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EFFECT OF RENAL FAILURE ON THE VALUE OF INTERLEUKIN-6, POTASSIUM, SODIUM AND CALCIUM

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Abstract:
This study was conducted on patients with renal failure in Tikrit Teaching Hospital - Division of the Artificial Kidney during the period from the beginning of January 2021 to the beginning of March 2022. The current study dealt with the estimation of electrolyte concentrations (potassium, sodium, calcium), and the estimation of interleukin-6, as the number of patients with renal failure was (60) and healthy (30) people, including females and males, where the number of males for renal failure patients was (33) and (27) females, with ages ranging from (20-70) years. As for the healthy (control group), including (16) males and (14) females, the results were as follows. The presence of a high level of potassium, sodium and calcium in patients with renal failure compared to the healthy ones, and an increase in the level of interleukin-6 among patients with renal failure compared to the healthy ones. The results of the study also showed that there were no significant differences in the electrolyte and interleukin-6 values between males and females, with a significant increase in the sodium value in the age group 51 years compared to the two age groups (20-35) years and (36-50) years. The results also showed a positive relationship between sodium and potassium, and a positive relationship between all electrolytes (potassium, sodium, calcium). The results also showed a negative relationship between interleukin-6 and potassium, sodium and calcium.

Keywords: interleukin-6, potassium, sodium, calcium

INTRODUCTION:

The kidney is one of the important organs in the human body, and chronic kidney failure is one of the most common diseases that affect the kidneys. Early detection of kidney disease can avoid the high expenses spent on kidney diseases, including chronic kidney failure. The first motive for our study and for the study of many researchers is to prepare more studies in order to protect people from the effects of the disease, and given the expected increase in infection with this disease in the coming years, and as a result of high blood pressure and diabetes, there is an imbalance in the functions of the kidneys, which leads to the occurrence of kidney failure [1]. Chronic kidney failure is one of the most serious complications of diabetes, and this leads to a high mortality rate. In recent years, a significant increase in the number of patients with type 2 diabetes has been recorded, and one of the most vital organs in the human body exposed to complications of diabetes is the kidney [2]

Hronic kidney disease is a long-term condition that occurs due to the deterioration of the functioning of both kidneys and in some cases it becomes necessary to dialysis, or a kidney transplant, and the functions of the kidneys become abnormal, or their structure becomes abnormal [3], and when chronic kidney disease develops, the kidneys lose their ability to remove waste and fluid and electrolyte balance in the body [4], and patients in the end stage of kidney disease are susceptible to a variety of endocrine disorders [5].

Potassium is the primary positive ion in intracellular fluid [6] and is essential for the functioning of nerves, heart, arteries and muscles, and also has a significant effect in modifying acids harmful to the body [7]. The potassium ion rate within cells and in human serum is (135-150 MEq/L and 3.5-5.0 MEq/L), respectively [8], as the rate of sensitization, irritability, impulse reception and stimulation, such as cardiac muscle cells, and nervous tissue cells , dependent on intracellular potassium ion to extracellular potassium ion rate [9]. Potassium is the most lost ion (Hypokalemia), and there is a relationship between potassium ion deficiency and high blood pressure. Medicines that are used to treat blood pressure may cause a deficiency in potassium ion [10] [11] [12] of its causes: vomiting, diarrhea, burns, sweating, taking diuretics, increased aldosterone, and heart failure [13] [14]. Increased potassium (Hypercalmia): It expands blood vessels because it inhibits smooth muscles, so it is noticed when the kidneys are disturbed, and its rise is a strong indication for starting the process of blood flow in patients with chronic renal insufficiency [15] [16], and the increase in potassium in extracellular fluids causes expansion Severe in the heart

muscle, slowing its speed, and then stopping the heart, and high potassium concentration can lead to a limit of 8-12 meg/L, which is two to three times the normal limit, that is, it generates a very weak heart and an abnormal pattern that leads to death [17].

Sodium is the extracellular backbone [6], and is essential for nerve, muscle, and stomach functions, as well as for maintaining proper water balance and the proper pH of the blood [7]. The kidneys regulate the sodium ion in the body, and when the value of the sodium ion decreases, the kidneys store it, but if the sodium ion level increases, it is excreted in the urine [18], where the kidneys filter and reabsorb (173 L) of water and 2400 MEq/L of sodium ion. Daily, the kidney regulates the amount of sodium ion in the body through two methods: the change in the glomerular filtration rate, and the change in the tubular reabsorption [11]. Adission disease, which is characterized by excess sodium loss, is caused by adrenal cortical insufficiency during pregnancy and may be caused by the formation of sodium-retaining hormones and lipids, It has also been observed that the placenta develops some hormones that have effects on sodium retention. It is believed that these hormonal substances are responsible for the retention of sodium and water, accompanied by a rapid increase in weight and we usually notice during certain periods of pregnancy in pregnant women, but the increase in sodium in the serum is a rare case, and it may sometimes occur as a result of taking sodium salts or it may be due to the hyperactivity of Adrenal cortex as in Cushing Syndrome after taking Corticotropin Cortisone, some sex hormones, may cause an increase in the concentration of sodium ion in the blood serum due to the excretion of water outside the cells [6] and an increase in the secretion of aldosterone hormone [13], and excessive sodium or water loss leads to an inability to secrete Anti-Dieurtic Hormone (ADH), which the kidneys need to maintain the amount of water [17], and the lack of water taken is a result of difficulty swallowing, coma and nausea [19].

Calcium ion is one of the body's basic and internal ions in many physiological processes, and it is one of the essential elements as it helps maintain human health and bones, and it also acts as an aid to the maintenance and preservation of the nervous system as well as the mechanism of muscle tissue contraction, blood clotting and in the formation of materials the basic structure of the device digestive system [20]. Regardless of a woman's age, when she becomes pregnant, calcium will be a very important element for her because she takes it in through food, because it is necessary for the development of the fetus. It enters into the formation of its skeleton during the embryonic stage inside the womb, and the fetus withdraws the calcium it needs from the placenta, and what the mother gets [21] and estrogen, which plays an important role in helping to increase calcium absorption from the bones [22].

