (Arthur ,2000) .

2.3.2 Chronic renal failure :

Chronic renal failure is a progressive loss in renal function over a period of months or years . The symptoms of worsening kidney function are non -specific , and might include feeling generally un well and experiencing a reduced appetite . Often ,chronic kidney disease is

diagnosed as result of screening of people known to be at risk of kidney problems ,such as those with high blood pressure or diabetes and those with a blood relative with chronic kidney disease .Chronic kidney disease may also be identified when it leads to one of its recognized complications , such as cardiovascular disease ,anemia or pericarditis .(National kidney ,2002) .

Chronic kidney disease is identified by a blood test for creatinine . Higher levels of creatinine indicate a lower glomerular filtration rate and as a result a decreased capability of the kidneys to excrete waste products . creatinine levels may be normal in the early stages of chronic kidney disease , and the condition is discovered if urine analysis (testing of a urine sample) shows that the kidney is allowing the loss of protein or red blood cells into the urine . To fully investigate the underlying cause of kidney damage ,various forms of medical imaging , blood tests and often renal biopsy (removing a small sample of kidney tissue) are employed to find out if there is a reversible cause for the kidney malfunction . Recent professional guidelines classify the severity of chronic kidney disease in five stages , with stage 1 being the mildest and usually causing few symptoms and stage 5 being a severe illness with poor life expectancy if untreated .Stage 5 is often called End Stage Renal Disease (ESRD) and is synonymous with the now out dated terms chronic kidney failure (CKF) or chronic renal failure (CRF) . (National kidney ,2002) .

People with chronic kidney disease suffer from accelerated atherosclerosis and are more likely to develop cardiovascular disease than the general population .Patients afflicted with chronic kidney disease and cardiovascular disease tend to have significantly worse prognoses . There is no specific treatment unequivocally shown to slow the worsening of chronic kidney disease . In more advanced stages treatments

may be required for anemia and bone disease . Severe chronic renal failure requires renal replacement therapy ,which may involve a form of dialysis ,but ideally constitutes a kidney transplant .

(Adrogue and Madia ,1981) (Bacchetta et al,2012) .

2.4 Dialysis :

Dialysis is a method of removing toxic substance or wastes from the blood when the kidneys are un able to do that .

Dialysis is most frequently used for patients who have kidney failure , but may also be used for quickly remove drugs or poisons in acute situations , dialysis can be life saving in people with acute or chronic kidney failure . Dialysis is done by using a special fluid called dialysate which is amixture of pure water and chemicals that filtrate the blood with out removing substances of the body needs .Dialysis acts as an artificial kidney . (Mayne 1994) .

2.4.1 Types of dialysis :

(1) Haemodialysis :

In haemodialysis ,blood from the patients is pumped through an array of semi permeable membranes which bring the blood into close contact with dialysate ,following countercurrent to the   blood .The plasma biochemistry changes towards that of the dialysate owing to diffusion of molecules down their concentration gradients (Alan,2008) .

(2)peritoneal dialysis :

It has been used for treating acute and chronic renal failure since 1923, in peritoneal dialysis a fluid is put into patient abdomen .The fluid called dialysate ,captures the waste products from patient blood . (Mayne, 1994) .

2.5 Renal Transplantation :

Renal transplant is an operation in which aperson with kidney failure

receives a new kidney . It is the treatment of choice for a patients with end -stage renal disease (ESRD) .

2.5.1 Classification of renal transplantation :

kidney transplantation is typically classified as deceased -donor or living donor .

1. Living donors :

Potential donors are carefully evaluated on medical and physiological grounds .This ensures that the donor is fit for surgery and has no disease which brings undue risk or likelihood of apoor out come for either the donor or recipient . The psychlogical assessment is to ensure the donor gives informed consent and is not coerced .In countries where paying for organs is illegal ,the authorities may also seek to ensure that a donation has not resulted from a financial transaction . The relationship the donor has to the recipient has evolved over the years , the first successful living donor transplants were between identical twins . In the 1960 -1970 live donors were genetically related to the recipient . Now the elasticity of the donor relationship has been stretched to include acquaintance and even stranger .

2. Deceased donors :

Deceased donors can be divided in two groups :

(A) Brain - dead donors :

Although brain dead donors are considererd dead , the donors heart continues to pump and maintain the circulation . This makes it possible for surgeons to start operating while the organs are still being perfused (supplied blood) . During the operation , the aorta will be cannulated , after which the donor׳s blood will be replaced by an ice-cold storage solution for a rapid cooling , the heart will stop pumping .

(B) Donation after cardiac death :

Donation after cardiac death donors are patients who do not meet the

brain -dead criteria but due to the un likely chance of recovery , have elected via a living will or through family to have support withdrawn .

2.5.2 Compatibility :

In general the donor and recipient should be ABO blood group and crossmatch (HLA antigen) compatible .

2.5.3 Complications :

Problems after a transplant may include :

- Transplant rejection (hyperacute , acute , chronic)
- Infections due to the immunosuppressant drugs that are required to decrease risk of rejection .
- Imbalances in electrolytes including calcium and phosphate which can lead to bone problems .
- Side effects of medications including gastrointestinal inflammation and ulceration of the stomach .

2.5.4 Transplant rejection :

The most important problem that may happen after transplant is rejection of the kidney .

2.5.4.1 Pathology of rejection :

The principal function of the immune system is to defend against infections . Fundamental to this function is the capacity of the immune system to discriminate between self and non-self antigens . The immune response recognize of foreign antigens , activation of antigen -specific lymphocytes,and the effectors phase of graft rejection . If the transplant is between genetically different individuals of the same species ,it is referred to as an allogenetic graft this allograft stimulates an immune response , which is mediated by alloreactive lymphocytes . However, grafts can also be autologous

(from an individual back into that same individual) , syngenetic

 (between genetically identical individuals) and Xenogeneic (between

individuals of different species).

Rejection is classified clinically as hyperacute , acute and chronic .
(Davasion ,2005) .

1. Hyperacute rejection :

Within minute or hours of renal transplantation occurs when the kidney donors ABO blood group is incompatible with the recipient , or when as a result of pregnancy , blood transfusion or a previous transplant , the recipient has developed cytotoxic HLA antibodies reaction with the donor cell . (Muirs ,2008) .

2. Acute rejection :

Many renal transplant recipients have an episode of acute rejection within a few weeks of transplantation . The graft tends to become enlarged and the patient may develop a fever and fall in urine volume . However , in cyclosporine treated patients ,clinical features may be non-existent and the only due to rejection arise in serum creatinine . Vascular rejection often occurs at early stage after transplantation and the response to immunosuppressive   therapy is less good than cellular rejection . Frequently of course , cellular and vascular rejection occurs together . (Muirs,2008) .

3. Chronic rejection :

Usually occurs after several months or years and often in the patients who have had acute rejection at an earlier stage . It presents clinically with progressive   deterioration in renal function usually with heavy proteinurea and hypertension . Chronic rejection leads to progressive deterioration in renal function and some times also to a nephritic syndrome . Graft loss with eventually result and there is no response to anti- rejection therapy . (Muirs,2008) .

To avoid renal transplant rejection from begining patient will need to take immuno suppressant medicine every day and also need to follow a special

diet. (National kidney foundation ,2015)

2.6 Electrolytes

Electrolytes are ions capable of carrying an electric charge .They are classified as anions or cations based on the type of charge they carry . Anions have a negative c harge and move to ward the anode ; cations have a positive charge and migrate to ward the cathode . Electrolytes enter the body through the diet and leave the body primarily through the kidneys ,roles are also important such as sweat and the gastro intestinal tract hormones , secreted by endocrine gland , and control the absorbance of electrolyte by the renal tubules and thus play a vital role in maintaining homeostasis . One of the most important functions of electrolyte to maintain the acid-base balance of the body , such, electrolysis as sodium , potassium , chloride , phosphate ,bicarbonate and carbonic acid are in same way related tothis process . Osmotic balance is maintained by sodium potassium and chloride , in addition potassium play role in active transport materialagainst the concentration gradient . Some ofelectrolytes also play important constituent of the body structure and alsoplay important role in imbalance in the body is fluid loss throughdiarrhea ,vomiting and sweating .

