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(RESEARCH ARTICLE)

Evaluation of some hormones and trace elements in renal failure patients

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Abstract

Renal tissue has a crucial role in electrolyte and acid-base balance maintenance. Failure of kidney functions will develop a condition termed renal failure (RF), which leads to various disorders, including anemia, metabolic acidosis, and endocrine dysfunction. The current research aims to study certain trace elements and hormones related to renal failure; the study included 200 dialysis patients and 70 healthy controls who visited Azadi Teaching Hospital from December 2023 to April 2024. All participants were assessed for biochemical and hormonal tests, including renal function, trace elements, complete blood count, and erythropoietin and vasopressin levels.

Our data illustrated that renal failure (RF) patients had lower GFR levels (58.67±40.20). Our data showed that the average levels of erythropoietin (EPO) at 42.71 ng/dl and vasopressin (AVP) at 55.87 mg/dl were much lower in RF patients compared to the control group, with a significance level of $P<0.05$. Additionally, serum selenium was significantly lower (at 89.41 ng/dl for Se) in RF patients than in the control, while serum nickel was significantly higher in RF patients, with a mean of 62.72 ng/dl for Ni. In conclusion, our data revealed a significant decline in erythropoietin and vasopressin hormones in RF patients. Additionally, the selenium level decreased. However, the nickel level in the blood was higher in the patient group, which can lead to impaired renal filtration and an increased risk of renal injury.

Keywords: Trace Elements; Renal Failure; Renal Tissue; Erythropoietin; Vasopressin

1. Introduction

The kidneys are essential organs that maintain the body's fluid, electrolyte, and acid-base balances, ensuring a steady environment for tissue and cell metabolism. They balance solute and water transport, excrete metabolic waste products, conserve nutrients, and control acid-base balance [1]. Some of the common causes of renal illness are diabetes and proteinuria, in addition to chronic use of anti-cancer medications [2]. Acute kidney necrosis significantly increases the risk of renal function impairment, leading to high risks of morbidity and mortality [3]. In chronic renal failure (CRF), the body is no longer able to maintain balance in the electrolytes as well as metabolic waste clearance, hence acidosis, uraemia, anemia, and metabolic disorders. RF's most prominent etiologic factors include diabetes, polycystic renal disorders, elevated blood pressure, and glomerular inflammation [4;5].

One of the kidneys' most critical hormones is erythropoietin (EPO), which controls the process of erythropoiesis in the bone marrow. Individuals with renal failure often suffer from anemia due to low levels or failure in the production of this hormone, which impacts the patient's quality of life and general well-being. The standard therapy for this illness is erythropoietin, which includes erythropoiesis-stimulating medications like epoetin alfa and beta and its counterpart, darbepoetin alfa. However, disagreement exists over the ideal haemoglobin (Hb) concentration for managing side effects and reducing the risk of systemic hypertension, site access thrombosis in dialysis patients, and an increase in cardiovascular events [6].

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Vasopressin, also known as antidiuretic hormone or arginine vasopressin, is a substance found in high amounts in certain areas of the hypothalamus, including the PVN, supraoptic nuclei, and suprachiasmatic nuclei. Vasopressin is a hormone that aids in blood vessel constriction and helps the kidneys regulate the body's salt and water balance. This process aids in lowering blood pressure and the volume of urine produced [8]. The hypothalamus, a brain region, produces vasopressin, which the pituitary gland secretes into the bloodstream. Some tumour types release excess vasopressin, leading to low blood salt levels and water retention. Other names for it include arginine vasopressin and antidiuretic hormone [9]. Unsurprisingly, ADH has significant clinical importance, given its essential involvement in several processes. ADH increases the production of water transport proteins in the collecting duct and late distal tubule, which helps the kidneys take in more water.

