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The Role of the Hormone Apelin and Some Biochemical Variables in Patients with Kidney Stones

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Abstract

There is a significant correlation between kidney stones, type of food, environment, and the variety of medication taken, as well as genetic conditions, as well as the effect of the level of electrolytes on the formation of stones. This study was conducted in the laboratories of Kirkuk General Hospital and the Public Health Laboratory in Kirkuk Governorate from 1/12/2019 to 1/1/2021. , Where the study included (60) samples of people with kidney stones ranging in age from (30-72) years, the number of men (32) men and the number of women (28) women, as well as (30) blood samples were collected from healthy people, where the number of men was (15) men and the number of women was (15) women, and they were chosen randomly from the residents of Kirkuk governorate.

This study also includes some biochemical variables: levels of the hormone apelin, aldosterone, and measuring the sodium ion (Na^{+}), calcium ion (Ca^{++}), and body mass index. In addition to studying the relationship of ages and studying the number of times the formation of stones and gender, and comparing it to the control group.

There were no significant differences between patients with kidney stones and the control group in their effect on the level of the hormone apelin, the results also showed that there was no significant difference in the levels of apelin in all the studied factors. It was also noted that there was a significant decrease ($p < 0.0001$) in the levels of the hormone aldosterone among the group of patients with kidney stones for the age groups of patients. There is a decrease in the age group (30-49) compared to the age group (50-72). For patients, also a significant decrease ($p < 0.0001$) was found in the levels of the hormone aldosterone among the group of patients with kidney stones who had stones for the first time compared to the group of patients who had stones more than once, while there was no significant increase in patients for the rest of the variables studied in This study, as for calcium, the results showed that there were no significant differences between kidney stone patients and the control group, as well as no significant difference for the rest of the variables studied in this study. As for sodium, there was a significant decrease ($p < 0.0001$) in the blood serum of patients with kidney stones compared to the control group, as well as a significant decrease ($p < 0.0001$) in the blood serum of patients with kidney stones in the age group (50-72) compared with the age group (30). -49), Also, there was a significant decrease ($p < 0.0001$) in the blood serum of kidney stone patients for patients who had stones more than once compared to patients who first formed them. There was no significant difference for the rest of the variables studied in this study.

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1-Introduction

Apelin (APLN), a bioactive neuropeptide derived from 77amino acids[(1)], is an endogenous ligand for APJ receptors(APLNR) [(2)], first acquired from bovine gastric tissue[(3)].The prepeptide of APLN was cleaved and processed by protease to form various derived molecular forms, such as apelin-36, apelin-26, pyr-apelin-13, and apelin-12, and themost active form is apelin-13[(4)]. Apelin is a novel adipocytokine that acts on G protein-coupled receptors (APJ)through APJ signaling[(5)].Receptor protein APJ is an intron-free gene in the codingregion, mainly binding to apelin-13 specificity, and the sequence is similar to the angiotensin receptor type 1 (AT1) gene[(6)]. APJ can be detected in a variety of organs and tissues other than APLN, including the brain, heart, skin, retinal endothelium, adipose tissue, blood vessels, and cardiovascular system. As we all know, the apelin/APJ system plays a key physiological role in cardiovascular action, neovascularization[(8)] , energy metabolism, glucose metabolism, and pain[(9)] and is involved in cardiovasculardisease, metabolic syndrome, and diabetes[(10)]. Evidence suggests that the antioxidant activity of APLN is significant in some areas[(11)].

Kidney stones are mineral concretions in the renal calyces and pelvis that are found free or attached to the renal papillae. By contrast, diffuse renal parenchymal calcification is called nephrocalcinosis[(12)]. Stones that develop in the urinary tract (known as nephrolithiasis or urolithiasis) form when the urine becomes excessively supersaturated with respect to a mineral[(13)], leading to crystal formation, growth, aggregation and retention within the kidneys[(14)]. Globally, approximately 80% of kidney stones are composed of calcium oxalate (CaOx) mixed with calcium phosphate (CaP). Stones composed of uric acid[(15)], struvite and cystine are also common and account for approximately 9%, 10% and 1% of stones, respectively[(16)]. Urine can also become supersaturated with certain relatively insoluble drugs or their metabolites, leading to crystallization in the renal collecting ducts (iatrogenic stones). For example, patients with HIV who are treated with protease inhibitors such as indinavir and atazanavir are at risk for developing nephrolithiasis[(17)]. Both indinavir and atazanavir are metabolized by the liver, with a considerable proportion of the drug excreted in the urine unchanged, leading to their crystallization and the formation of kidney stones[(18)]. Even when given as part of a multiple drug regimen, atazanavir can crystallize in the urine and form kidney stones[(19)].

