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Biochemical studies for some enzymes in sera of patients with renal failure

((دراسة كيموحيوية لبعض الانزيمات في امصال مرضى الفشل الكلوي))

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Abstract

This study conformed on patients who have renal failure. Thirty four patients were chose for this study complaining of renal failure in two types (acute renal failure and chronic renal failure).

Full history about patients were taken including (age, sex, occupation, cigarettes smoking, drinking and history of diseases).

In this work we assessed the enzymes (acid phosphatase and alkaline phosphatase) in serum in the state of renal failure, when we compared the tests results with control groups. The number of the control groups were twenty-two healthy person. Also we compared the result of enzymes with other tests including (globulin, albumin, total protein, A/G ratio, urea, creatinine) in the same patient or among patients in the case of renal failure and tests result the control group.

ألخلاصه

جرت هذه الدراسة على مرضى الفشل الكلوي (الحاد والمزمن) وكان عدد المرضى في هذه الدراسة 34 مريض منهم 8 من النساء و28 من الرجال وهم مرضى يراجعون مستشفى الديوانيه التعليمي. حيث تم تسجيل كل المعلومات التي تخص المرضى وهي العمر, الجنس, العمل, العادات وتاريخ المريض الطبي. كان اغلب المرضى يعانون من ارتفاع ضغط الدم ومرض السكر.

تم العمل على قياس تركيز اليوريا والكرياتيين في مصل الدم ولوحظ زيادة كبيرة في تركيز المادتينز. كذلك تم تقدير البروتين الكلي والالبومين و الكلوبيولين في مصل المرضى ولوحظ

انه البروتين الكلي كان ضمن النسبة الاعتيادية والالبومين كان اقل من النسبة الاعتياديه

اما الكلوبيولين كان اعلى من النسبة الاعتيادية. كذلك تم العمل على الفوسفيتيز القاعدي لوحظ ارتفاع في مستوى الانزيم في مصل المرضى بالفشل الكلوي كذلك تم العمل على الفوسفتيز الحامضي ووجدنا مستوى الانزيم ضمن المستوى الطبيعي للنسبةالاعتيادية ولكن يزداد عند الرجال اذا ماقورنة بالنساء

INTRODUCTION:

Renal failure or kidney failure is a condition in which the kidneys fail to function adequately. It is divided into acute and chronic forms; either form may be due to a large number of other medical problems[1]. Traditionally diseases of the kidneys are divided into four major groups according to the predominant involvement of corresponding morphologic components :

1-Glomerular diseases:

2-Tubular diseases:

3- Interstitial diseases:

4- Vascular diseases:

The term "azotaemia" is used in biochemical abnormality characterized by evelation of the blood urea nitrogen (BUN) and creatinine levels[2]. Renal failure can broadly be divided into two categorie:acute renal failure and chronic kidney diseases[3]. Kidney failure can occur from an acute situation or from chronic proplems[4]. And the more pronouncement symptoms of renal failure which include:

1-Decrease in amount of urine (oliguria)
2-Urination stops (anuria)
3-Excessive urination at night
4-Ankle, feet and leg swelling
5-Generalized swelling and fluid retention
6-Decreased sensation, especially in the hands or feet
7-Decreased appetite
8-Metallic taste in mouth
9-Persistent hiccups
10-Changes in mental status or mood
a.Agitation
b.Drowsiness
c.Lethargy
d.Delirium or confusion
e.Coma
f.Mood changes
g.Trouble paying attention
h.Hallucinations
11-Slow, sluggish, movements
12-Seizures
13-Hand tremor (shaking)
14-Nausea or vomiting, may last for days
15-Brusing easily
16-Prolonged bleeding
17-Nosebleeds
18-Bloody stools
19-Flank pain (between the ribs and hips)
20-Fatigue
21-Breath odor
22-High blood pressure[1,3].

Chemically it is typically detected by an elevated serum creatinine.in the other wise the most important tests responsible to diagnoses of renal failure or renal disease like (glomerular disease, tubular disease, interstitial disease and vascular disease) by uric acid and creatinine tests because kidney The kidney is the major site for removal of uric acid and accounts for two-thirds to three-fourths of the daily losses. Urate excretion is believed to depend on a system that includes four components : glomerular filtration, proximal tubular reabsorption, secretion, and postsecretory reabsorption. In primary hyperuricemia and gout, most patients demonstrate a defect in the renal handling of uric acid[5].