Interleukins include a group of protein compounds that were first seen on white blood cells. The molecules act as a signal for many different cells, and their interaction contributes to controlling the functioning of the immune system, a type of cytokine known as Lymphokinase, and Cytokinases are peptides released by tissue cells and the immune system, leukocytes secrete interleukins and have the ability to influence the immune response [23 It is secreted mainly by mononuclear cells, which are observed to stimulate the growth and differentiation of lymphoid and stem cells [24], and interleukin represents a message between leukocytes as an inflammatory response, or an immune response. It is also mentioned that interleukins act as a mediator of inflammatory immune processes, and oxidative stress has been found to play a major role in increasing the level of interleukins on cardiac cells, especially for people who suffer from heart disease, as it causes a lack of myocardial ischemia or insufficiency [25], as is the case in patients with myocardial infarction, causes an increase in the level of secreted interleukins [26]. This family of cytokines includes: Different types of interleukins, which are symbolized by IL, such as IL-6, IL-10 and many others [27]. Given the increasing number of patients diagnosed with kidney failure, which leads to the development of serious diseases, it is very important to explain the mechanisms of its formation and development, and this is undoubtedly one of the biggest challenges facing modern medicine. That's why many researchers have created multi-level, multidisciplinary teams aimed at explaining a small part of the aetiology of kidney disease that has to do with the role of the immune system. The important role of interleukins in the development of several kidney diseases classified as AKI, CKD and kidney transplantation has been demonstrated. Due to the multidirectional mechanisms of action and the number of interleukins in the human body it is very difficult to determine the clear effects of individual cytokines, interleukins play an important role in maintaining the homeostasis of the immune system and cellular processes that occur in the human body [28].

IL-6 is a typical omnidirectional cytokine that regulates a variety of physiological events in vertebrates, such as cell proliferation, differentiation, survival and apoptosis [29]. IL-6 leads a role in the immune system, the endocrine system, the nervous system and blood, and in bone metabolism [30] [31]. There are many types of immune cells that produce IL-6 including T cells, B cells, and multiple cells. polymorphs, eosinophils, monocytes/macrophages, and mast cells, [32]. Other cell types known to produce IL-6 are chondrocytes, osteoblasts, endothelial cells, skeletal and smooth muscle cells, thyroid cells, fibroblasts, meningeal cells, keratinocytes, some cancer cells, adipose tissue cells, microglia and astrocytes [33]. Summarize the role of IL-6 in many kidney diseases, such as immunoglobulin nephropathy, lupus nephritis, diabetic nephropathy, and acute kidney And endothelial cells In addition to immune and inflammatory cells, endothelial cells will actively respond to IL-6 and IL-6 has already been shown to be involved in renal cell injury and repair as well as a variety of immunity and metabolism. The aim of the current study is to study the relationship of interleukin-6 with potassium, sodium and calcium in patients with renal failure.

MATERIALS AND WORKING METHODS:

About 5 milliliters of blood was drawn for each patient, and this amount of blood was put into several tubes, depending on the type and nature of the test to be performed. Where 2.5 milliliters of the blood sample was placed in tubes containing a gel material (gel), which helps to separate the blood drawn from the serum [34]. As for the rest of the tests that need to be determined using blood serum, plastic tubes that do not contain Anticoagulants (normal tube), where 5 milliliters of blood were put into the plastic tubes, then left for (10-15 minutes) at room temperature, then samples were placed in a centrifuge (5 minutes) at speed (3000 rpm)) to separate the serum from the blood, and the blood serum was frozen after being divided into several tubes in order to conduct the biochemical tests required to be studied. The study was conducted in (Tikrit Teaching Hospital - Artificial Kidney Division) for the period from the beginning of (January 2021) to the beginning of (March 2022). A personal interview was conducted with patients with renal failure to record information about each patient, such as gender, age, marital status, housing, and diseases associated with renal failure. The study included (60) sick people, and (30) healthy people.

Blood samples were collected for (30) healthy people, including (16) males and (14) females, and their ages ranged between (20-60) years, and they were accompanying patients and laboratory staff. They were confirmed to be free of signs and symptoms of failure. Kidney disease, diabetes and high blood pressure. Also, (60) blood samples (33 males and (27) females) were collected, their ages ranged between (20-70) years from patients with chronic renal failure who had undergone dialysis. The SmartLyte plas device shown in Figure (1) was used to estimate the level of potassium, sodium and calcium in the blood serum.

Figure (1) SmartLyte plas device

The level of interleukin-6 was measured using (ELASA) technique shown in figure (2)

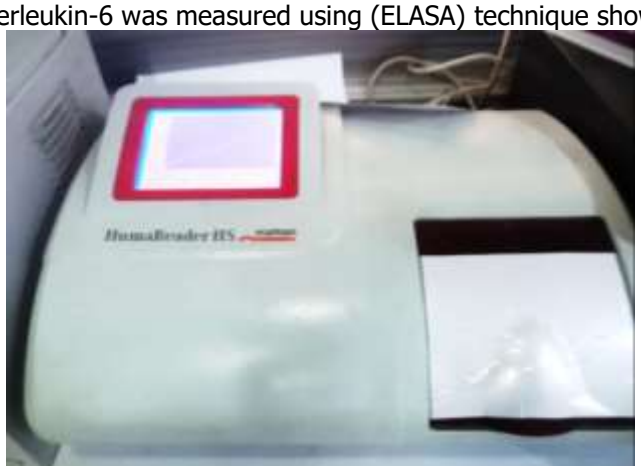

Figure 2 (ELASA) technique

STATISTICAL ANALYSIS:

The results were statistically analyzed using the (SPSS) program, as the significant levels of the variables were calculated between two different sets of data using the (ANOVA) and (t-test), and the correlation factor (r) was calculated between some of the studied traits [35].