Selenium (Se) is a trace element that functions as a cofactor in several enzymes (selenoproteins) that regulate the immune system, enzymatic antioxidant defences, and thyroid hormone metabolism [11]. Patients with chronic renal illness or severe kidney damage frequently have low serum Se levels [12]. According to reports, those over 35 who have low serum Se levels and renal insufficiency are at a higher risk of dying from coronary heart disease and all causes combined [13]. According to some research, oral and intravenous selenium supplementation improves renal patients' immunological function and selenium status while lowering oxidative stress products [14]. Even though there are interesting links between selenium's role in the body and various health issues related to both sudden and long-term kidney disease, the clinical effects of low sodium levels in these patients have not been studied in depth yet.

Nickel is a metal that exists naturally and may be found in soil, water, and the air. Overconsumption of Ni can cause harmful health consequences in humans, including cancer, illness, dizziness, asthma, heart problems, and problems related to the lungs, nose, throat, and prostate [15]. The human body can absorb Ni from polluted air, food, and drink. Many studies connect the creation of reactive oxygen species to the cell-killing properties of Ni compounds [16]. One of the most significant indicators of both apoptosis and cell growth is the production of ROS [17;18]. Nickel's oxidative damage increases ROS production, and it's believed that these ROS contribute to apoptosis. Nevertheless, it is uncertain whether raising ROS is necessary for the apoptotic process [19,20]. This study aimed to evaluate the levels of some heavy metals and biochemical parameters, in addition to erythropoietin and vasopressin hormone levels, in patients with chronic renal failure.

2. Materials and Methods

2.1. Sample collection

The study involved sampling renal failure patients admitted to a dialysis center in Kirkuk City between 15-11-2023 and 15-3-2024. All patients were previously diagnosed clinically and confirmed in the laboratory as renal failure patients. A control group of healthy subjects with no health issues was also involved in the study.

2.1.1. Biochemical tests

All blood samples from patients and controls were checked for various biochemical tests, kidney function tests, and glomerular filtration tests using a Cobas automated biochemistry analyzer, as well as for trace elements like lead and selenium using graphite furnace atomic absorption (GF-AAS).

2.1.2. ELISA

Quantitative ELISA kits for vasopressin and erythropoietin (Paramedical PKL, Italy) were utilized to assess those hormones' levels using an ELISA reader (Paramedical, Italy).

2.1.3. Statistical analysis

was performed via GraphPad Prism version 10.1. A significant result was estimated when $P<0.05$, whereas $P>0.05$ is considered statistically insignificant.

2.1.4. Ethical approvals

The study was approved by the Medical of College/University of Kirkuk, issue number 1161, on 13/5/2024. All participants obtained the written consent form before commuting to the study.

3. Results

Our data revealed that most renal failure patients fell within the age groups 31-40 years (15.5%), 41-50 years (23.5%), 51-60 years (34.5%), and >60 years (20.5%), while the least affected group was in the 20-30 years (6.0%), as depicted in Table 1.

Table 1 distribution of age for RF patients and control group.

Age	Patients (n=200)		Control (n=70)	
	No	%	No	%
20-30	12	6.0	9	12.8
31-40	31	15.5	11	15.7
41-50	47	23.5	14	20
51-60	69	34.5	23	32.9
>60	41	20.5	13	18.6
Total	200	100.0	70	100.0

The study revealed that most renal failure patients fell within the gender group, with 48% of men and 52% of women in the patient group and 50% in the control group, as depicted in Table 2.

Table 2 distribution of Gender for RF patients and control group.

Gender	Patients		Control	
	No	%	No	%
Male	96	48	35	50
Female	104	52	35	50

The hematology assessment of kidney failure and the control group shows a notable increase in kidney function tests, such as haemoglobin concentration, hematocrit percentage, and serum ferritin level, with average values of 12.42 and 7.76 g/d for Hb, 41.7 and 26.7 % for PCV, and 107.1 and 8.26 ng/ml for ferritin, with P=0.0192, 0.0053, and 0.0013, respectively. The Mann-Whitney T-test was used, as shown in Table 3. The Mann-Whitney T-test was applied, as depicted in Table 3.