While alkaline phosphatase are widely dishibuted different tissues possessing one (occasionally more) characteristic and analytically distinguishable form of liver, bone, placenta and intestine are clinically important sources of plasma ALP activity. It is possible to determine the tissue of origin of increased alkaline ALP activity[6].

In the other hand acid phosphatase enzymes are found throughout the body,and biochemical test for this enzyme has unimportant role to diagnosis renal failure.

Acute Renal Failure : ARF is defined as a precipitous and significant (> 50%) decrease in glomerular filtration rate (GFR) over a period of hours to days with accumulation of nitrogenous wastes in the body[7]. (ARF) is the name implies, a rapidly progressive loss of renal function, generally characterized by oliguria (decreased urine production, quantified as less than 400 mL per day in adults, less than 0.5 mL/kg/h in children or less than 1 mL/kg/h in infants); body water and body fluids disturbances; and electrolyte derangement[1]. ARF can result from a large number of causes. The causes of ARF may be classified as pre-renal, intra-renal and post-renal in nature[8].

Chronic Renal Failure: CRF is a syndrome characterized by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma eventually terminating in death when sufficient number of nephrons have been damaged[9]. Acidosis is the major problem in CRF with development of biochemical azotaemia and clinical uraemia syndrome.All chronic nephropathies can lead to CRF. The diseases leading to CRF can generally be classified into two major groups: those causing glomerular and tubulointerstitial pathology[10].

METHODS and MATERIALS:-

Patients :Acute and chronic renal failure patients was examined and included in this study.Thirty four patients admitted in hospital (26 males and 8 females), they were proved to have renal failure (acute and chronic).We have to deaw venous blood samples from the patients arms. Five ml of blood was obtained from each patient and was pushed slowly in to plain disposable tubes from the syringes without anticoagulant. Blood was allowed to clot for 10-15 minutes. The clot shrinks and serum was obtained by centrifuging 2500 rpm for approximately 10-15 minutes to separate the serum from other content of the blood. After obtaining.The serum from all patients we must conduct a full investigation: Blood of urea,Blood of cretinine, Blood of total protein,Blood of albumin,Blood of globulin,A/G ratio. , Blood of ALP and Blood of ACP.

The control groups: The control group consisted of twenty-two healthy people who had the following features: they were not smokers,they did not have any history of chronic diseases, they did not take any treatment for diseases like diabetes mellitus and hypertenusion and they don`t drink spirits. The ages and sex were nearly the same as the experimental group. These data were analyzed statistically.

RESULTS AND DISCUSSION:

Figure (1) demonshated the effect age on patients with renal failure in the two types (acute and chronic) was between 19 to 87 years.