Electrolyte concentrate are expressed either as mill equivalent per liter (mEq/L) or mmol per liter(mmol/L) because1 mEg/L in equal 1mmol/L for monovalent ions .(Bishop et al,2000) .

2.6.1 Sodium (Na+) :

Is the major positive ions in the fluids out side of cells , representing 90% of all extracellular cations . The concentration of sodium in side cells is only about 5mEq/L , compared with 140 mEq/L out side .The sodium content of the blood is a result of a balance between the amount in the food and everages body consume ,and the

amount of kidneys excrete . (In addition ,asmall percent is lost through the stool and sweat) . There is active reabsorption of sodium in the proximal tubules up to about 75% of sodium in the filtrate ,further reabsorption occurs in the loops of Henle only about 10% reaches the distal tubules .The kidney reabsorbs quite a large amount of sodium each day, the amount which passes in the filtrate is about 6259mmol/day ,the transport of sodium in the distal tubules in an active process ,which occur against concentration gradient from the tubular cell to the tubular fluid .This net movement of sodium creates negative electrical potential inside the tubular lumen , the active sodium transport also result in the pumping of potassium into the cell .

In healthy plasma sodium level (135-145 mmol/L) it s primary functions in the body are to maintain osmotic pressure and acid -base balance chemically and transmit nerve impulses .The body has a strong tendency to maintain a total base content and only slight changes are found even under pathologic conditions . (Juhap et al,1986) (Bishop et al ,2000) .

2.6.1.1 Regulation :

Mechanisms for maintaining a constant sodium level in the plasma and extra- cellular fluid include renal blood flow, hormones .

Three major hormones are involved in regulating sodium and water absorbance in the body at the level of the kidney

(1) AntiDiuretic Hormones (ADH) :

Secreted from the posterior pituitary acts on the kidney to promote water reabsorption ,thus preventing its loss in the urine .

(2) Aldosterone :

Secreted from the adrenal gland acts on the kidney to promote sodium reabsorption ,thus preventing its loss in the urine .

(3) Atrial Natriuretic Hormone (ANH) :

Secreted from the atrium of the heart acts on the kidney to promote

sodium excretion so that it is excreted in the urine .(Juhap et al ,1986) ,(Bishop et al,2000) .

2.6.1.2 Reference value :

Adults	136 -145m Eq/L (136-145mmol/L)
Children	136-145m Eq/L (136-145mmol/L)
Full term infants	133- 142m Eq/L (133-142mmol/L)
Pre-mature infants	132- 140m Eq/L (132-140mmol/L)

 (Kaplan et al, 1999)   , (Fischbach ,2000) , (William et al ,2004) .

2.6.1.3 Hyponatremia : (lower than normal sodium level)

classified according to total body water :

(1) A decrease in total body water (hypovolemic hypo natremia) indicates dehydration ,over diuresis , ketonuria ,vomiting or diarrhea .

(2) Near normal total body water   (normovolemic hyponatremia) indicates syndrome of inappropriate anti-diuretic hormone secretion (SIADH) , hypothyroidism ,or addison disease .

(3) An increase in total body water (hypervolemic hyponatremia) indicates kidney failure ,congestive heart failure, nephrotic syndrome ,or cirrhosis of the liver .

(Zilva et al,1993) ,   (Maxwell et al,1987) .

 2.6.1.4 Hyper natremia : (Greater than normal sodium level)

Classified according to the amount of fluid that is outside cells   (extra cellular volume) :

(1) In extra- cellular volume is low , water lost due to burns ,excessive sweating , and diarrhea or osmotic /loop diureties (usually not thiazides) .

(2) In extra -cellular volume is normal , this may indicate diabetes .

(3) In extra -cellular volume is high , this may indicate hyper - aldosteronism , Cushing syndrome , salt or sodium bicarbonate ingestion . (Zilva et al ,1993) , (Max well et al,1987).

2.6.2 Potassium (K+) :

Is the major positive ion within cells . The total body potassium of a 70kg body man accounts about 3500mmol , 98% of this in intra - cellular since most intra- cellular potassium is within muscles cells .

In health plasma potassium level (3-5 mmol/L) .Potassium is one of the most important electrolytes , since it is needed for neuron scular activity and myocardial contractility .There fore both sever hypokalemia and hyperkalemia are dangerous .

Potassium is important in muscles for glycogen synthesis and maintains the intra-cellular content of muscles , and properties of cell membrane .

Potassium in association with sodium plays a primary role in maintenance of intracellular fluid volume and pressure .

Potassium acts as activator for the enzyme, sodium -potassium activated adenosine triphosphate (Na ,K -ATpase) which is present in large amount . In active tissues such as nerve ,kidney and epithelial potassium levels are mainly controlled by the steroid   hormone aldosterone . Aldosterone is secreted from the adrenal gland when level of potassium increase,aldosterone , in turn , cause the body to get rid itself of the excess potassium . (Juhap et al,1986) , (Bishop et al,2000) .

2.6.2.1 Reference value :

Adults	3.5 - 5.2 m eq/L (3.5 - 5.2mmol/L)
Children	3.4 - 4.7 m eq/L (3.4 - 4.7mmol/L)
Infants (7days-1year)	4.1 - 5.3 m eq/L (4.1 - 5.3mmol/L)
Neonates (1-7days)	3.7 - 5.9 m eq/L (3.7 -5.9 mmol/L)

 (Kaplan et al,1999) , (Fischbach ,2000) ,   (William et al ,2004) .

2.6.2.2 Hypokalemia : (Lower than normal levels of potassium)

- The person is not getting enough potassium intake in the diet .
- Excessive potassium loss beacause of gastrointestinal disorder -

eg- chronic diarrhea or use of laxatives .

- Vomiting .
- Diuretic use .
- Renal artery stenosis (narrowing   of the major blood vessels to the kidney) .
- Hyper aldostronism .
- Hypokalemic periodic paralysis .
- Cushing·ssyndrome(rare).   .

    2.6.2.3 Hyperkalemia:(Greater than normal levels ofpotassium)

- Crushed tissue from an injury .
- Kidney failure .
- Red blood cells destruction .
- Metabolic or respiratory acidosis .
- Transfusion of haemolyzed blood .
- Hyper kalemic periodic paralysis (potassium is elevated during episodes of paralysis) .
- Addisons disease (rare) .
- Hypo aldosteronism (very rare) .

(Zilva et al,1993) , (Maxwell et al ,1987) .

2.6.3 Calcium :

Calcium is a divalent cation with an atomic weight of 40 , is present in the body in larger amount than any other cation .Almost all of it is in the bones and teeth . The very small quantity not in the skeletal structures is in the body fluids and is in part ionized . Ionized calcium is of great importance in blood coagulations ,in the function of the heart ,muscles, nerves ,and in the permeability of membrane .

2.6.3.1 Sources :

Dietary sources of calcium include milk, cheese , egg yolk ,beans ,muts ,

turnip greens, and asparagus .

2.6.3.2 Absorption :

The ability of diferent individual to utilize the calcium in food varies considerably .On a high-protein diet ,15% of the dietary calcium is absorbed ,in a low -protein diet ,5% of the dietary calcium is absorbed .

Intestinal factors which influence absorption of calcium include :

1- PH : The more alkaline the intestinal contents , the less soluble the calcium salts .

2-Phosphate : If the Ca : P ratio is high the absorption diminished

3- Presence of free fatty acid reacts with calcium to form insoluble calcium soaps .

4- Vitamin D promotes the absorption of calcium from intestine . (Roerick ,1992) .

2.6.3.3 Normal homeostasis :

The total body calcium content is about 25 to35 mole over 9% is in skeleton , less than 0.5% occurs in the soft tissues and less than 0.1%resides in the ECF .

2.6.3.4 Calcium intake :

Calcium balance is determined by the relation -ship between calcium intake and calcium absorption and excretion .A striking feature of the system is that relatively small changes in calcium absorption and excretion can neutralize a high intake or compensate for a low one .There is a wide variation in calcium intake between countries , generally following the animal protein intake and depending largely on dairy product consumption . The lowest calcium intakes occur in developing countries ,particularly in Asia , and the highest in developed countries , particularly in North America and Europe . (FAO/WHO,1998) .