Aldosterone

It is a steroid hormone that stimulates the renal tubes to retain sodium and water, and thus increases the volume of fluid in the body, which raises blood pressure[(20)]. Many drugs affect blood pressure by affecting aldosterone [(21)]. Aldosterone is part of the renin-angiotensin system, which is a system that helps the body maintain blood pressure. Aldosterone is a steroid hormone secreted by the adrenocortical region [(22)]. Aldosterone activity is decreased in Addison's disease and increased in Conn's syndrome [(23)].

Calcium ion (Ca2 +) is one of the body ions necessary in many life processes, as its regulation includes bone, intestine, kidney, parathormone (PTH), calcitonin (CT), and the active vitamin D3 complex, a hormone-like substance called cholecalciferol, and three types of The cells are osteocytes, osteoclasts, and osteoblasts [(24)].

Sodium (Na +) is the most important component of ECF Extra Cellular Fluid, as it plays a central role in maintaining osmotic pressure [(25)]. And on the normal state of the acid-base balance and water, which is important in the work and activation of tissues that transmit nerve impulses. The concentration of sodium in the blood is regulated by the hormone aldosterone, which is secreted from the adrenal cortex, and increases its absorption by the kidney tubes, and the sodium is excreted through the kidneys and the skin [(26)] .

2-Materials and Methods

Samples

Patients group: This study was conducted in the laboratories of Kirkuk General Hospital and the Public Health Laboratory in Kirkuk Governorate from 12/1/2019 to 1/1/2021, where the study included (60) samples of people with kidney stones whose ages ranged from (30-72) years. The number of men is (32) men and the number of women is (28) women. Pathological cases with kidney stones were confirmed after conducting clinical examinations and referring them to the specialist doctor and conducting an ultrasound examination (sonar).

group control:(30) blood samples were collected from healthy people, where the number of men was (15) men and the number of women was (15) women, and they were randomly selected from the population of Kirkuk governorate.

Collection Of Blood Samples: The blood was drawn from the vein using a needle (syringe) in the size of (ml5) and the blood was placed in a vacuum tube containing GEL (Tube gel), which is free from the anticoagulant substance EDTA, and the blood was left in this tube at room temperature for (30

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minutes) The serum was separated by a Centrifuge at a speed (3000 rpm) for a period of (20 minutes). Then, it was transferred to its plain plastic tube and stored at -20 ºC. The exact questions of the patients and companions were recorded through a special questions form for each patient.
Diagnostic kits (Apelin.Aldosterone) : the manufacture company Bioassay Technology laboratory. Calcium ion the manufacture company Biolabo
Sodium ion in blood serum were directly quantified by the Easylyte Na^+ analyzer based on Ion Selective Electrodes (ISE) technology[27].

3-Results

The study included results for two groups, a control group and a patient group. Where the groups were divided according to age into two groups: (30-49) and (50-72) years, and by gender to Female and Male, in addition to the classification of patients according to body mass BMI into two groups: group (25-29) and group (30) -33), as well as how often the pebbles are once or more than once.

Table (1) show the mean ± standard deviation (SD) of the concentration of apelin in blood serum of both the control group and the patient group. There were no significant differences between patients with kidney stones and the control group in their effect on the level of the hormone apelin, and the results were (55.9345 ± 3.47031), (54.6473 ± 2.896l35 for patients and healthy subjects, respectively, despite the patients' superiority compared to the control group, as noted in Table 1. -3) which shows a comparison of the level of the hormone apelin between the age groups of patients and the control group that there are no significant differences between the male and female patients and the control group and the results for the age group (30-49): (55.748 ± 2.809), (54.244 ± 2.009) for patients and the control group Respectively, as well as the age group (50-72) (56.032 ± 3.348), (3.433 ± 54.875) for patients and the control group, respectively.Also, there were no significant differences in the female patient group compared to the female control group (56.741 ± 3.147), (3.075 ± 54.555) for patients and the control group, respectively, as well as the absence of significant differences in the male patient group compared with the male control group (55.904 ± 3.888). , (3.112 ± 53.904) for patients and the control group respectively, as well as no significant increase in the group of patients whose body mass ranges between (25-29) (50.814 ± 4.830), (2.432 ± 54.622) for patients and the control group, respectivelywith a group of patients whose body mass ranges between(30-33)(59.384 ± 6.498), , (54,576±4.691) for patients and the control group, respectively.Also, there was no significant increase in the morale of patients who had stones more than once compared with the group of patients who had stones for the first time, as the patients who had stones for the first time (56.323 ± 4.107), (2.356 ± 55.323) for the patients and the control group, respectively, and the patients who had stones for the first time. They had stones more than once (53.731 ± 3.153), (55.731 ± 2.532) for the patients and the control group, respectively.