RESULTS AND DISCUSSION:

Figure (3) shows a significant increase in the value of potassium in patients with renal failure compared to healthy persons, as the value of potassium level, respectively, for patients (mmol/L 0.973±6.370) and for the healthy(mmol/L 0.160±4.335) And at a moral level P≤ 0.0006 As shown in Table (1). The glomerular filtration rate (GFR) is the main cause of hyperkalemia, and with a low glomerular filtration rate, the rate of excretion of potassium from the body will decrease, and this leads to an increase in the level of potassium in the blood and the speed of reabsorption by the kidney tubules [36], and the effectiveness of the ATP pump. Sodium-potassium phosphatase (Na+-K+ ATPase), where the increase in potassium can be attributed to many reasons, including the role of the kidneys in excreting approximately (90 to 95%) of potassium entering the body. When chronic renal failure occurs, the efficiency of this process diminishes [37]. The results of the current study agreed with [38] [39].

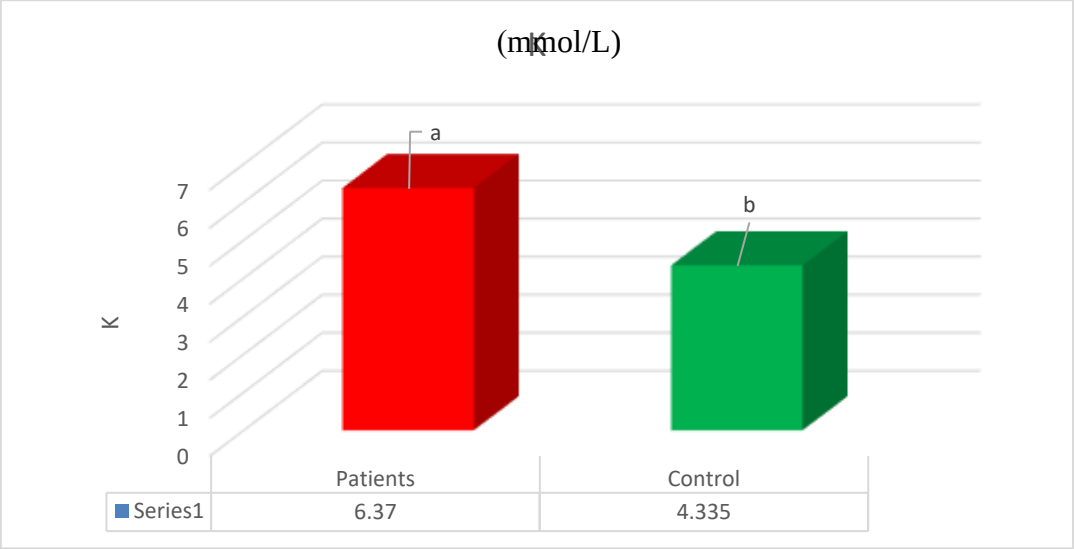

Figure (3) Potassium level for patients and healthy people

Table (1) Electrolyte concentrations in patients with renal failure compared to healthy controls

P - value	Mean ± SD		الفئات
	healthy (30)	patients (60)	
P ≤0.0006	0.160 ± 4.335	0.973 ± 6.70	K (mmol/L)
P ≤0.0008	3.09 ± 133.69	3.31 ± 150.21	Na (mmol/L)
P ≤0.0007	0.0743 ± 1.178	0.858 ± 3.723	Ca (mmol/L)
P ≤0.0008	1.17 ± 7.98	15.4± 202.5	IL - 6 (Pg/ml)

Figure (4) shows a significant increase in the value of sodium in patients with renal failure compared to healthy patients, as the value of the sodium level was respectively in patients (mmol/L 3.31±150.21) And for the healthy (mmol/L 3.09±133.69) And at a moral level P≤ 0.0008. Sodium is one of the electrolytes that the body needs in relatively large amounts. Electrolytes carry an electric charge when dissolved in body fluids, such as blood. Most of the body's sodium is found in the blood and in the fluid surrounding cells. Sodium helps maintain the normal fluid balance in the body and plays an active role in the normal functions of nerves and muscles. Sodium can be obtained through food and drink, and is lost through sweat and urine.

A healthy kidney works to maintain a constant level of sodium in the body, and this is done by balancing the amount excreted in the urine. The total amount of sodium is affected by the disturbance of the balance in the amount of sodium lost and ingested, as it becomes very high and its increase is detected by sensors in the heart, blood vessels, and kidneys, thus alerting the kidneys to increase sodium excretion, which leads to the return of blood volume to its normal position. Excess sodium is caused by poor water intake, kidney failure, diuretic use, and diabetes. The results of the sodium value for the current study did not agree with [38], because in the current study the samples were collected before the patient undergoes dialysis, where an increase in sodium arises due to a large deposition of sodium in the water and this is due to the inability of the kidneys to excrete the excess water outside the body Because of chronic renal failure, which leads to an increase in the concentration of sodium inside the cells compared to the percentage of sodium outside the cells. This, in turn, will lead to an increase in the concentration of sodium in the plasma, causing a rise in the potassium ion concentration due to the mechanisms of ineffective transport of potassium out of cells as well as the electrochemical gradient of potassium ion secretion [40]. The significant increase in sodium is due to a decrease in the efficiency of the glomerular filtration rate, as it reduces sodium filtration and increases its concentration in the blood serum, and this is consistent with the results of [41] and differs with [42]. The reason for the difference is, the decrease in the level of sodium concentration in the blood serum is due to the deficiency of the hormone aldosterone, which increases the loss of sodium ions in the urine.