2.6.3.5 Control of homeostasis :

The two major controllers of calcium homeostasis are parathyroid hormones (PTH) and vitamin D . Other factors that are known to influence calcium metabolism but play a minor ,if any , role in the normal subject are : calcitonin ,thyroid hormones , adrenal steroids ,prostaglandins , osteoclast activating factor ,PTH-related protein .

(1) parathyroid hormone (PTH) :

Parathyroid hormone is secreted in rsesponse to a decrease in the plasma ionized calcium level , influences calcium homeostasis by:

a- Directly effecting calcium and phosphate re-absorption by the kidney

b- Influencing bone mineralization and calcium flux from bone .

c-Stimulating 1.25-dihydroxy cholecalciferol (1.25-DHCC) synthesis by the kidney .

(2) Vitamin D :

Stimulates renal 1 a-hydroxylase activity which increases the production of 1.25-DHCC .

(3) Kidney :

a- Increases calcium re-absorption by the distal nephron through the adenyl cyclase-cyclic AMP mechanism .

b- Decreases phosphate reabsorption by the proximal tubule .

c- Increases 1.25-DHCC production and subsequently increases the absorption of calcium in the gut .

(4) Calcitonin :

This is 32-amino acid polypeptide secreted by the parafollicular cells of the thyroid gland .In high doses in patient with increased bone turnover ,it inhibits osteoclastic bone reabsorption and increases the renal excretion of calcium and it can lower the plasma calcium level such patient with hypercalcaemia due to increased bone turnover .

(5) Thyroid hormones :

These hormones increase the rate of calcium removal from bone .
(Bishop ,2010) .

2.6.3.6 Output :

The major calcium excretion route is via the kidneys ,where depending
on the   intake, ,some 2.5 to 7.5 mmol of calcium are excreted daily
.Approximately   250mmol/24h of calcium   are filtered   by the
glomerulus but most of this is reabsorbed by the renal tubules with
only about 1-5% appearing in the urine .

2.6.3.7 Tubular re-absorption :

Calcium re-absorption occurs along the whole length of the nephron and
is mainly   under   the control   of   PTH which   influences calcium
absorption in the distal nephron .

Proximal tubule :65%reabsorbed ascending   limb of loop of Henle   ,
20%reabsorbed (in thick portion) distal convoluted and collecting duct
, 15% reabsorbed (influenced by PTH) .

2.6.3.8 Hypocalcaemia :

Hypocalcaemia is defined as aplasma calcium level is below the lower
limit of the reference range ,less than 2.15mmol/L

Causes of hypocalcaemia :

Decreased intake ,hypoalbuminaemia , vitamin D deficiency , citrated
blood , malabsorption , inadequat parenteral nutrition , PTH deficiency
,hypo parathyroidism , increased bone uptake ,acute pancreatitis ,renal
failure .

Mild hypocalcaemia occurs   in acute renal failure and most cases of
chronic renal failure .It is of multifactorial origin some of the causes
being :Dereased intestinal uptake due to :

a- Decreased 1.25-DHCC production .

b- Precipitation of calcium in the gut as insoluble in vivo precipitation of

calcium ,phosphate .

c- Decreased renal reabsorption of calcium and bone resistance to PTH .

2.6.3.9 Hypercalcaemia:

The definition of hypercalcaemia depends on the reference range provided by the laboratory and the precision of the analytical method with reference range of 2.15 - 2.55mmol/L a value in excess of 2.60mmol/L should be considered to be sufficiently abnormal to warrant further evaluation .

Causes of hypercalcaemia :

Malignancy , solid tumors ,multiple myeloma , leukaemia , Hodgkins disease , hyper parathyroidism , multiple endocrine adenosis ,vitamin D excess syndromes , increased bone reabsorption thyrotoxicosis ,post acute renal failure, decreased renal excretion ,Addison's disease, phaeoctromocytonia .(Roerick,1992) (Bishop ,2010) .

2.6.4 Phosphate :

Phosphate is found in every cell of the body , but most of it in bones and teeth .

The biological roles of phosphate include :

- Combination with calcium to form the mineral component (hydroxyl
 apatite) of bones and teeth .

-Participation as essential   agents (high energy phosphate bonds) in energy transfer in the metabolism of carbohydrates and fat.

-Crucial urinary buffer constituting most of the titratable acidity .

- Maintenance of cell wall integrity

- Enzyme regulation

- Regulation of oxygen transport through 2,3-diphosphoglycerate .

2.6.4.1 Distribution :

The total body content is 25moles with 80% complexed with calcium in bones , 10% incorporated into organic compounds , and 10% combined

with carbohydrates ,and lipids .In its various forms , it comprises the principal intracellular anion ,less than 1% is found in extracellular fluid.

2.6.4.2 Intake :

About 80% of the dietary phosphate intake of 20-40mmol/day is absorbed in the small intestine .The rate of absorption is increased by parathyroid hormone and 1,25-dihydroxy vitamin D. (Campbell,2005).

2.6.4.3 Output :

The major route of phosphate excretion is the kidney . About 100-200mmol of phosphate is filtered daily by the glomerulus , 80 -90% is reabsorbed in the proximal tubules and the remainder excreted in the urine.The two major factors influencing renal phosphate excretion are :

PTH and the intake , other factors include the extracellular volume ,growth hormone ,calcitonin and sodium intake .

Increased renal excretion associated with :

- Increased sodium intake

- Increased PTH secretion

- Increased extra cellular volume

- Increased phosphate intake

Decreased renal excretion associated with :

- Decreased extra cellular volume

- Decreased phosphate intake

- Decreased PTH

2.6.4.4 Plasma phosphate

In the adult subject the plasma inorganic phosphate concentration is around 0.60 to 1.25 mmol/L with 12 to 15% bound to protein .The level varies with age ,being higher infancy and childhood .

2.6.4.5 Hypophosphataemia :

This disturbance, although not as common as hyperphosphataemia ,has the potential to cause more damage   to the patient because of the

importance of phosphate sufficiency for optimization of various metabolic processes .

Causes of Hypophosphataemia :

- Respiratory alkalosis

- Hyper alimentation

- Nutritional recovery syndrome

- Phosphate binding in the gut (medication with aluminium hydroxide)

- Recovery from burns

- Treatment of diabetic ketoacidosis

2.6.4.7 Hyperphosphataemia :

The definition of hyperphosphataemia depends on the reference range provided by the laboratory and the precision of the analytical method with reference range 0.6 -1.25mmol/L

causes of Hyperphosphataemia :

- Tissue destruction

- Artificial

- Hypoparathyroidism

- Bone release (malignancy)

- Haemolysis

- Renal failure

- Acidaemia (lactic acidosis)

- Age related (infancy ,childhood)

- Growth hormone excess

- Diabetes mellitus (insulin deficiency)

- Decreased renal excretion

Early in renal insufficiency the plasma phosphate level remains normal because of increased excretion by the remaining functional nephrons. The plasma level begins to rise when the GFR falls to below 20ml/min .(Campbell,2005) .

3.Materials and Methods

3.1 Study approach :

Aquantitative methods were used to measure sodium, potassium, calcium and phosphorous in sudanese renal transplant patients in khartoum state , during a period from April to August 2015 .

3.2 Study design :

Analytical Case - control study .

3.3 Study population :

The study covered 50 individuals randomly selected from renal transplant people with different age . And 50 apparently healthy individuals participate in this study as control .

3.4 Inclusion criteria :

The criteria of inclusion of the test group based on a renal transplant patients (males and females) from different ages .

Control groups : healthy volunteers .

3.5 Exclusion criteria :

Patients with bone disease ,malnutrition ,hyper and hypo-thyrodism, hyper tension , Diabetes .

3.6 Study variables :

Dependent variables are :plasma sodium ,potassium ,calcium and phosphorous level . Independent variables : ages , duration of transplantation .

3.7 Ethical consideration :

An approval was taken from faculty mangement and verbal consent from individuals under study .