Table 3 Hematology test associated with RF patients and control group.

Parameter	Mean ±SD		P-Value
	Control (n=70)	Patient (n=200)	
Hb (g/l)	12.42±5.31	7.76±4.26	0.0241
PCV (%)	41.7±21.23	26.7±18.51	0.0062
ferritin (ng/ml)	107.1±74.65	8.26±6.42	0.0018

Regarding the biochemical assessment of renal failure and the control group, it reveals a significant elevation of renal function tests, including blood urea and serum creatinine, with a mean of 24.39 and 90.94 mg/dl for urea and 0.71 and 3.85 mg/dl for creatinine, with P = 0.0072 and 0.0021, respectively, when the Mann-Whitney T-test was applied, as depicted in Table 4. In the same way, GFR was shown to increase significantly in RF patients compared to controls, with means of 58.67 and 105.29 ml/min and P=0.0541. Similarly, for S. K+, there was a significant elevation with a mean of 4.4 and 8.94 mmol/L and a P value of 0.0034. At the same time, S. albumin levels were slightly reduced in the patient group compared to the control (4.27 and 2.78 g/dl), P = 0.0672.

Table 4 Biochemical test associated with RF patients and control group.

Parameter	Mean ±SD		P-Value
	Control (n=70)	Patient (n=200)	
Urea (mg/dl)	24.39±6.27	90.94±12.53	0.0072
Creatinine (mg/dl)	0.71±1.476	3.85±0.221	0.0021
GFR (ml/min)	105.29±80.42	58.67±40.20	0.0541
S. K^+ (mmol/l)	4.4±1.81	8.94±5.42	0.0034
S. Albumin (g/dl)	4.27±3.62	2.78±1.68	0.0672

The amounts of erythropoietin and vasopressin were much lower in RF patients than in the control group, with average levels of 282.23 and 42.71 ng/dl for EPO and 217.32 and 55.87 mg/dl for AVP, and the differences were statistically significant, as shown in Table 5.

Table 5 Comparison of Erythropoietin and Vasopressin levels in patents and control groups

Parameter	Mean ±SD		P-value
	Control (n=70)	Patient (n=200)	
Erythropoietin (ng/dl)	282.23±194.46	42.71±28.42	<0.0001
Vasopressin (ng/dl)	217.32±68.52	55.87±47.31	0.0038

Regarding trace element assessment of renal failure and the control group, serum selenium declined significantly. Similarly, the level of serum nickel was higher in renal failure patients compared to the control group, with average values of 99.72 ng/dl for selenium and 57.8 ng/dl for nickel in the control group, and 131.0 ng/dl for selenium and 46.33 ng/dl for nickel in the renal failure group, with P values of 0.0294 and 0.0211, respectively, as shown in Table 6.

Table 6 Comparison of trace elements concentration in patents and control groups

Parameter	Mean ±SD		P-Value
	Control (n=70)	Patient (n=200)	
Selenium (ng/dl)	140.29±109.54	89.41 ±69.62	0.0242
Nickle (ng/dl)	38.23±30.11	62.72±38.31	0.0191