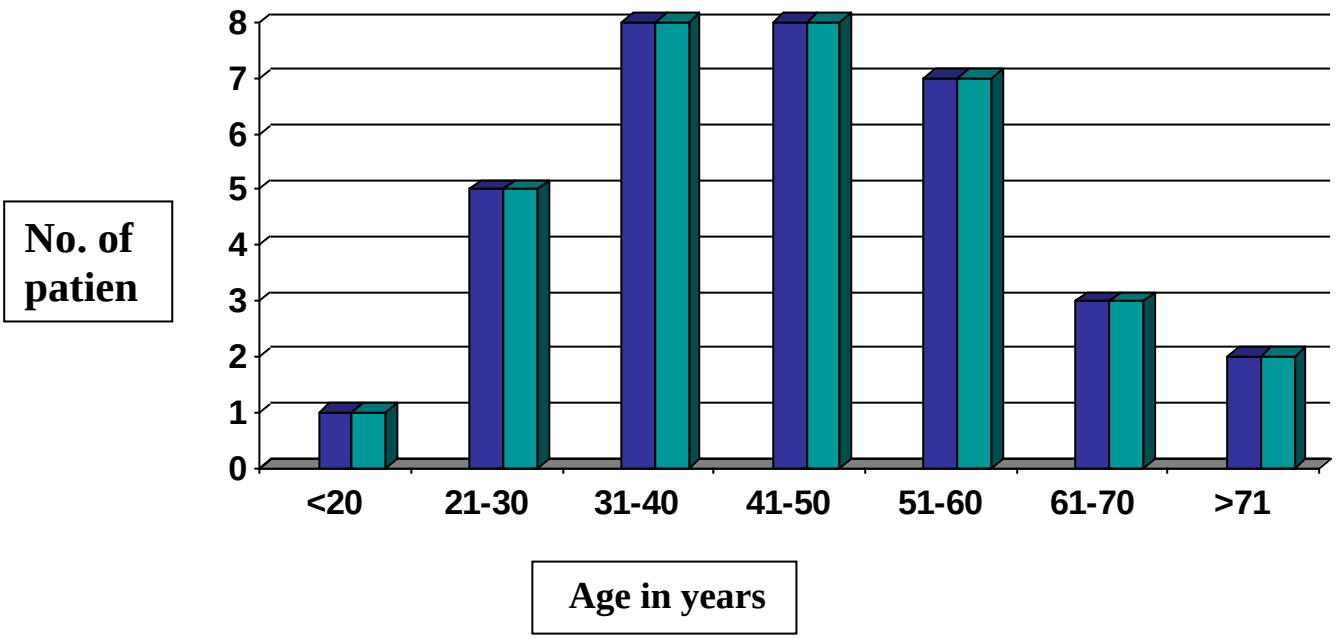

Figure (1): Age distributions among patients with Renal Fialure

The mean age of patients with renal failure (acute and chronic) was 45.6 years.

According to the figure of age distribution of renal failure of patients shows a peaks levels in age (31-40 and 41-50) years, its high levels and lower than the two high was age (51-60) years and the lower in age (21-30)years and the lower in age (61-70) years and the lower in >71 years and the last lower age <20 years.

while figure (2) show the ratio of males to females was 3.25 in the renal failure (acute and chronic).

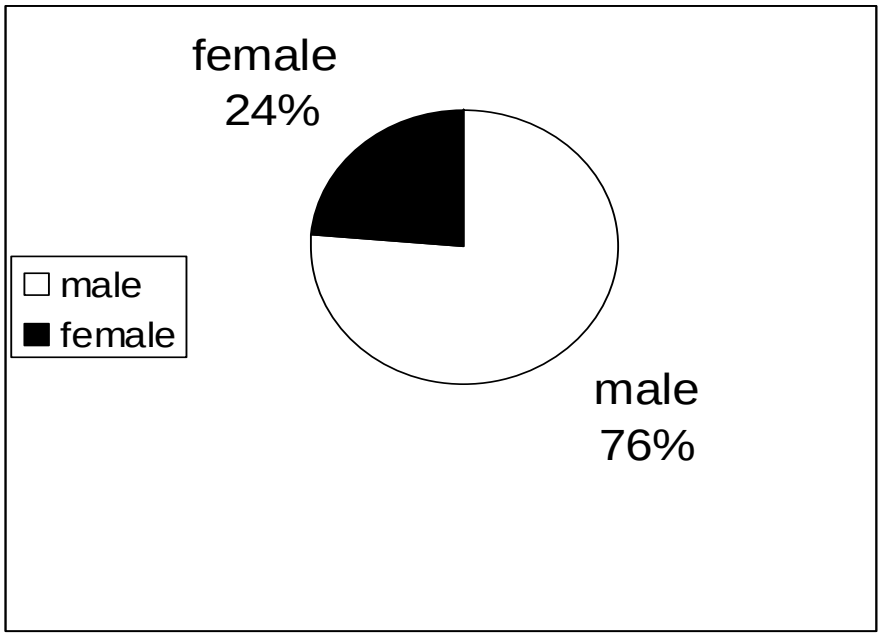

Figure (2): the rate of the males to females patients with renal failure

However from a bove we can discuss the result to mesangial fractional volume increased in all CRF. CRF showed an increase of glomerular sclerosis index (GSI) and tubulointerstitial damage (TID) but in a smaller proportion in male castrated; the opposite occurred with females: castration induced an increase of these parameters. CRF showed increased cortical and glomerular fibronectin (FN) rates. Castration decreased glomerular and cortical FN rates in CRFM but not in females. In conclusion, proteinuria was higher in CRFM and probably led to glomerular and interstitial damage, as well as to FN accumulation, castration seems to protect against development of PTN, TID and FN accumulation in males. Castrated female rats presented mesangial expansion, with no changes in PTN, TID and FN rates. It seems that female sex hormones do not protect against renal disease progression, instead, we suggest that male sex hormones lead to acceleration of CRF[11].