3.8 Data collection :

Data were collected using structural interviewing questionnaire , which was designed to collect and maintain all information concerning the study to determine including or excluding certain individuals in or from

study respectively

3.9 Collection of samples :

After informed consent and use of local anti septic for the skin (70% ethanol) ,a sample of venous blood (3ml) was collected using sterile disposable syring from each individual included in the study ,then emptied in a heparinized containers and centrifuged at 4000 rpm for 10 minutes , after that the plasma is separated and transferred in a plain containers and processed .

3.10 Method of measuring plasma sodium and potassium :

Ion - selective electrodes method

principle of the method :

Ion selective electrode is a transducer (or sensor) that converts the activity of a specific ion dissolved in a solution into an electrical potential , which can be measured by a voltmeter or PH meter . The voltage is theoretically dependent on the logarithm of the ionic activity , according to the Nernst equation . The sensing part of the electrode is usually made as an ion-specific membrane , along with a reference electrode .

3.11 Method of measuring plasma calcium :

Principle of the method :

Calcium in the sample reacts with methylthymol blue in alkaline medium forming a coloured complex that can be measured spectrophotometry .

3.12 Method of measuring plasma phosphate :

Principle of the method :

Inorganic phosphate in the sample reacts with molybdate in acid medium forming aphosphomolybdate complex that can be measured spectrophotometry .

3.13 Instruments :

Spectrophotometer model BTS 302 ,centrifuge , automatic pipette .

3.14 Quality control :

The precision and accuracy of methods used in this study were checked and was analyzed by including commercially prepared control sera .

3.15 Data analysis :

The data collected in this study was analyzed using Statistical Package for social science (SPSS) computer programme .

The means and standard deviation of the plasma electrolytes (sodium , potassium , calcium and phosphate) were obtained to both test group and control group and independent T- test was used for comparison .

Pearson correlation was used to assess correlation between the duration of transplant, age of patient and plasma level of electrolytes.

4.Results

The levels of biochemical parameter of blood electrolytes (sodium , potassium , calcium , phosphate) were measured in renal transplant patients and compared with the values of other apparently healthy volunteers as control group , the result presented as follow:

Table (4-1) show the distribution of sex in both groups of the study

60% were males in patients and also control , where females 40% in both case and control also . Males are demounting in both group .

Table (4-2): represents the mean of parameters sodium, potassium , calcium and phosphate in control and RT patients . It is appeared that sodium and potassium levels in renal transplant patients were not significantly altered nearly the same as in control values being (138mEq/L) and (139 mEq/L) for patients and control respectively (p.value =0.1) this for sodium ,while potassium values were (4.0mEq/L) and (4.2mEq/L) for RT patients and control respectively (p.value =0.08) . But calcium level showed significant elevation being (11.4mg/dl) and (8.9 mg/dl) for renal transplant patients and control respectively (p. value = 0.00) . Phosphate levels were significantly reduced in renal transplant patients in comparison with control values being (2.3 mg/dl) and (3.8 mg/dl) for patients and control respectively (p. value = 0.00) .

Table (4-3): indicated that sodium , potassium , calcium and phosphate concentrated in males were not significantly altered nearly the same as in females .

Figure(4-1) :Ascatter plot show no correlation between the level of sodium and ages of R T patient (r=0.23 ,p. value =0.09)

Figure (4-2) : Ascatter plot show no correlation between potassium and ages of RT patients (r=0.15, p.value = 0.3)

Figure (4-3) : Ascatter plot show negative moderate correlation

between the level of calcium and ages of RT   (r= - 0.64 ,pvalue =0.00)

Figure (4-4) : Ascatter plot show negative moderate correlation between the level of phosphate and ages of RT (r = - 0.47, p value =0.00)

Figure (4-5) : Ascatter plot show no correlation between the level of sodium and duration of transplant in RT patients (r=0.22 , p value = 0.1)

Figure (4-6) :   Ascatter plot show no correlation between the level of potassium and duration of transplant in RT patients (r= 0.06 , pvalue = 0.5)

Figure (4-7) : Ascatter plot show negative moderate correlation between the level of calcium and duration of transplant in RT patients (r = - 0.51 , p value = 0.00)

Figure (4-8) : Ascatter plot show negative moderate correlation between the level of phosphate and duration of transplant in RT patients (r = - 0.49 , p. value = 0.00) .

Table (4-1) : Distribution of sex in both study groups

Sex	Patients NO	Patients %	Controls NO	Controls %
Male	30	60%	30	60%
Female	20	40%	20	40%
Total	50		50	

Table (4-2) : Means of biochemical parameters in controls and RT

Patients   participated in the study

Parameters	Test group (n=50)	Control group (n=50)	P.value
Plasma Sodium	138 ± 2.5 (135-143)	139 ± 2.3 (135-144)	0.1
Plasma potassium	4.0 ± 0.47 (3.2-4.9)	4.2 ± 0.41 (3.5-5.0)	0.08
Plasma calcium	11.4 ± 0.54 (8.7-12.5)	8.9 ± 0.45 (8.5-10.0)	0.00
Plasma phosphate	2.3 ± 0.29 (2.0-3.3)	3.8 ± 0.61 (3.7-5.0)	0.00

-Result given in mean and SD deviation.

-Range between brackets

-P.value < 0.05 consider significant

Table (4-3) :Means of biochemical parameter in RT Patients according to sex

Parameter	Male No=30 Mean +SD	Female No=20 Mean+SD	p.value
Sodium mEq/L	138 ± 2.2	138 ± 2.1	0.5
Potassium mEq/L	4.0 ± 0.48	3.9 ± 0.43	0.1
Calcium mg/dL	11.4 ± 0.50	11.3 ± 0.59	0.5
Phosphate mg/dL	2.2 ± 0.23	2.3 ± 0.33	0.1