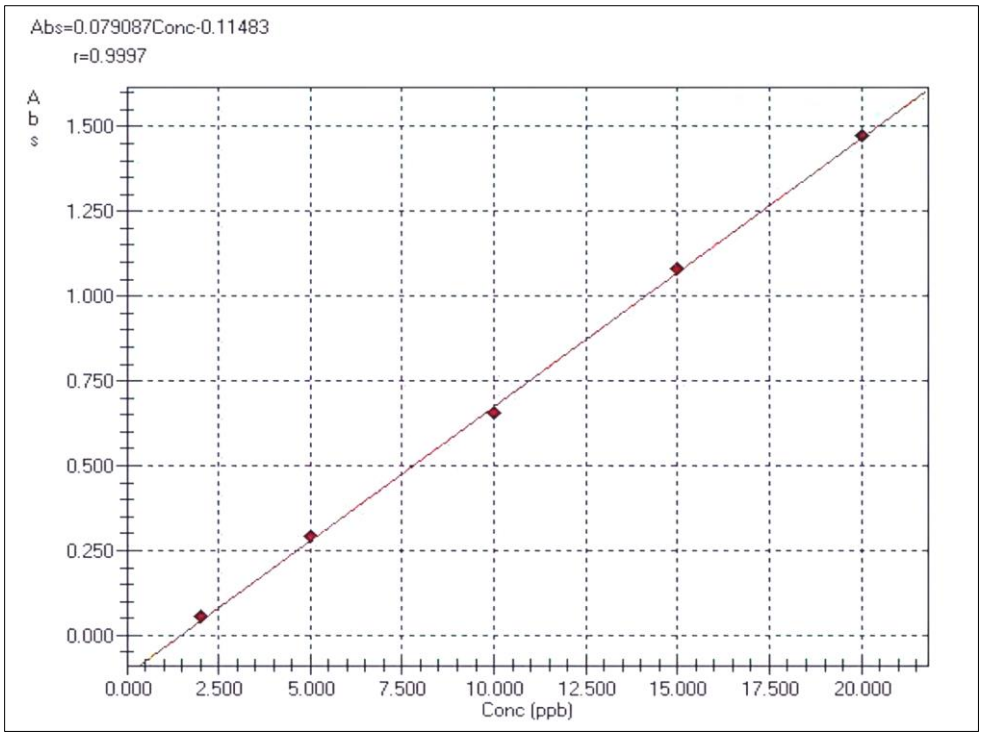

Figure 1 Standard Curve of Selenium

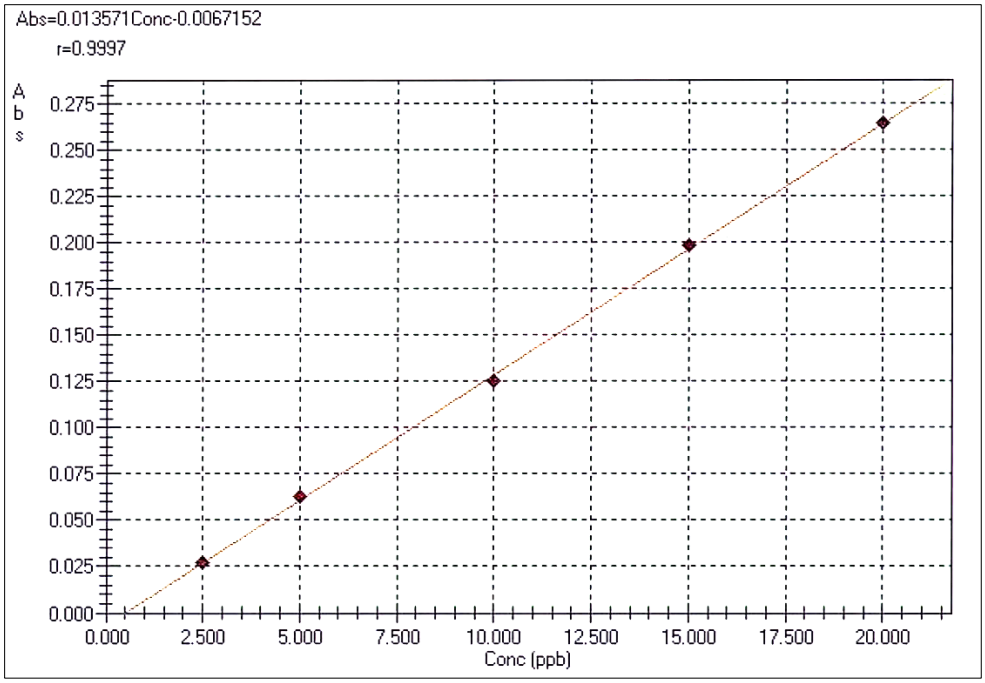

Figure 2 Standard Curve of Nickle

3.1. Correlation of age with multiple parameters

A correlation of age with multiple variables associated with RF patients was made via the Kruskal-Walli's test, and it revealed a significant correlation ($P < 0.05$) of age with urea, creatinine, GFR, EPO, and AVP with r values of 0.4772, 0.391, 0.418, 0.5617, and 0.6094, respectively.

Table 7 Correlation of patients age with multiple parameters**.**

	Age vs Urea	**Age vs Cre**	**Age vs GFR**	**Age vs S. K^+**	**Age vs S. Alb**	**Age vs EPO**	**Age vs AVP**	**Age vs Se**	**Age vs Ni**
P value	<0.05	<0.05	<0.05	>0.05	>0.05	<0.05	<0.05	>0.05	>0.05
r value	0.4772	0.391	0.418	0.1467	0.2297	0.5617	0.6094	-0.6347	-0.1670

4. Discussion

In this study, we assessed the levels of some hematological, biochemical, and immune parameters related to renal failure in patients. All the cases were on dialysis, and most of the patients affected by the disease were males, with men aged more than 57 years, while the mean age of the affected females was 51 years. These data are in line with another report that denoted more male patients affected by renal failure than females [21]. On the contrary, more female patients were affected than males, with a mean age of less than 50 years [22]. Regarding hematological parameters, the mean Hb in the patient's group was significantly lower than in the control group, with $P<0.05$. These data are parallel with another research study conducted on renal failure patients, which recorded a decline in the Hb levels compared to control subjects [23].

Additionally, there was a substantial decrease in ferritin in the sick group compared to the control, with $P<0.05$. The information presented here is consistent with research on renal failure cases that discovered a drop in ferritin levels compared to the control group [24]. Additionally, renal failure cases showed a substantial decline in the PCV ratio with $P < 0.05$. These data are close to other reports conducted on RF patients [25]. This decline in the levels of PCV in RF