In the other hand we can note the relation between hypertention and renal failure figure (3).

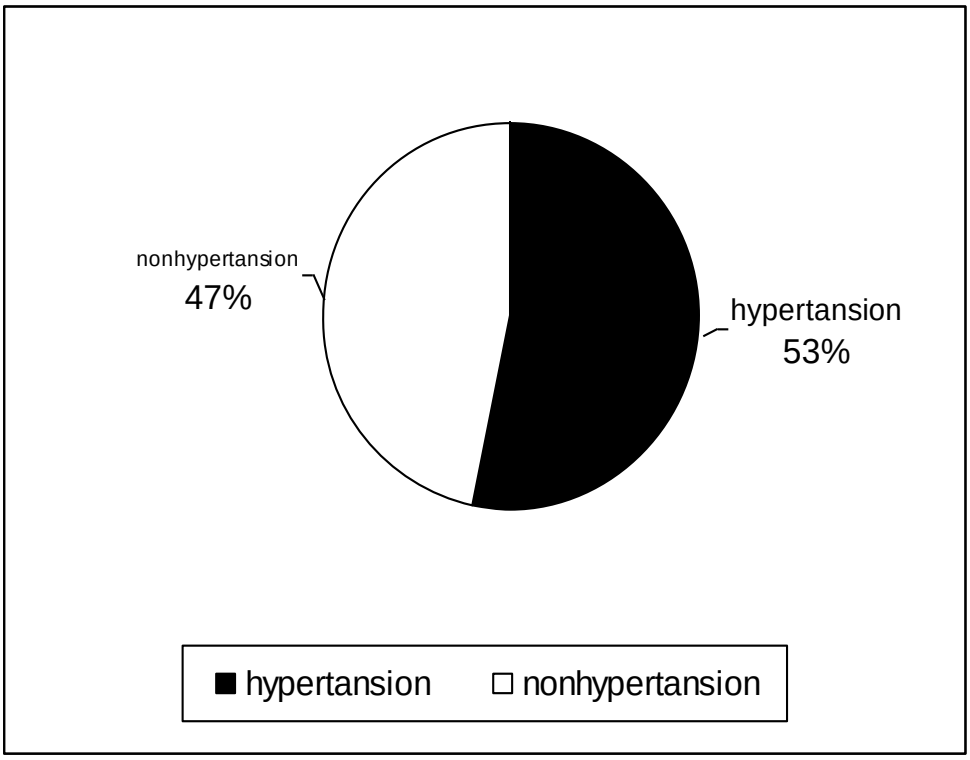

Figure (3): the rate of the hypertension to nonhypertansion for patients with renal failure

So this figure demonshated that males have hypertension more than females because the Atherosclerosis decrease in females compared with males, where the male can disorder to Coronary Insufficiency more than female, that have Estrogen hormone which keep them (female) from the Atherosclerosis[12,13].

This cause due to hypertension in males more than females.Atherosclerosis happen because hypertension due to decrease blood flow to kidney and getting Nicrosis in Glomeruli and other effects. The renal decay due to hypertension also hypertension due to renal decay. Renal decay increase hypertension higher and due to increase renal decay that is end to renal failure[14,15,16].
And form figure (4) we can notes relation between diabetes and non diabetes with renal failure and the percent of them %50 in which used 17 patients with diabetes and 17 patients nondiabetes,while these percent can expansion by diabetes can lead to kidney diseases
but. It is clear that diabetes can lead to kidney disease, but just why high blood sugars that should damage the glomeruli unclear is.High blood pressure (hypertension) is a known risk factor for kidney disease and people with diabetes are prone to hypertension.The renin-angiotensin system - which helps regulate blood pressure - is also thought to be involved in the development of diabetic nephropathy [17,18].