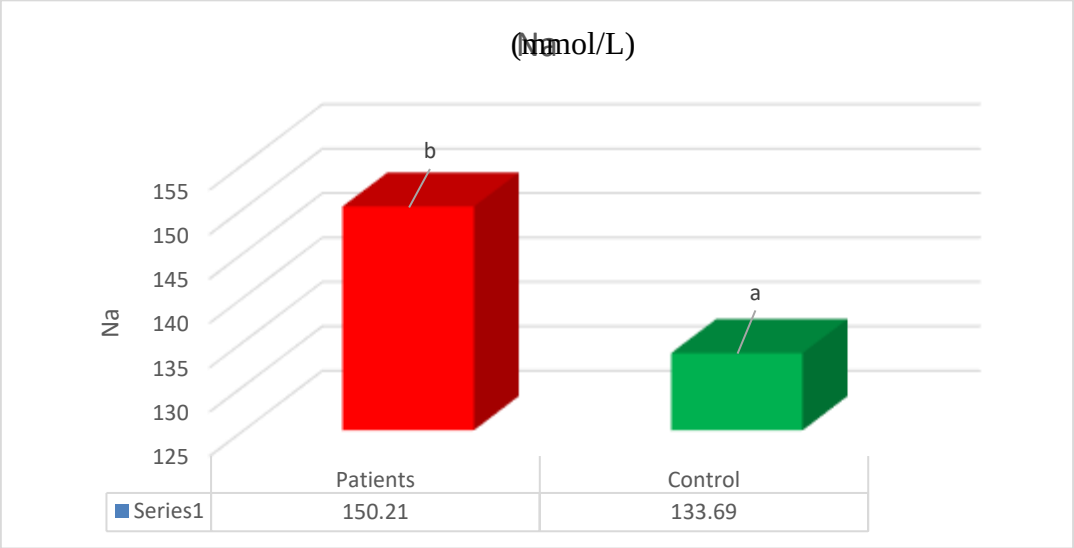

Figure (4) Sodium level for patients and healthy people

The results of Figure (5) showed a significant increase in the value of calcium in patients with renal failure compared to healthy ones, as the value of calcium level, respectively, for patients (mmol/L 3.723±0.858)and for the healthy (mmol/L 1.178±0.743) And at a moral level P≤ 0.0007. Hypercalcemia is usually caused by thyroid and parathyroid glands. Excess calcium stresses the kidneys, which can lead to excessive thirst and frequent urination. The ability of the kidneys to clean the blood and get rid of fluid. An increased calcium concentration may be caused by the overuse of antibiotics, calcium and vitamin D supplements, and the overuse of medications such as lithium and some diuretics. The age group has a major role in increasing calcium, its imbalance and its deposition inside the body, and the results of the current study agree with [43], and the results of the current study did not agree with [44] because in the current study samples were collected before the patient undergoes dialysis.

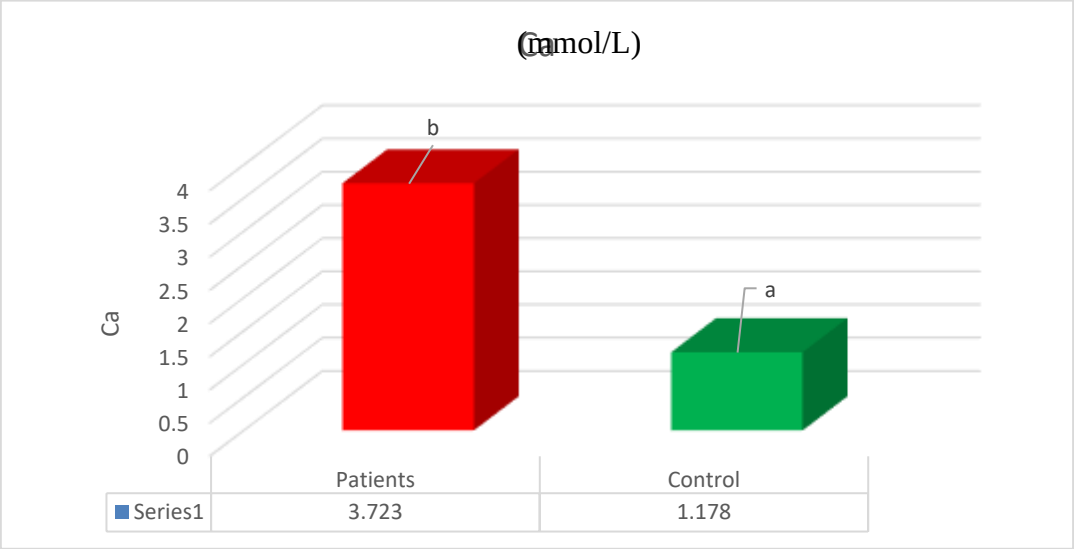

Figure (5) Calcium level for patients and healthy people

Figure (6) shows a significant increase in the IL-6 . value P≤ 0.0008 in patients with renal failure compared to healthy subjects, the value of the IL-6 level for the patients was (Pg/ml 51.4±202.5) And for the healthy (Pg/ml 1.17±7.98) Straight. IL-6 is the main mediator of the acute phase response, its value is high in the plasma of patients with ESRD, which is a strong indicator of the outcome. There are a number of factors prevalent in patients with ESRD, such as high blood pressure, obesity, insulin resistance, Excess fluid and persistent inflammation can all be associated with blood pressure. IL-6 levels are directly or indirectly associated with decreased kidney function and with elevated IL-6 and genetic differences may be of interest.. This cytokine is considered as a central regulator of the inflammatory response in patients with ESRD [45] and [46]. The results of the study agree with the results of [47].