-Result given in mean and SD deviation

-P .value $<$ 0.05 consider significan
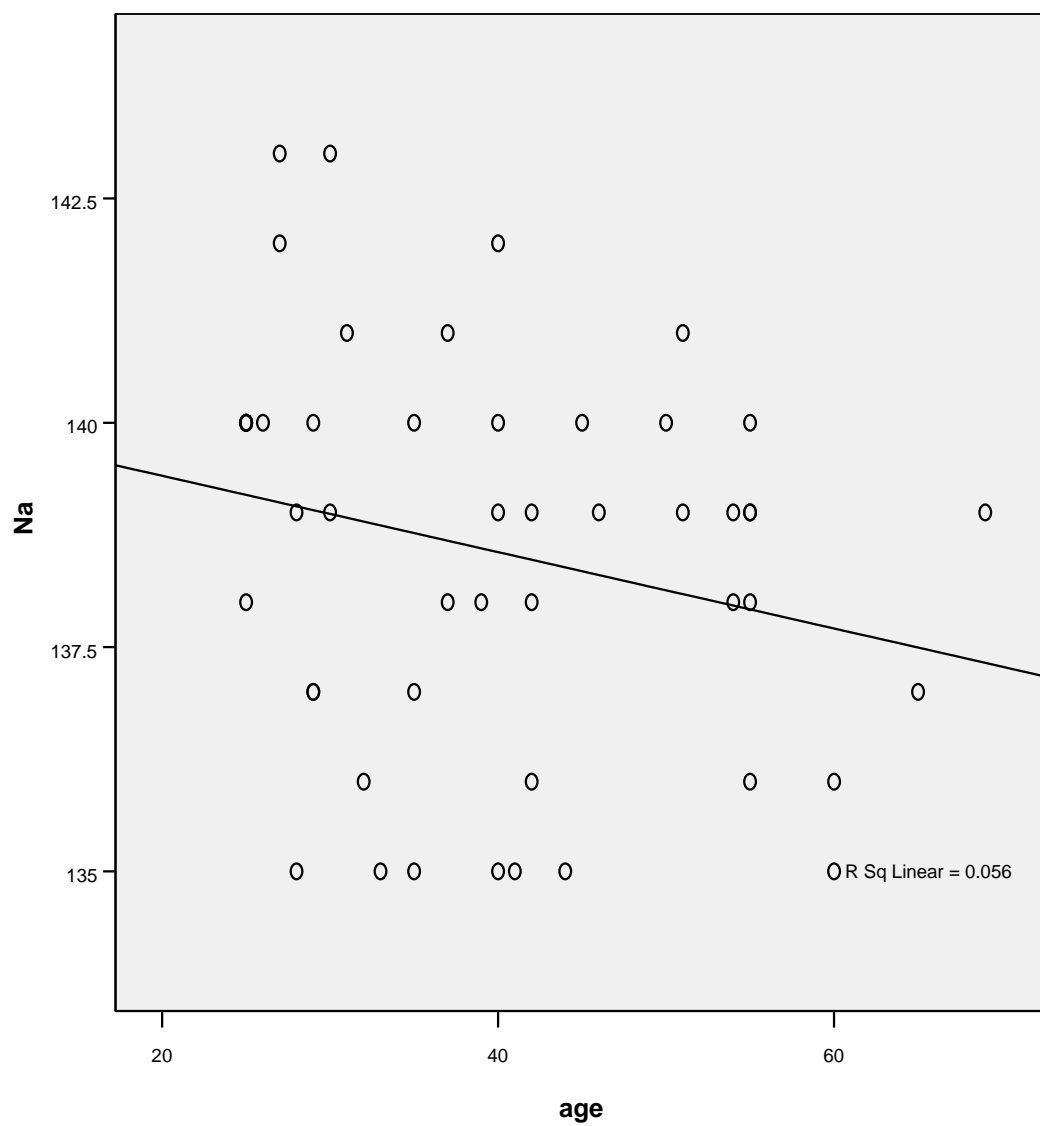
Figure (4-1) : correlation between the level of sodium and ages of RT
patients (r = 0.23 , p value = 0.09)
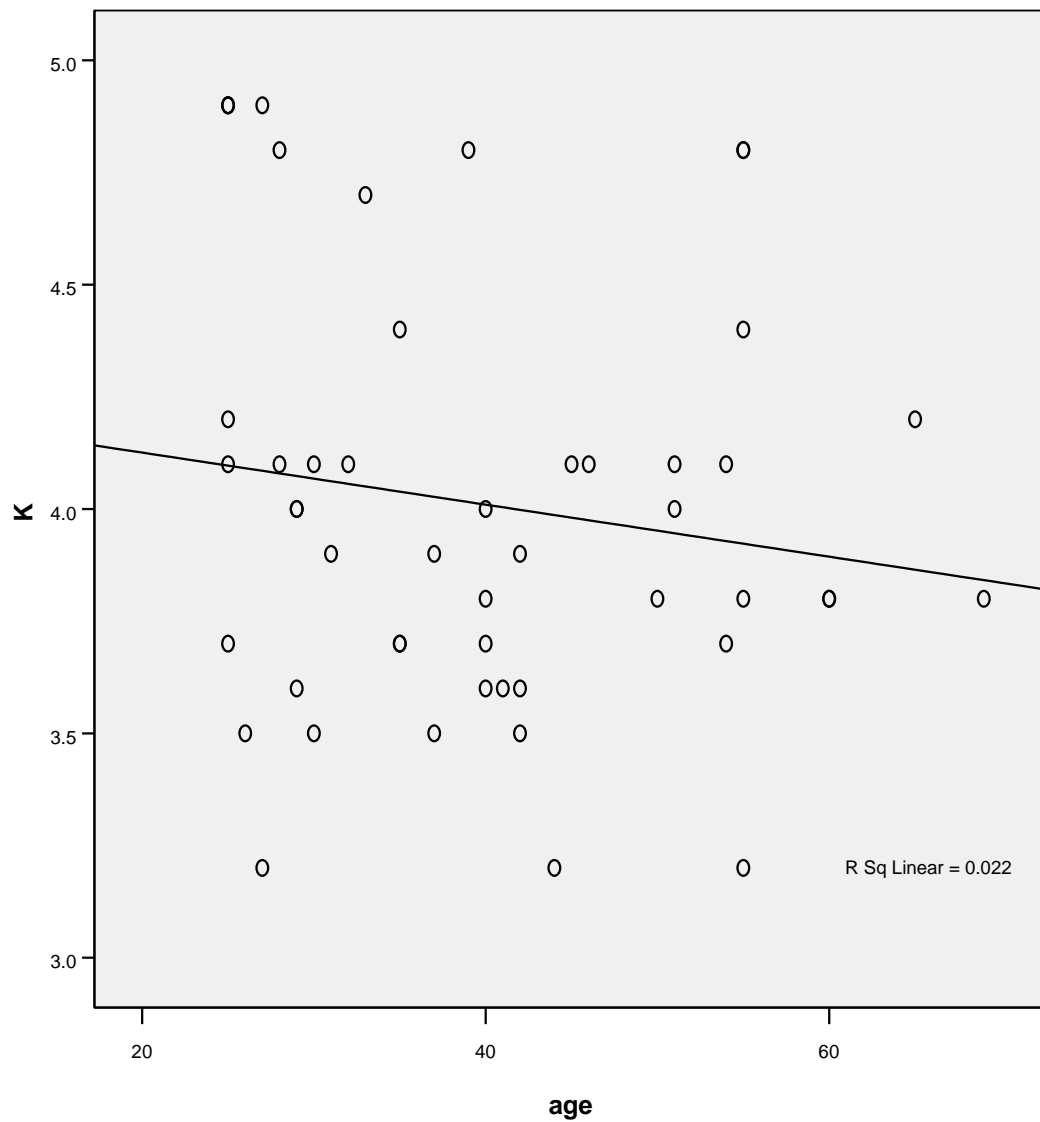
Figure (4-2) : correlation between the level of potassium and ages of RT
patients (r = 0.15 ,p value = 0.3).
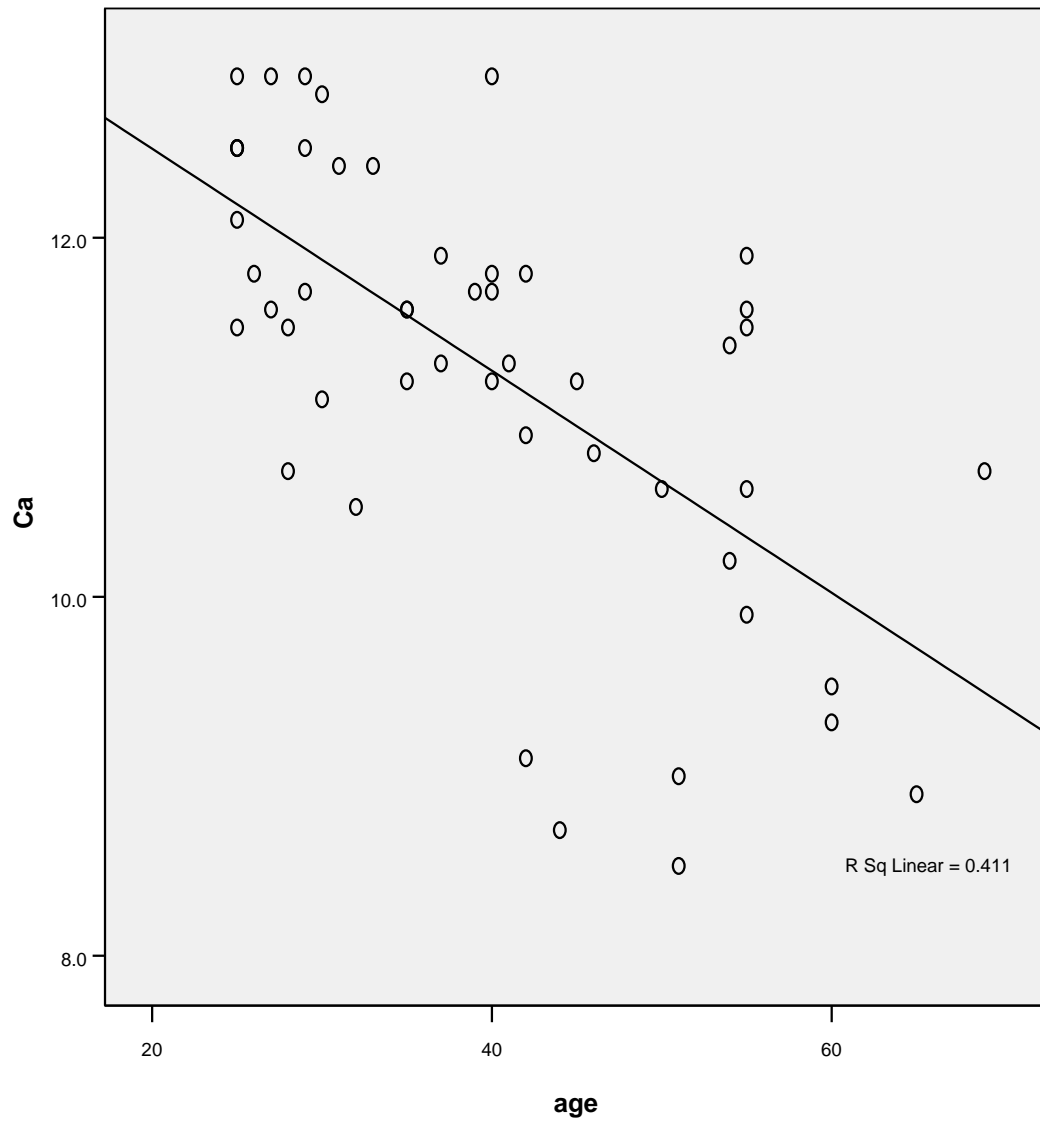
Figure (4-3) : correlation between the level of calcium and ages of RT
patients(r = - 0.64 , p value = 0.00).