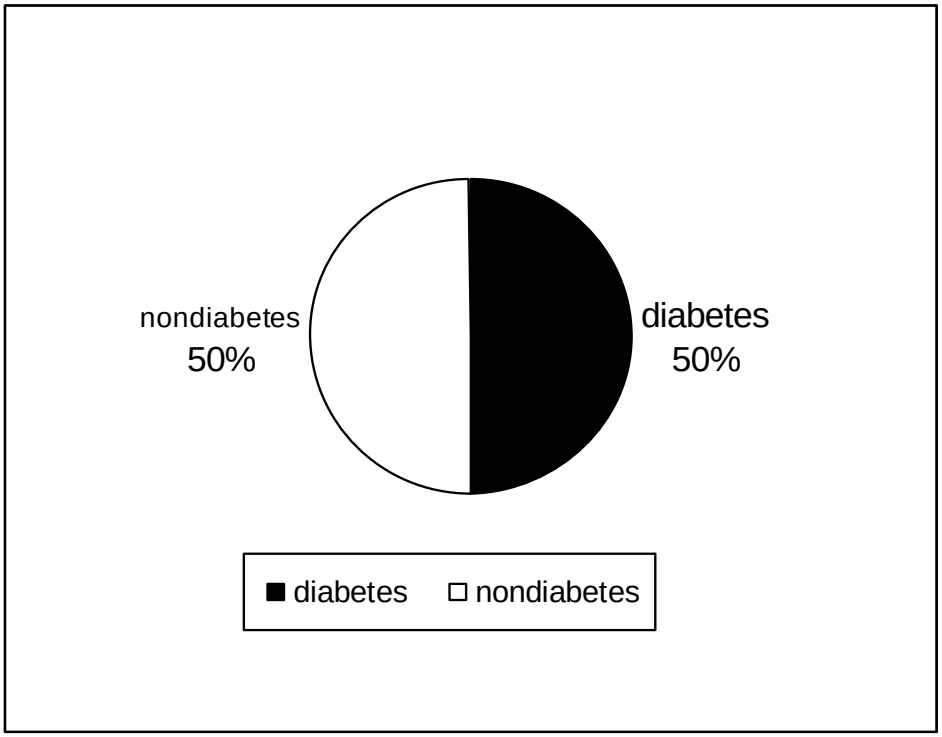

Figure (4): the rate of diabetes to nondiabetes patients with renal Failure

Figure (5) show the rate of smokers to non-smokers with renal failure patients in which the smokers in renal failure in this study the smokers in Renal failure groups were 15 patients (it`s 44%) and the non- smokers were 19 patients (56%),some of smokers are give up smoking after falling in this disease.