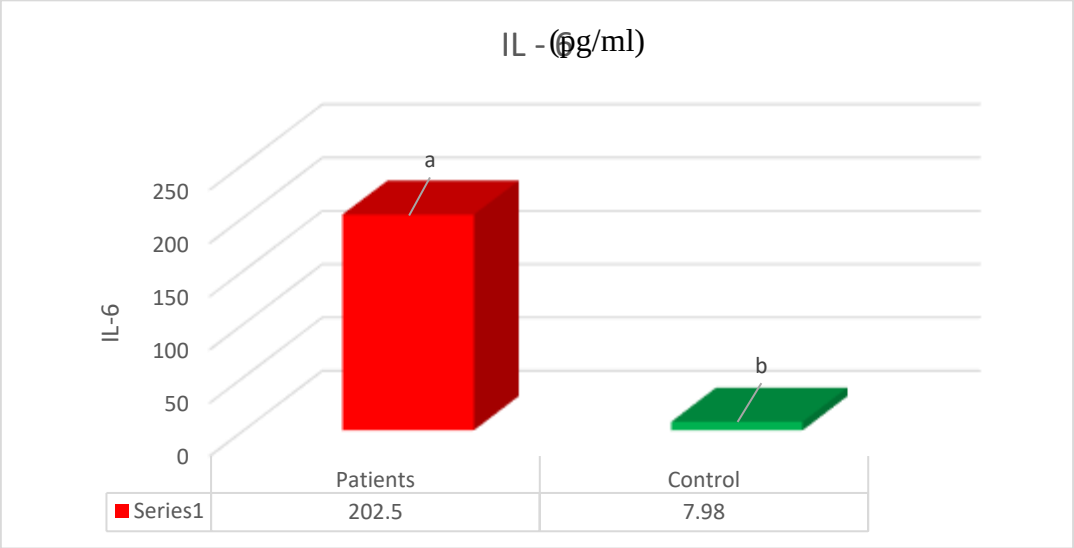

Figure (6) Interleukin-6 level for patients and healthy people

Figures (7), (8) and (9) showed the values of electrolyte concentrations measured in patients with renal failure, divided (by sex) and compared with each other and compared with the control group. We note that there are no significant differences shown in Table (2).