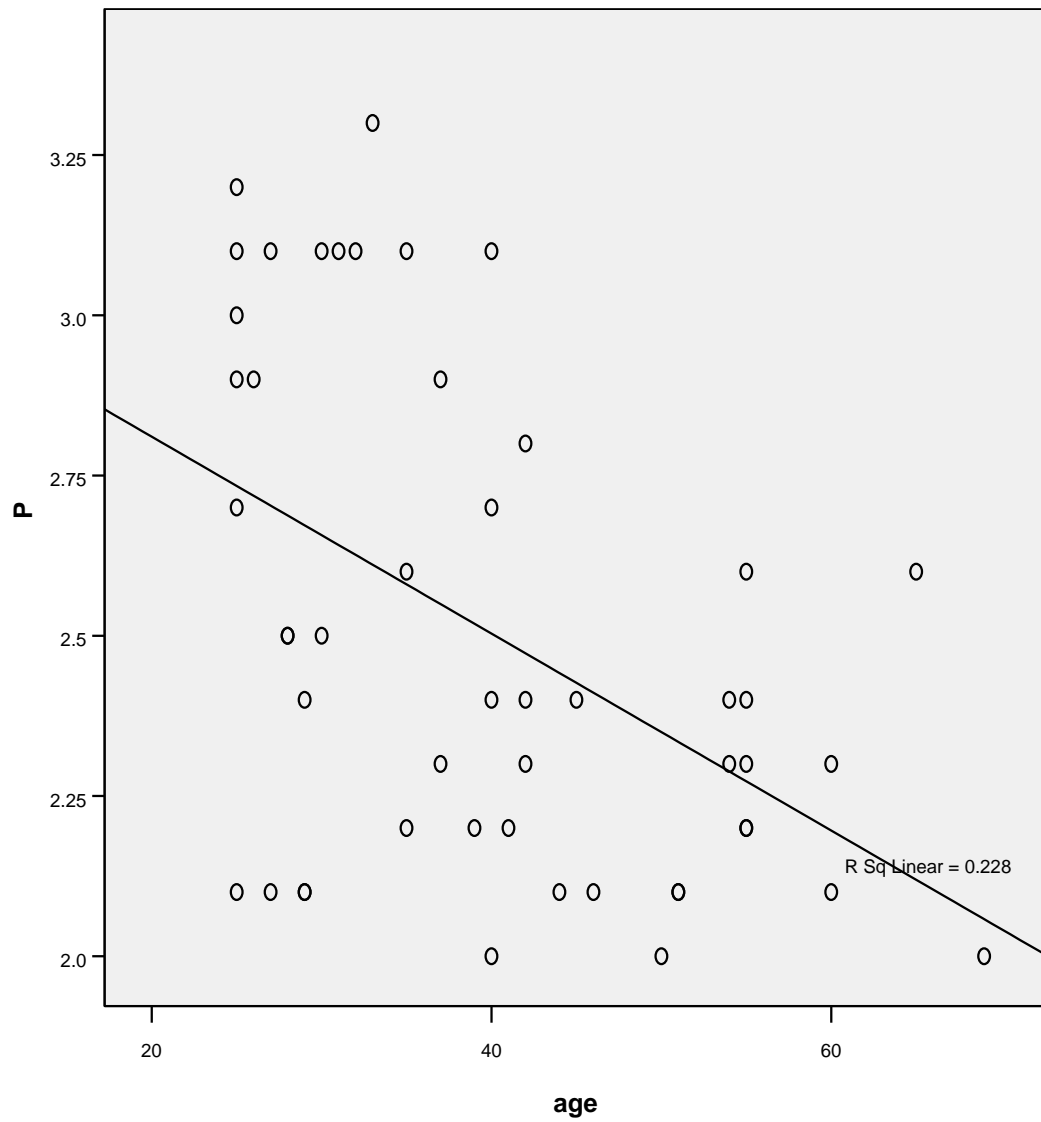Figure (4-4) :   correlation between the level of phosphate and ages of RT
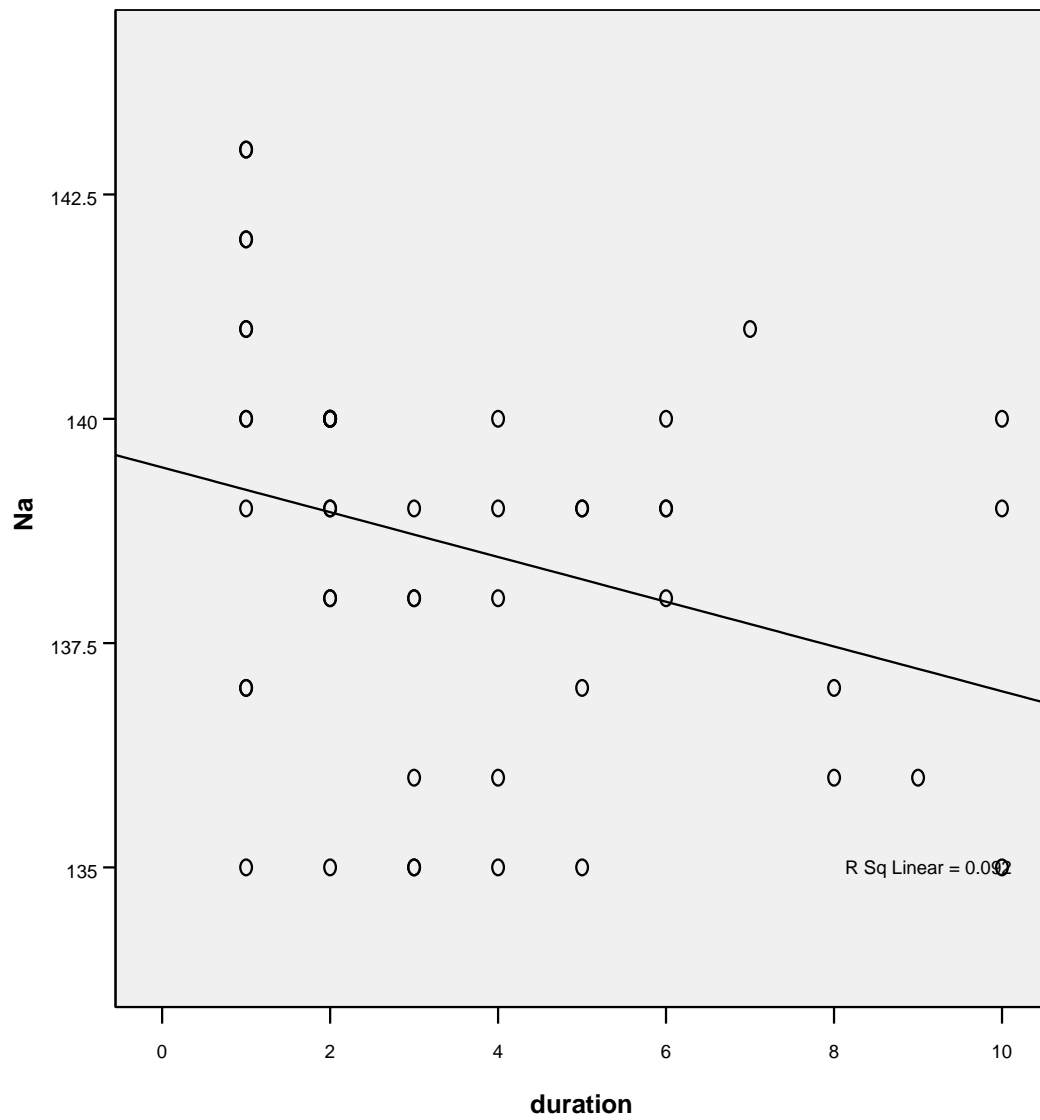patients (r = - 0.47, p value = 0.00) .