Table (1) levels of the hormone apelin ng / l in the serum of the control group and the patient group depending on age, gender, body mass and number of times stones

Groups		Apelin ng/l	
		Mean ± SD	
		Control	**Patients**
Total		**54.6473±2.896**	**55.9345±3.470**
Age year	**(49-30)**	**54.244±2.009**	**55.748±2.809**
	(72-50)	**±3.43354.875**	**56.032±3.348**
Gender	**Male**	**±3.112 53.904**	**55.904±3.888**
	Female	**±3.07554.555**	**56.741±3.147**
BMI	**(25-29)**	**±2.43254.622**	**50.814±4.830**
	(30-33)	**± 4.69154.576**	**59.384±6.498**
How often	**Once**		**56.323±4.107**
	More than once		**53.731±3.153**
P value			
Total		**0.084**	

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Age year	**(49-30)**	**Patients**	**0.862**
	(72-50)		
	(49-30)	**Control**	**0.921**
	(72-50)		
Gender	**Male**	**Patients**	**0.766**
	Female		
	Male	**Control**	**0.922**
	Female		
BMI	**25-29**	**Patients**	**0.101**
	30-33		
	25-29	**Control**	**0.877**
	30-33		
How often	**Once**	**Patients**	**0.09**
	More than once		

Aldosterone

Table (2) show the mean ± standard deviation (SD) of the concentration of the hormone testosterone in the blood serum of both the control group and the patient group. Where there was a significant increase ($p < 0.0001$) in the levels of the hormone aldosterone among the group of patients with kidney stones compared to the control group, as well as a significant decrease ($p < 0.0001$) in the levels of aldosterone hormone among the group of patients with kidney stones for the age groups of patients where there was a decrease for the group. (30-49) compared with the age group (50-72) of patients, and also a significant decrease ($p < 0.0001$) was found in the levels of the hormone aldosterone among the group of patients with kidney stones who had stones for the first time compared to the group of patients who had stones more One time, while there was no significant increase in patients for the rest of the variables studied in this study.

Table (2) Levels of the hormone aldosterone ng / ml in the serum of the control group and the patient group depending on age, gender, body mass and number of times stones

Groups	**Aldosterone ng/ml**	
	Mean ± SD	
	Control	**Patients**
Total	± 1.72917.267	± 4.35850.183
Age year	**(49-30)**	± 5.193 44.428
	(72-50)	± 5.83558.427
Gender	**Male**	± 4.16950.355
	Female	± 6.35350.215
BMI	**(25-29)**	50.279 ± 6.189
	(30-33)	± 4.60349.985
How often	**Once**	± 3.43942.421
	More than once	± 3.737 59.697
P value		

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	Total		0.00001
Age year	**(49-30)**	**Patients**	0.009
	(72-50)		
Gender	**Male**	**Patients**	0.933
	Female		
BMI	**25-29**	**Patients**	0.860
	30-33		
How often	**Once**	**Patients**	< 0.0001
	More than once		

Calcium ion

Table (3) shows the mean ± standard deviation (SD) of calcium ion in serum of both the control group and the patient group. The absence of significant differences between patients with kidney stones and the control group, as well as the absence of a significant difference for the rest of the variables studied in this study.

Table (3) Calcium ion levels mg / dl in the blood serum of the control group and the patient group depending on age, gender, body mass and number of times stones

	Groups		**Calcium ion mg/dl**	
			Mean ± SD	
			Control	**Patients**
	Total		**± 0.4759.460**	**± 0.4469.403**
	Age year	**(49-30)**		**± 0.387 9.375**
		(72-50)		**± 0.5099.450**
	Gender	**Male**		**± 0.422 9.506**
		Female		**± 0.454 9.335**
	BMI	**(25-29)**		**± 0.402 9.500**
		(30-33)		**± 0.4689.363**
	How often	**Once**		**± 0.478 9.396**
		More than once		**± 0.409 9.419**
		P value		
	Total		**0.580**	
Age year	**(49-30)**	**Patients**	**0.552**	
	(72-50)			
Gender	**Male**	**Patients**	**0.142**	
	Female			
BMI	**25-29**	**Patients**	**0.227**	
	30-33			
How often	**Once**	**Patients**	**0.912**	
	More than once			