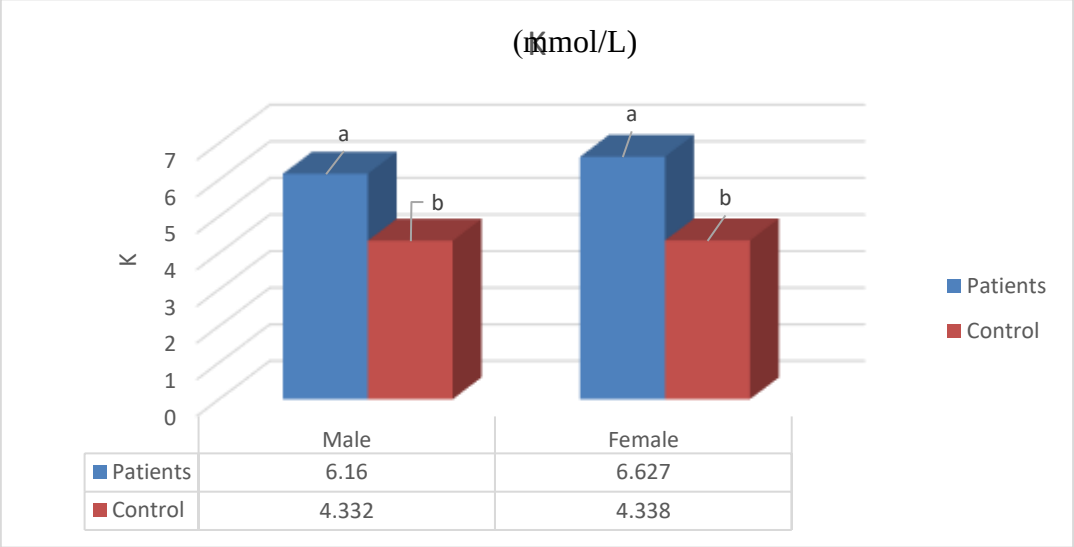

Figure (7) Potassium level by gender for patients and healthy people

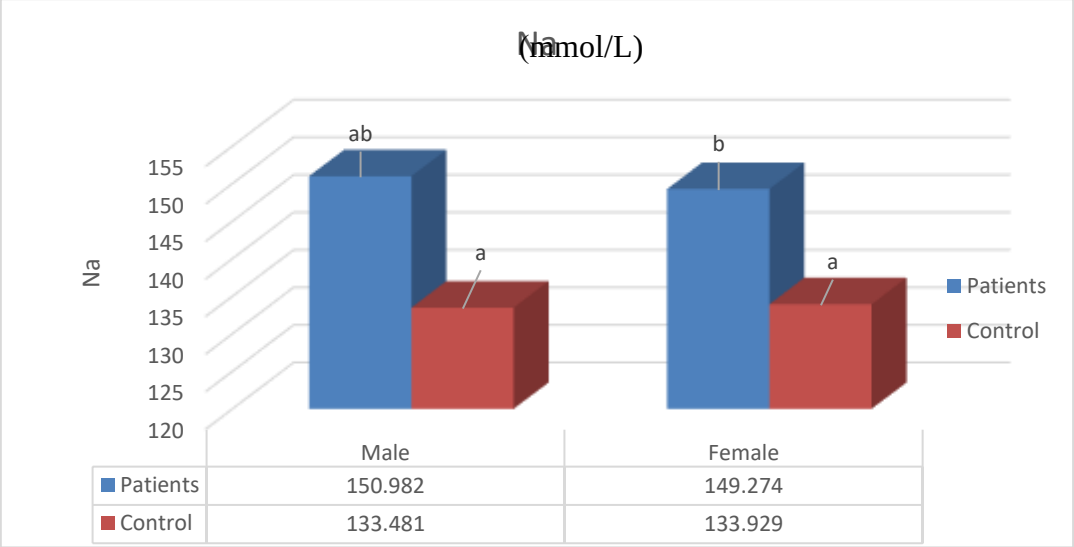

Figure (8) Sodium level by gender for patients and healthy people

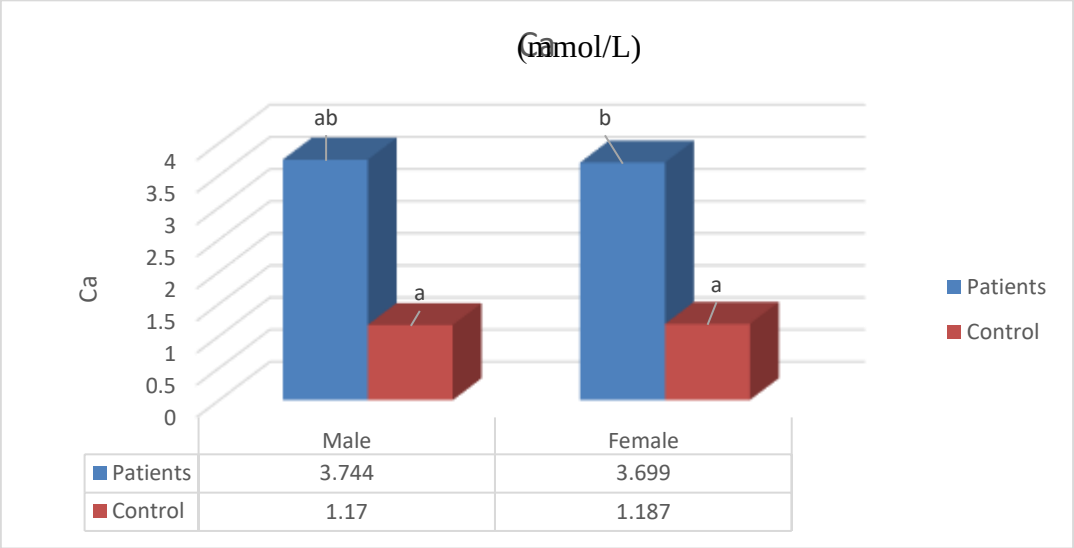

Figure (9) Calcium level by gender for patients and healthy people

Table (2) Electrolyte Concentrations in Renal Failure Patients Compared to Healthy People (by Gender)

P - value	Female		Male		adjectives
	14 Healthy (N) Mean ± SD	(N) 27 Patients Mean ± SD	(N) 16 Healthy Mean ± SD	33 Patients (N) Mean ± SD	
P ≤0.000	0.1529 ± 4.338 b	0.922 ± 6.627 a	0.1712 ± 4.332 b	0.976± 6.16 a	K (mmol/L)
P ≤0.00005	3.115 ± 133.929 b	3.390 ± 149.274 a	3.145 ± 133.481 b	3.079± 150.982 a	Na (mmol/L)
P ≤0.00003	0.0700 ± 1.187 b	0.769 ± 3.699 a	0.0792 ± 1.170 b	0.939± 3.744 a	Ca (mmol/L)
P ≤0.00006	1.353 ± 7.907 b	13.2 ± 196.69 a	1.022 ± 8.050 b	10.25± 207.33 a	IL – 6 (Pg/ml)

Note: Similar letters mean there are no moral differences, different letters mean there are moral differences.

Figure (10) showed that there were no significant differences in the level of interleukin-6 for patients with renal failure, compared to the control group, as shown in Table (2).

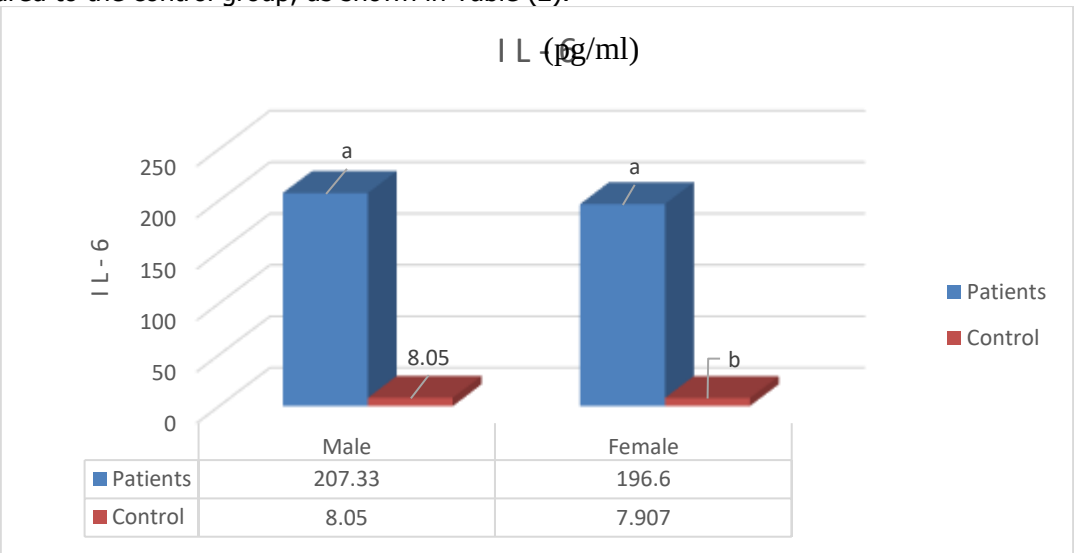

Figure (10) Interleukin-6 level according to gender for patients and healthy people

The study showed, as shown in Figures (11) and (12) and (13), which were divided into three age groups (20-35 years), (36-50 years), and (51 - etc.), where it was found that There is a significant increase in the value of sodium in the age group 51, and the reason for this is due to not drinking enough amounts of water, and sometimes respiratory diseases, the use of some medicines, antibiotics, diuretics, high pressure and blood sugar, and the absence of significant differences in the value of potassium and calcium according to the age groups mentioned , as shown in Table (3).