patients could be attributed to the fact that the concentration of ferritin and other hematopoietic resources is decreasing due to the failure to produce this potent hormone, which is the primary regulator of the erythropoiesis process in the bone marrow. A significant decline in the size and shape of the erythrocytes directly correlates with any decline in its levels [26].

One important function of the kidneys is controlling the haematocrit levels to optimize the demands of peripheral tissues for oxygen consumption. This function is controlled via the synthesis of erythropoietin [27].

Regarding biochemical parameters, the mean urea and creatinine were significantly higher in RF patients than in controls, with $P<0.05$. These data are in parallel with those who recorded an incline in the level of renal function test 10-fold in renal failure patients compared to control. Additionally, another report has revealed similar data regarding renal function tests in the RF group [28]. Moreover, the GFR in the patients' group was significantly lower compared to the control group, with $P<0.05$. These data are close to the other study on renal failure patients, which found a decline in GFR levels compared to the control group [29]. The drop in kidney function test results can be understood because renal failure patients experience a significant decrease in kidney function, either from damage to the kidney's filtering units or from problems with removing waste from the blood due to lower filtration rates in the kidneys. Any damage to the renal glomeruli or the renal tubular cells will potentially affect the filtration process, thereby increasing the levels of the end products of cellular metabolism in the circulation, which is reflected in the elevation of the renal function tests and a drop in the GFR levels [30]. Our data showed that potassium levels were much higher than in the control group [31;32]. This matches another study that found high potassium and albumin levels in patients with kidney failure, as indicated by lower albumin tests. In contrast, other studies indicated patients had lower potassium concentrations but elevated albumin [33;34].