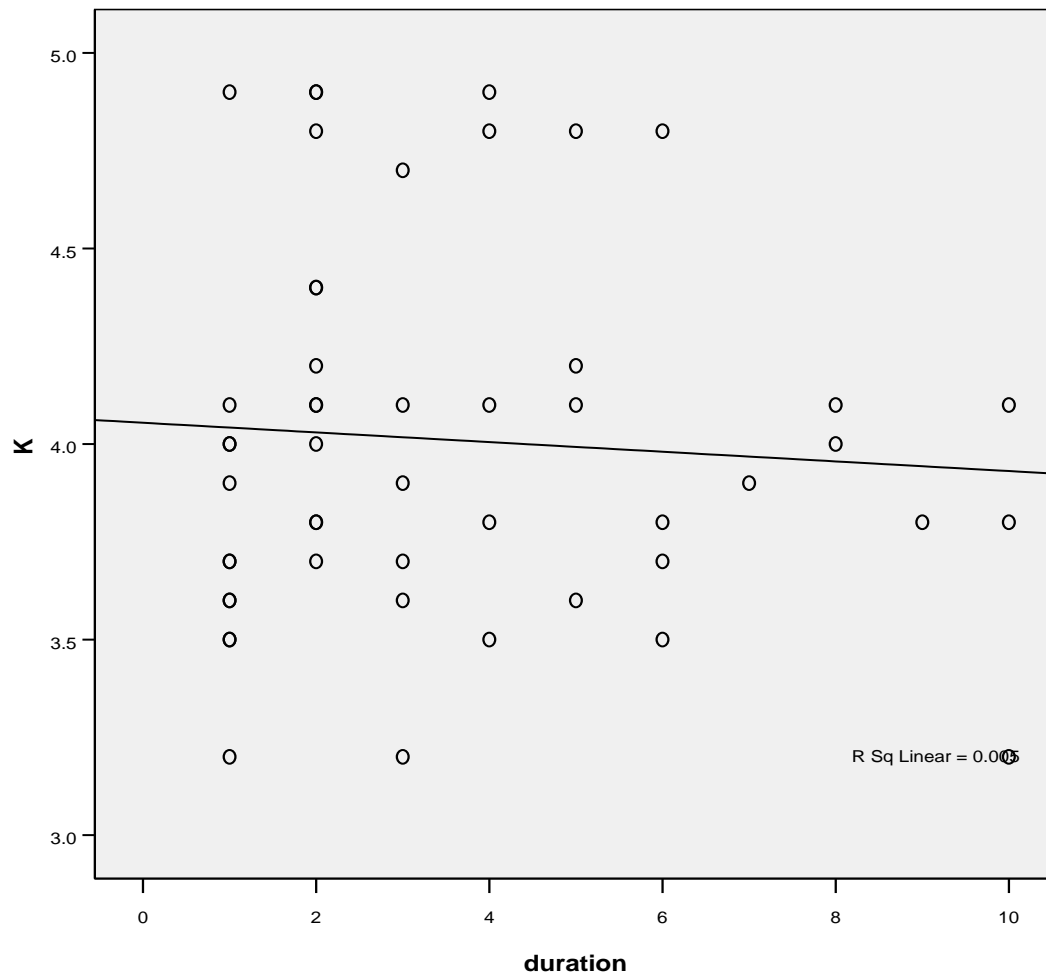Figure (4-5) : correlation between the level of sodium and duration of transplant in RT patient (r = 0.22 , p= 0.1)