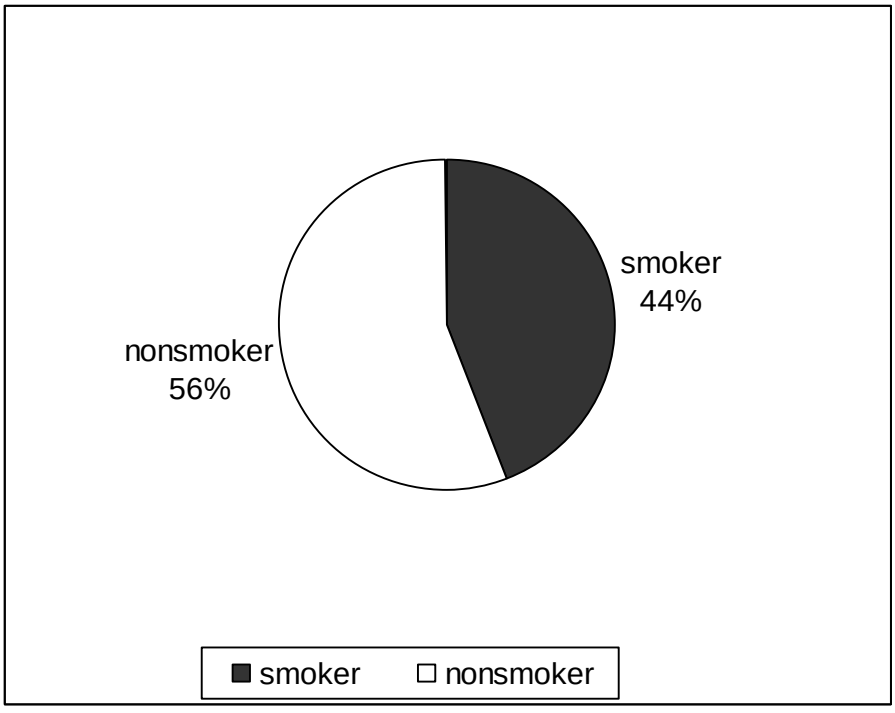

Figure (5): the rate of smokers to non-smokers with Renal Failure Patients

And this rate can be explained as follow: smoking might theoretscally initiat renal disease because it adversely affects renal function in healthy subjects [19,20]. However, there is a growing consensus that vascular risk factors such as smoking, hypertension, and hyperlipidemia act as promoters of preexisting renal disease regardless of the underlying cause [21]. In the light of the various ways that smoking might injure the kidneys, the effects of smoking are probably not uniform and may also

depend on underlying renal disease. Smoking induces both systemic and intrarenal hemodynamic alterations that can be significant for renal disease progression. Smoking may also injure the kidneys by damaging the renal microvasculature through oxidative stress, reduced nitric oxide generation, and increased endothelin plasma concentration. Smoking-induced tubular cell dysfunction may further contribute to tubulointerstitial injury and progression of CRF [22,23].
In the other hand table (1) demonstrated the mean value of urea and creatinine concentration in patients with renal failure and control groups.

Table (1):mean value of urea and creatinine conc. in patients with renal failure and control group.

Tests	Mean Values		+\- S D		P value
	patients	control	patients	control	
Urea (mmol/L)	23.8	4.63	12.04	0.99	9.44 E-11
Creatinine (mmol/L)	441.47	74.77	273.71	9.49	5.26 E-9

P < 0.01 Significant S D Standard Deviation

P > 0.05 not significant

It was observed that all patients with renal failure had hyperuraemia and increase in serum creatinine level, with a mean value 23.8 and 441.4 respectively. In this study the results were highly significant in the two tests(urea and creatinine) were of urea (9.44 E-11) and of creatinine (5.26 E-9).
With this result can retain to some researches had pointed out that urea and creatinine were the mainindicators for renal failure at both types (acute and chronic)[24] ,but others indicated that at all stages renal insufficiency, the serum creatinine was a mach more reliable indicator of renal function than blood urea because blood urea is far more likely to be affected by dietary and physiological conditions not related to renal function[25].

While table (2) show total protein serum albumin and globulin in sera of patient with renal failure.

Table(2) : mean value of total protein, albumin conc. , globulin conc. and ratio Alb./Glo. In patients with renal failure control group

Tests	Mean Values		+/_ S D		P value
	patients	control	patients	control	
Total protein g/L	70.94	71.54	10.66	6.1	0.0788
Albumin g/L	29.3	40.39	9.36	12.88	0.00134
Globulin g/L	41.65	33.88	7.82	6.89	0.00029
Ratio Alb/Glo	0.772	1.184	0.338	0.406	0.000322

$P < 0.05$ Signficant $0.05 >$ not significant

It was found that all patients understudy had normal concentration of total protein and low level of serum albumin and high level of serum globulin with a mean value 70.9 , 29.3 and 41.6 respectively.

The results of total protein not significant and Albumin , Globulin and ratio Alb/Glo were significant when compared to control group, as shown in table(14).

The results of normal total protein concentration and low albumin levels weren`t similar to those results obtained by other studies [26][27],who found that there was no significant difference when protein and albumin were reduced in their levels in the sera of patients with renal failure. Many findings had suggested that a marked total protein depletion existed in chronic uremia and that dietary treatment was not responsible for such a depleted state, instead. The depletion of protein stored observed in the steady phase of chronic uremia might have been originated by exaggeratedly increased catabolism in the early phase of renal failure, not compensated by a proportional increase of the synthetic rate. Due to both state of uremic intoxication and reduced dietary protein intake during the early phase[28]. And also increase in the globulin fraction usually result from an increase in immunoglobulins, but there can be an increase in other proteins in pathologic states that have characteristic electrophoretic patterns Malnutrition and congenital immune deficiency can cause a decrease in total globulins due to decreased synthesis, and nephrotic syndrome can cause a decrease due to protein loss through the kidney[29].