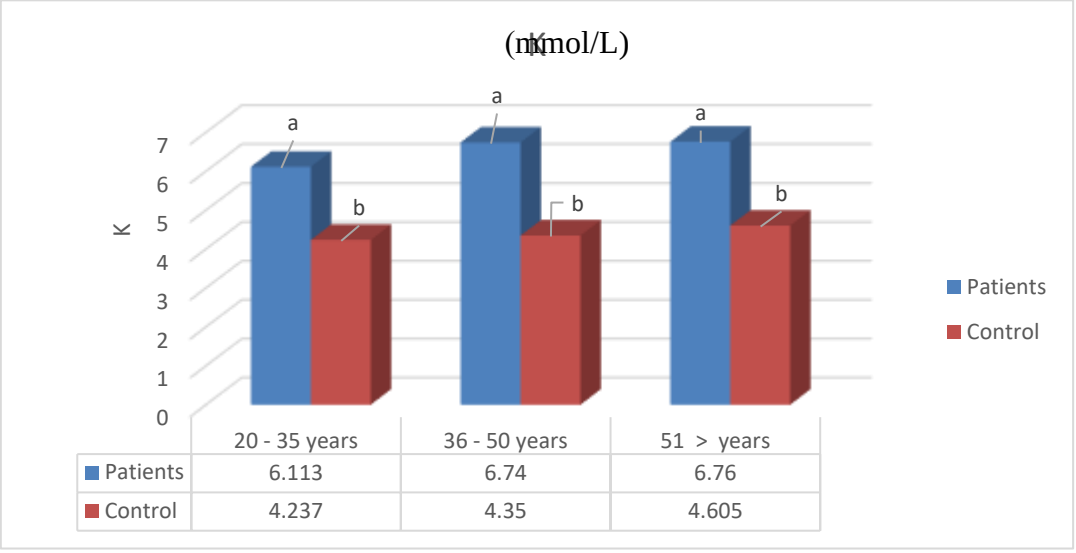

Figure (11) Potassium level according to the age groups of patients and healthy people

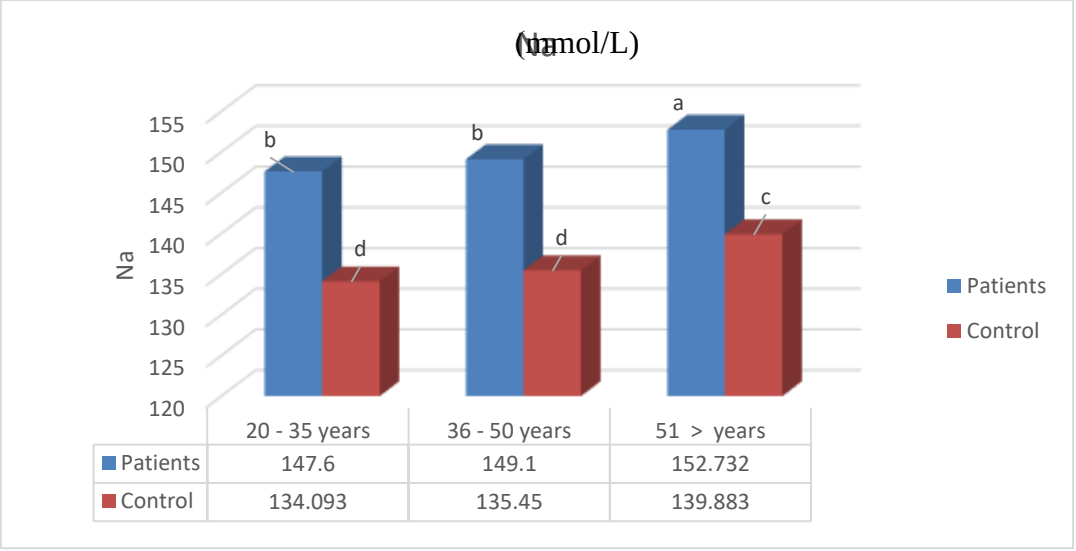

Figure (12) Sodium level according to the age groups of patients and healthy people

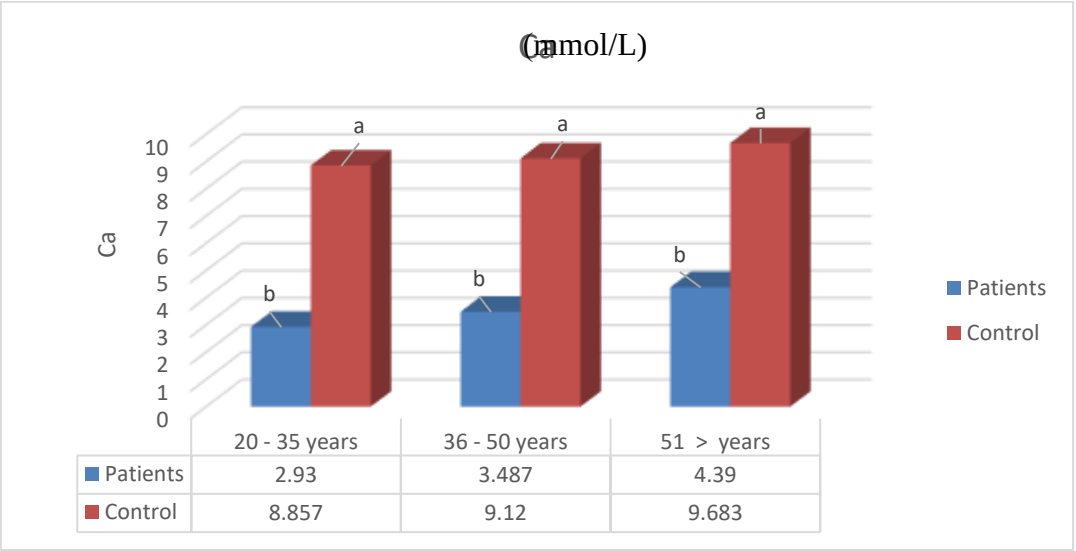

Figure (13) Calcium level according to the age groups of patients and healthy people