Figure (4-6): correlation between the level of potassium and duration of transplant in RT patients (r= 0.06 , p value = 0.5)
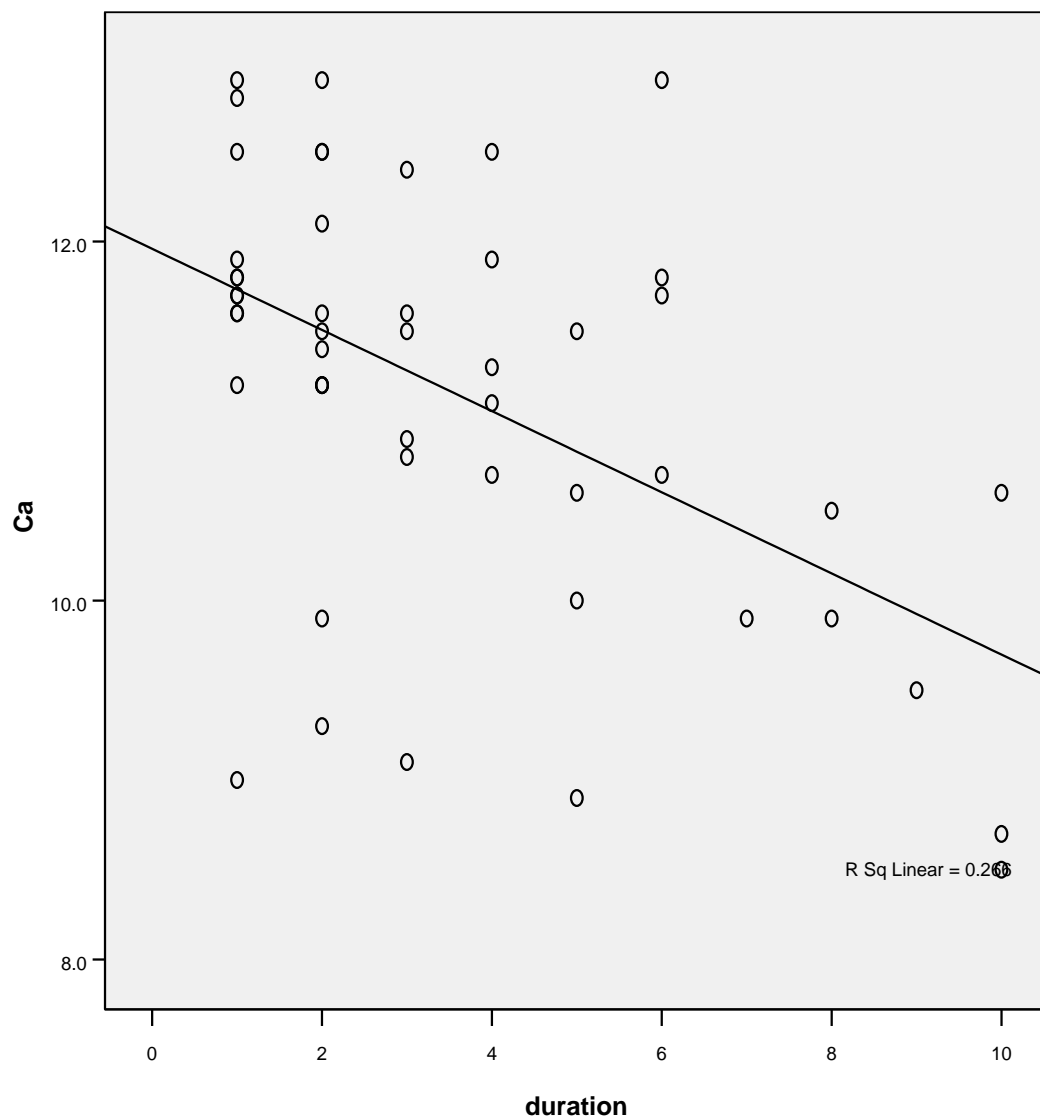
Figure (4-7) : correlation between the level of calcium and duration of transplant in RT patients (r = - 0.51 , p value = 0.00)
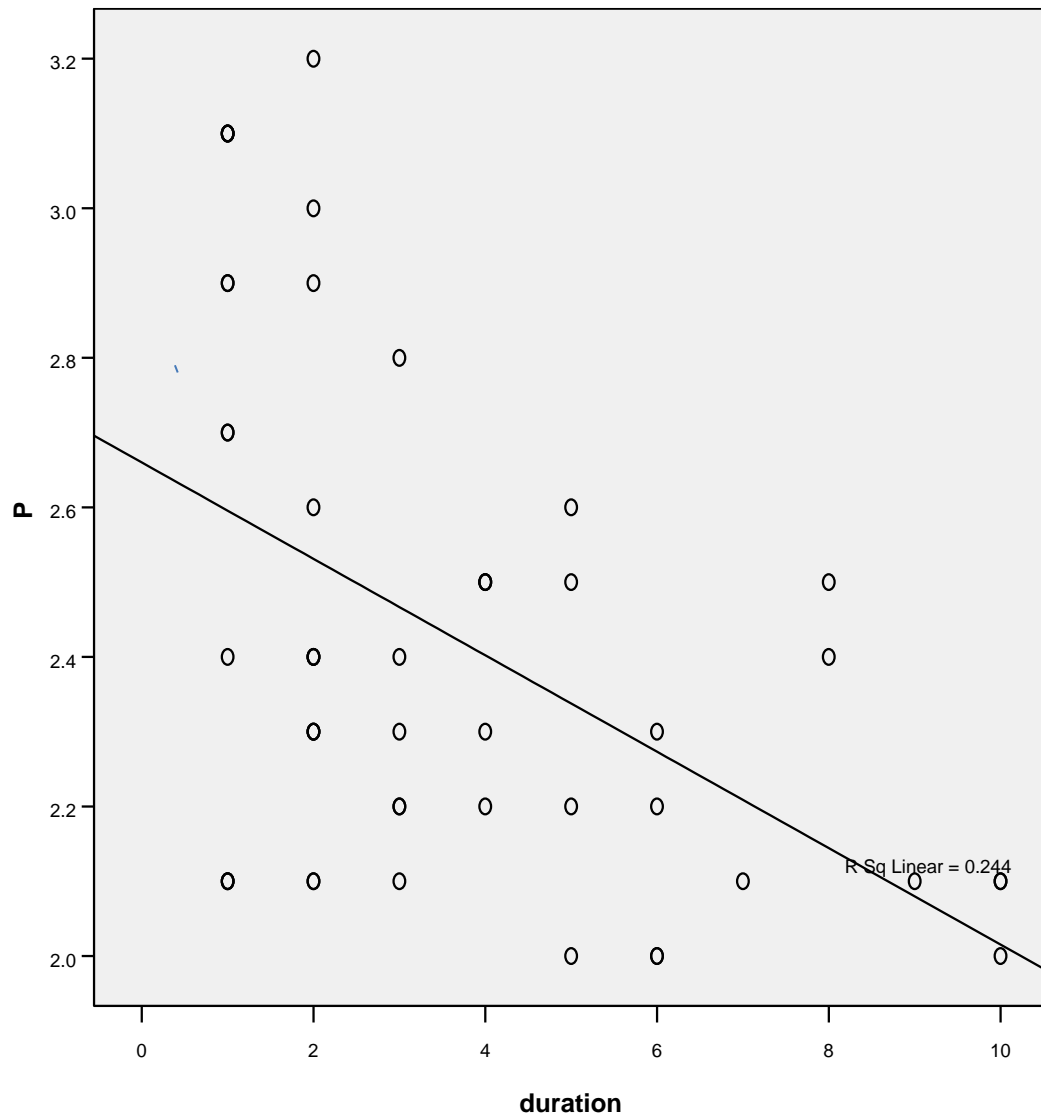
Figure (4-8) : correlation between the level of phosphate and duration of
transplant in RT patient (r = - 0.49 ,pvalue= 0.00)

5.1 Discussion :

Renal Transplantation remains the preferred modality of treatment for patients with end -stage renal disease . Renal failure has been recognized as amajor health problem occuring in almost all population of the world at avariable prevalence .

In sudan which is a large country with 30 million inhabitants it has been estimated from hospital records that the number of chronic renal failure patients is increasing in all socioeconomic classes . 60% of all sudanese with renal failure attending renal dialysis .Peritoneal dialysis was started in 1968 , while hemodialysis was started in 1973 .Renal Transplantation accounted for 28% of the total provided renal replacement therapies in sudan. The first renal transplant was in 1974 and till now. All the transplants have been from living donors . The scholars of Islam in sudan oppose to donation from cadavers . Although RT is ideal therapy for ESRD but some times can failed due to many complication can occurs after transplantation include : infection , electrolytes disturbance , graft rejection.

Abnormalitties in serum electrolytes serve as risk factors for graft dysfunction (Ahmadi F , Ali M, 2008) .

The findings obtained from this study revealed that the levels of sodim and potassium in the blood of renal transplant patients were nearly same as in control group there is no significant change . But calcium level was signifcantly elevated in the blood of RT patients compare with control value . On the other hand phosphate was significantly compare with control values . Our result demonstrated abnormalities in serum electrolytes specially in serum Calcium and phosphate level ,this finding also reported by other workers.

Abnormalities in serum electrolytes especially in serum calcium and phosphate level are frequently observed in renal transplant patients . More

over , hyper calcemia was observed in 66% of kidney transplant recipient . Many factor have been suggested as the putative causal factors . However the persistence of moderate , severe a secondary hyper parathyrodism associated with change in the set point of Ca controlled . PTH secretion is considered the most important factor (Messa P, J Nephrol 2010) .

Calcium increase post transplantation and reach apeak after about six months and persist for years . Hyper calcemia can negatively impact on both the graft and patient out come , increasing the incidence of nephrocalcinosis which can induce worse graft out come .(Evenepoel ,P . Nefrol , 2011)

Post transplantation hypophosphatemia being observed in up to 40% of patient, the putative causal factors for this metabolic alteration are persistent hyper parathyrodism , increased level of FGF -23tubular damage which make renal phosphate loss due to proximal tubules dysfunction . Hypo phosphatemia can negatively impact on both graft and skeletal and muscular system . (Falkiewicz , Kaminska D,et al, 2006) .

The para thyroid hormone cause mobilization of calcium and phosphate from bone to plasma and enhances re-absorption of calcium and loss of phosphate in the renal tubules . the over all action of parathyroid hormone is to increase plasma calcium and reduce plasma phosphate (Campbell and Farrel ,2005) .

In this study sex have no effect on the biochemical parameters measured in the plasma of RT patients participate in this study . There were no correlation between the duration of transplant , age of the patients and the level of sodium and potassium in R T patient . but there were moderate significant correlation between the duration , ages of patients and the level of calcium and phosphate in RT patients .

5.2 Conclusion :

From the findings and observation obtained from this study, we may conclude the followings:

1- Sodium and potassium in the blood of renal transplant patients were nearly same as in healthy volunteers (control group)

2- Calcium was significantly increased in RT patients compared with control

3-Phosphate was significantly decreased in RT patients compared with control

4-Sex have no effect on the level of the four parameters , sodium , potassium , calcium and phosphate in the blood of renal transplant patients .

5-There were no correlation between duration of transplant , ages of patients and the level of sodium and potassium in RT patients

6- There were negative moderate correlation between duration of transplant , ages of patients and the level of calcium and phosphate .

5.3 Recommendations :

from the results and findings of this study it's recommended that:

1- Electrolytes (sodium, potassium, calcium, phosphate) should be monitored in renal transplant patients.

2- Calcium and phosphate should be checked regularly in RT patients and phosphate supplementation should be given to RT, in addition they should receive treatment to lower their plasma calcium.

3-Pre transplant accurate treatment should be taken

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