In the other hand table (3) observation that alkaline phosphatase was tested in this study to show whether kidney failure had an effect on this enzyme. It was observed that alkaline phosphatase had increase above the normal values when compared to its values in normal individuals. The mean value of alkaline phosphatase in patients was 98.36(U/L). whereas the mean value in control groups was 77.2 (U/L).

Table (3): Mean value of alkaline phosphatase in patients with renal failure and control group. Also Standard Deviation.

Tests	Mean Values		+/- S D		P value
	patients	control	patients	control	0.074
ALK (U/L)	98.36	77.21	63.9	16.76	

P < 0.01 significant P > 0.01 not significant

According to these results there was not significant in alkaline phosphatase value in sera of patient with renal failure.

The increase of alkaline phosphatase may be attributed to the increase of ecto-5-nucleotiase the enzyme which involved converting adenine into adenosine.

Ecto-5-nucleotidase activity was present within alkaline phosphatase activity and indicated by some investigators[30][31]. The presence of high activity in ecto-5-nucleotidase in the sera of patients with renal failure would result in turn in accumulation of adenosine in the serum and in some body tissues and this accumulation may also be related to the decrease in the activity of adenosine deaminase which was diminished in patients with renal failure.

Also for the sex the mean value of alkaline phosphatase was (86)in male patients and (137) in female patients and it was found that there were significant difference in mean value of alkaline phosphatase between both sex ,the results are shown in the below table.

Table (4): Distribution of Alkaline phosphatase mean value in patients with renal failure and control groups according to patients sexes.

Patients sex	Number	Mean -/+ SD	P value
Male	26	86.3 -/+ 53.7	0.13
Female	8	137 -/+ 81.5	

P < 0.05 significant P > 0.05 not significant

This result was similar to that obtained by some studies which found that alkaline phosphatase value were similar in female and male patients with renal failure[32].

The table (5) show the mean value of acid phosphatase in patients with renal failure and control group. It was observed that acid phosphatase was tested in this study to show whether kidney failure had an effect on this enzyme. It was observed that Acid phosphatase had increase but with normal values when compared to its values in normal individuals. The mean value of acid phosphatase in patients was 8.23 (U/L). whereas the mean value in control groups was 4.92 (U/L). the results were not significant difference of value Acid phosphatase when compared with the control group, the results of the study are in the following table.

Table (5): Mean value of Acid phosphatase in patients with renal failure and control group.

Tests	Mean Values		+/- S D		P value
	patients	control	patients	control	
ACP (U/L)	8.23	4.92	3.53	1.92	3.42

P > 0.05 not significant P < 0.05 significant

However acid phosphatase (APS) are members of the hydrolase class of enzymes catalyze the hydrolysis of orthophosphate monoesters under acidic conditions[33]. The concentration of human APs undergo pronounced changes in particular diseases, resulting in unusually high or low concentrations. Thus, AP levels are often used as clinical markers of disease. The levels of prostate acid phosphatase (PAP) have long been used as an indicator of prostate cancer, while an increased level of tartrate resistant acid phosphatase (TRAP) is often indicative of bone disease[34].
While the results of our study show that the ACP in men is higher than woman patients but with normal values it was found that there were not significant difference in mean value of acid phosphatase between both sex ,the results are shown in the below table.

Table (6): Distribution of Acid phosphatase mean value in patients with renal failure and control group according to patients sexes.

Patient sex	Number	Mean -/+ SD	P value
Male	26	8.3 -/+ 3.5	0.79
Female	8	7.9 -/+ 3.7	

P > 0.05 not significant P < 0.05 significant

Prostate-specific antigen (PSA) occurs in different molecular forms in serum: free PSA (fPSA) and complexed PSA (cPSA), the sum of which corresponds to total PSA (tPSA). In addition to tPSA, percent fPSA is widely used in the detection of prostate cancer. Free PSA, is eliminated by glomerular filtration. Previous data showed that men with end-stage renal dysfunction requiring chronic dialysis have increased percent fPSA

The percent fPSA is importantly influenced by moderately impaired renal function in men with chronic kidney disease. For such men, use of the current clinical decision limits for percent fPSA could cause some men with prostate cancer to be misdiagnosed as having beign disease, and therefore fPSA should not be used to diagnose prostate cancer in these patients[35].

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