Table (3) Electrolyte Concentrations in Renal Failure Patients Compared to Healthy People (by age)

P - value	the age (51 - etc)		the age (36 - 50)		the age (20 - 35)		adjectives
	اصحاء 6 (N) Mean ± SD	مرضى 25 (N) Mean ± SD	اصحاء 10 (N) Mean ± SD	مرضى 19 (N) Mean ± SD	اصحاء 14 (N) Mean ± SD	مرضى 16 (N) Mean ± SD	
P ≤0.0008	0.0826± 4.605 b	0.937± 6.760 a	0.1171± 4.350 b	0.603± 6.074 a	0.0875± 4.237 b	1.202± 6.113 a	K (mmol/L)
P ≤0.00007	1.320± 139.883 c	2.460± 152.732 a	3.092± 135.450 d	2.707± 149.100 b	2.841± 134.093 d	2.262± 147.60 a	Na (mmol/L)
P ≤ 0.000002	0.1941± 9.683 a	0.742± 4.390 b	0.2530± 9.120 a	0.501± 3.487 b	0.1697± 8.857 a	0.445± 2.930 b	Ca (mmol/L)
P ≤0.00003	1.078± 8.62 b	26.59± 194.46 a	1.035± 7.74 b	29.8± 204.40 a	1.273± 7.89 b	29.1± 212.80 a	IL - 6 (Pg/ml)

Figure (14) showed that there were no significant differences between renal failure patients compared to the control group, which were divided according to age groups, as shown in Table (3).

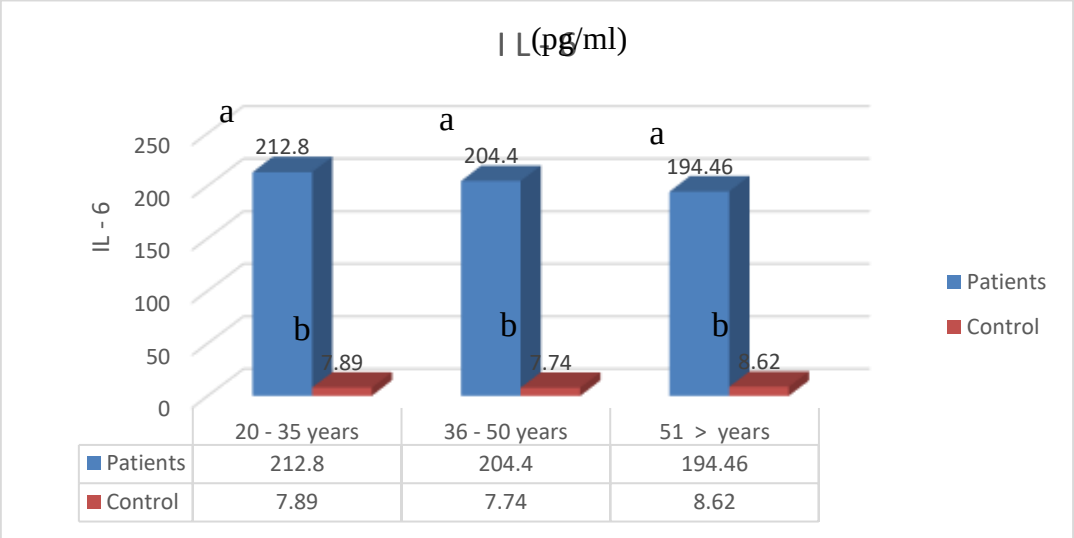

Figure (14) Interleukin-6 level according to the age groups of patients and healthy people

The results of the study also showed a relationship between interleukin-6 (IL-6) and all electrolytes (potassium, sodium, calcium) were negative ($r = -0.023$), ($r = -0.106$) and ($r = -0.221$) respectively in patients with renal failure, and the reason for the increase in interleukin 6 is due to the immune response And the inflammation between interleukin-6 and kidney receptors, which has a role in IgM nephropathy, lupus nephritis, and diabetic nephropathy by residing cells in the kidneys [47]. The reason for the low electrolyte level is due to an imbalance in the role of urea and creatinine, which in turn plays a critical role in regulating sodium and potassium ions and the presence of thyroid and adrenal disorders.

CONCLUSIONS:

1. High level of sodium and calcium in patients with renal failure compared to healthy persons.
2. High level of interleukin-6 in patients with renal failure compared to healthy persons.
3. There is a significant increase in the value of sodium in the age group ≥ 51 compared to the two age groups (20-35) and (36-50).
4. A negative relationship exists between interleukin-6 and all electrolytes (potassium, sodium, calcium) ($r = -0.023$), ($r = -0.106$) and ($r = -0.221$) respectively .
5. There were no significant differences in the electrolyte and interleukin-6 values between males and females.
6. Increase in the IL-6 . value P≤ 0.0008 in patients with renal failure compared to healthy subjects, the value of the IL-6 level for the patients was (Pg/ml 51.4±202.5) And for the healthy (Pg/ml 1.17±7.98) respectively .
7. Increase in the value of calcium in patients with renal failure compared to healthy ones, as the value of calcium level, respectively, for patients (mmol/L 3.723±0.858)and for the healthy (mmol/L 1.178±0.743) And at a moral level P≤ 0.0007.

8. Increase in the value of sodium in patients with renal failure compared to healthy patients, as the value of the sodium level was respectively in patients (mmol/L 3.31±150.21) And for the healthy (mmol/L 3.09±133.69) And at a moral level P≤ 0.0008.

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