Elevated potassium levels are due to renal filtration barrier breakdown. Renal potassium loss due to medication use is a common cause of hypokalaemia in adults, especially with thiazide diuretics, which are associated with a 5-fold increased risk. [35]. In patients undergoing dialysis, the predominant causes of hypokalaemia are low potassium dialysate, low dietary potassium intake, and malnutrition. The risk of mortality associated with hypokalaemia may be greater than that associated with hyperkalaemia, even in patients with CKD and patients undergoing dialysis; however, studies relating hypokalaemia to adverse outcomes are observational and subject to uncontrolled confounding [35]. Regarding erythropoietin and vasopressin hormones, there was a significant decline in the levels of erythropoietin and vasopressin ($P < 0.001$ and $P < 0.0049$), respectively. These data are parallel with another research that reported a significant drop in the levels of erythropoietin hormone in patients with chronic renal failure [27]. Another study noted a significant drop in the levels of the vasopressin hormone in RF patients [36]. Erythropoietin is vital to controlling and

maintaining the normal volume and number of red cells in circulation. This process is accomplished in parallel with the ability of the renal cells to sense the oxygen tension in the peripheral circulation, which can be controlled via the excretion of more water and salts or retaining them in the circulation. Anaemia is a relatively common complication of CKD. The most important factor contributing to this anaemia is the relative deficiency of erythropoietin. Iron deficiency is also a common contributing factor. However, erythropoietin is crucial for maintaining the blood synthesis process and providing adequate red blood cells to cover the need for oxygen demand on the cellular level. Due to the weakening hormone production by the kidneys in relation to renal failure, the receptors responsible for responding to the hormone are no longer occupied due to the lack or deficiency of its levels in circulation [37]. In the case of vasopressin, our data were close to other studies that indicated a significant decline in the levels of this hormone in RF cases [38]. Vasopressin could explain this, acting through its three receptors, which can exert actions far beyond its role in regulating water permeability in the renal collecting duct and the contraction of smooth muscle cells. Another study provides insight into the role of vasopressin in the pathogenesis of diabetes mellitus, metabolic disorders, and their associated cardiovascular complications via activation of hepatic V1a and pancreatic islet V1b receptors [39]. Regarding trace element parameters, the mean selenium was significantly lower in RF patients than in controls, with $P = 0.0294$. These data are in parallel with another report that recorded a decline in the level of trace elements tested in renal failure patients compared to controls [40]. The role of selenium is important in many interactions due to the importance of this molecule as a cofactor enhancing the function of the thyroid. In addition to supporting the synthesis of DNA and reducing cellular damage, these processes are achieved through the interaction with selenoprotein, an important protein that maintains the functionality of selenium. In addition, selenium may play an important role in protecting against heavy metal toxicity [41]. Reported from a study revealed that selenium deficiency resulted in inflammatory injuries in renal tubular atrophies in experimental animals, leading to impaired kidney function and downregulation of different variants of selenoproteins [42]. Regarding nickel, the mean nickel concentration was significantly higher in RF patients compared to the control, with $P = 0.0211$. Comparable data from another research group have demonstrated an incline in the concentration of this trace element in RF patients [43]. In renal failure, a patient's Ni intoxication and resulting systemic and renal effects could explain the clinical signs observed during early high Ni concentrations, which result in impaired renal filtration. Another report indicated an association with an increased risk of renal injury, systemic inflammation, and anaemia associated with high nickel concentration [44]. Moreover, the physiology of nickel elevation in the circulation may primarily involve generating harmful reactive oxygen species, modifying gene expressions, and modulating or inhibiting metabolic pathways. Elevated Ni also causes direct DNA damage, inhibits repair systems, and prevents methylation [45].

5. Conclusion

In conclusion, our data revealed a significant decline in erythropoietin and vasopressin hormones in RF patients. In addition, selenium levels were also decreased, but nickel levels in the blood were higher in the patient group, which can lead to impaired renal filtration and an increased risk of renal injury.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no competing interests.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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