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Sodium ion

Table (4) shows the mean ± standard deviation (SD) of the sodium ion in blood serum of both the control group and the patient group. The presence of a significant decrease ($p < 0.0001$) in the blood serum of patients with kidney stones compared to the control group, as well as the presence of a significant decrease ($p < 0.0001$) in the blood serum of patients with kidney stones in the age group (50-72) compared with the age group (30-49).), As well as the presence of a significant decrease ($p < 0.0001$) in the blood serum of patients with kidney stones for patients who had stones more than once compared to patients who formed them for the first time. There was no significant difference for the rest of the variables studied in this study.

Table (4) The levels of sodium ion mEq / L in the blood serum of the control group and the patient group depending on age, gender, body mass and number of times stones

Groups			Sodium ion mEq/L	
			Mean ± SD	
			Control	Patients
Total			± 3.11348143.2933	± 6.62751129.0467
	Age year	(49-30)		± 6.001 139.528
		(72-50)		± 4.130120.891
	Gender	Male		± 6.778 129.671
		Female		± 6.048 128.873
	BMI	(25-29)		± 6.400 130.197
		(30-33)		± 6.753128.556
	How often	Once		± 4.845143.363
		More than once		± 5.350 115.497
	P value			
Total			0.00001	
Age year	(49-30)	Patients	< 0.001	
	(72-50)			
Gender	Male	Patients	0.378	
	Female			
BMI	25-29	Patients	0.126	
	30-33			
How often	Once	Patients	< 0.001	
	More than once			

4- Discussion

These results were consistent with what was indicated by researcher *Yasemin C. Yavuz*and et al 2016[27] ,who did not find any significant differences between the levels of the hormone abelin in the control

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group and the patients ,and contradict the researcher *Hamiyel Y. Yasar* and et al 2018[28]It contrasts with *Hamiyel Y. Yasar*and et al 2018, who found a decrease in the level of the hormone abelin in patients compared to the control group[29].

The results of the current study agree with what was reported by the researcher *Omar Bayomy* and et al his group 2020, and they found an increase in the levels of the hormone aldosterone in kidney patients [30], and the study also agrees with *Wessam Osman et al*his et al 2020 [31]. In promoting the growth of cells that are damaged by the movement of stones [32]. With regard to the increase of the hormone in the age group (50-72) compared to the age group (30-49) for patients, the reason may be attributed to the lack of sodium in the body, so the concentration of the hormone aldosterone increases to preserve sodium and prevent its excretion outside the body [33].Likewise, the level of the hormone aldosterone increased more than once in patients with kidney stones compared to patients who had stones for the first time, and this is consistent with what was reported by the researcher *Giovanni Maria Rossi* 2020 and his et al[34]. As for the rest of the variables that were studied on the hormone aldosterone in this study, they were not significant[33].

The results of the current study agree with what was reported by the researcher *Jing Xie* 2020 and his group [35], and it is believed that the reason for this is due to the high level of uric acid and the low level of magnesium and that the high level of uric acid caused the increase in acidity and the low level of magnesium and citrate, and all these factors contributed to the deposition of calcium on Stone formation and excretion of excess calcium in urine [36].

The results of the current study agree with what was reported by researcher *William G. Herringeton*2018 and his et al[37]. Perhaps the reason for the decrease in the level of sodium ion in the blood serum of kidney stone patients is due to the patients taking diuretics and thus the sodium is excreted outside the body and its level in the blood serum decreases [25], as well as the low level of sodium in the age group (50-72) years compared with the age group (30-50) years. These results are consistent with what was reported by the researcher *Mathilde R. Rivaud* 2020 and his et al[39]The reason for the low level of sodium may be attributed to the deterioration of kidney function, taking diuretics, and some diseases such as hypothyroidism, diabetes, and liver dysfunction [26]. As for the low level of sodium in patients who had stones more than once compared with patients who had stones first Once, this is consistent with what was reported by *Wonngarm Kittanamongolchai* 2018 and his et al[40]. Perhaps the reason for the low level of sodium is due to the deterioration of kidney function, the influence of nephrons, and the excessive use of diuretics [25].

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