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Study of the role some biochemical variables in patients with renal failure

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Abstract
Chronic renal failure (CRF), or chronic kidney disease (CKD), is a common condition that is associated with an abnormal renal function and progressive decline in glomerular filtration rate (GFR). The association of serum apelin with the progression of CKD is unknown. Therefore, this study investigated the association of serum apelin levels with end stage renal disease (ESRD). It aimed at providing additional details on the relationship between apelin hormone and biochemical markers in patients with ESRD (GFR <15 ml/min). This observational study involved 70 patients who gradually progressed to ESRD and 50 healthy as controls. Data were collected from selected dialysis centers within hospitals during a six-month study (December 2023 to May 2024) in Salahaldin Governorate, Iraq. The demographic, clinical, and biochemical data of all participants were recorded. Serum apelin was measured by enzyme-linked immunosorbent assay (ELISA). Blood urea (B-urea), serum creatinine (S-cr), serum uric acid (S-UA), calcium, potassium, sodium, serum albumin (S-alb), total protein (T. Prot) were analyzed using an Automated Biochemical Analyzer. Mean apelin level in patients (161.0± 15.1 pg/mL) was significantly decreased when compared to the healthy subjects (246.4±26.9 pg/mL). Serum apelin levels gradually and significantly declined with decreases in the estimated glomerular filtration rate (eGFR). Serum Apelin showed significant negative correlations with B-urea (r= - 0.441, p <0.001), S-cr (r = - 0,434, p < 0.001), S-alb (r= - 0.305, p < 0.01), potassium (r= - 0.395, p < 0.001), S-UA (r= - 0.293, p = 0.014), significant positive correlations with eGFR (r= 0.465, p < 0.001), calcium (r= 0.389, p < 0.001). This study could be an important step in the right direction for the accurate detection, diagnosis and counseling in ESRD.

Keywords: Apelin, blood urea, creatinine, calcium, albumin, total protein, potassium, sodium, uric acid.

Introduction

Renal failure is a disorder in which the kidneys are unable to control the fluid, electrolyte and remove metabolic waste products from the blood. Acute or chronic illness can lead to kidney failure. Acute renal failure (ARF) develops suddenly, but is often curable with proper diagnosis and care. The ultimate consequence of irreversible kidney damage is CRF. It takes time to mature, usually several years [1]. The frequency and burden of CKD is increasing globally, especially in poorer countries.

According to Ghelichi-Ghojogh *et al*., (2022) [2], the prevalence of CKD (all stages) is expected to be 8-16% globally. This figure could equate to millions of deaths per year. The prevalence of CKD has been identified as a major public health problem worldwide. For example, the prevalence of CKD in the Iranian adult population has been estimated at about 11.68%, and 1.3% of Iranian men and about 2.9% of Iranian women are expected to develop CKD each year [3]. The pathophysiology of CRF may be explained by a series of events that occur abruptly after acute injury in the case of ARF and gradually over time in the case of CKD. AKI can be broadly classified into three categories [4], There are five stages of kidney damage associated with CRF, ranging from minimal to complete failure. People with CKD stage 3 or 4 are believed to have moderate to severe kidney damage. Renal damage with stage 3 is divided into two stages: stage 3A (GFR level of 45-59 ml/min/1.73 m2) and stage 3B (GFR level of 30-44 ml/min/1.73 m2). Furthermore, GFR at stage 4 is of 15–29 ml/min/1.73 m2 according to Kimura *et al*. [5]. The classification scheme is based on the study of Forbes and Gallagher [6]. The Apelin/APJ system has a wide distribution *in vivo*. Apelin is an endogenous peptide. It is the natural ligand for the G protein-coupled receptor APJ [7]. Apelin and the Apelin receptor (APJR) are expressed in the human kidney from the glomerulus to the renal nephron collecting duct. The receptor is strongly localized to the juxtaglomerular apparatus involved in the control of systemic blood pressure. In models of renal disease, ligand expression is downregulated, but the receptor is unaffected [8]. Apelin peptide activation of the APJR has diverse physiological consequences, including vasodilation, enhanced cardiac contractility, angiogenesis, fluid balance, and regulation of energy metabolism [9]. Murali and Aradhyam (2023) [10] state that the APJR is important for maintaining fluid homeostasis, controlling blood pressure, and increasing cardiac output. In addition, it is effective in treating neurological, metabolic, respiratory, gastrointestinal, liver, kidney and malignant diseases. In the human kidney, Apelin and APJR are expressed from the glomerulus to the collecting duct of the renal nephron, and the receptor is strongly localized to the juxtaglomerular apparatus that regulates systemic blood pressure. Importantly, ligand expression is downregulated in a renal disease model, whereas receptors are unaffected [8]. Studies have shown that the high levels ofApelin are expressed in the inner stripe of the outer medulla oblongata of the kidney, which is important in the process of maintaining a healthy salt-water balance. Further studies support the idea that the Apelin/APJ system influences various renal functions. The apelin/APJ system can reduce renal interstitial fibrosis by reducing extracellular matrix accumulation. The Apelin/APJ system dramatically reduces renal ischemia/ reperfusion injury by preventing renal cell death. Furthermore, the course of polycystic kidney disease is predicted by the Apelin/APJ system. The Apelin/APJ system protects hemodialysis patients from various dialysis problems. In addition, the Apelin/APJ system reduces vascular calcification and thus the symptoms of CKD; therefore, the Apelin/APJ system has multiple functions in kidney disease and is a potential therapeutic target [11].

Despite the extensive research on Apelin, there is a limited number of researches on the renal Apelin system, especially in Iraq. Therefore, the aim of this study is to Investigate the relationship between serum Apelin levels and CRF and Provide additional details on the relationship between apelin hormone and biochemical markers (B-urea, S-cr, S-UA, calcium, potassium, S-alb, in patients with CRF (GFR <15 ml/min) in Salah Al-Din province, Iraq.

Materials and Methods

Subjects and Study Design

The study included 50 healthy participants and 70 patients with ESRD with eGFR less than 15 mL/min/1.73 m2 before or during dialysis. Patients were classified as having stage 5 CKD based on renal function according to Kidney Disease Outcomes/Quality Initiative criteria. The patient group, which included 26 females and 44 males with ages ranging from 13 to 79 years, was compared to 50 healthy participants. GFR, which appeared to be normal (eGFR ≥111.6 mL/min), was chosen at random from the control group, which included 27 females and 23 males, with ages ranging from 30 to 76 years. Data were collected from selected dialysis centers within hospitals during a six-month study (December 2023 to May 2024) in Salahaldin Governorate, Iraq. Patients who were available at the time of the interview were intentionally selected. After obtaining informed consent from the patients, a pre-test questionnaire was filled out with information regarding the patient's general and family history, presence of certain diseases, medication history, and readily available records. Patients admitted to non-dialysis units and patients with an undisclosed history of CKD or with normal renal function tests were selected as control subjects. Subject demographic and clinical data were obtained from medical records and questionnaire (e.g., gender, age, history of hypertension) and physical examinations (e.g., height, weight, blood pressure).

Blood Samples

Blood samples were taken from a peripheral vein after an overnight fast prior to dialysis. The samples were centrifuged at 3500 rpm for 10 minutes and left at room temperature for approximately 1 hour before serum separation. Serum Apelin was measured by enzyme-linked immunosorbent assay (ELISA). Kit Thermo Fisher Scientific Inc Austria.

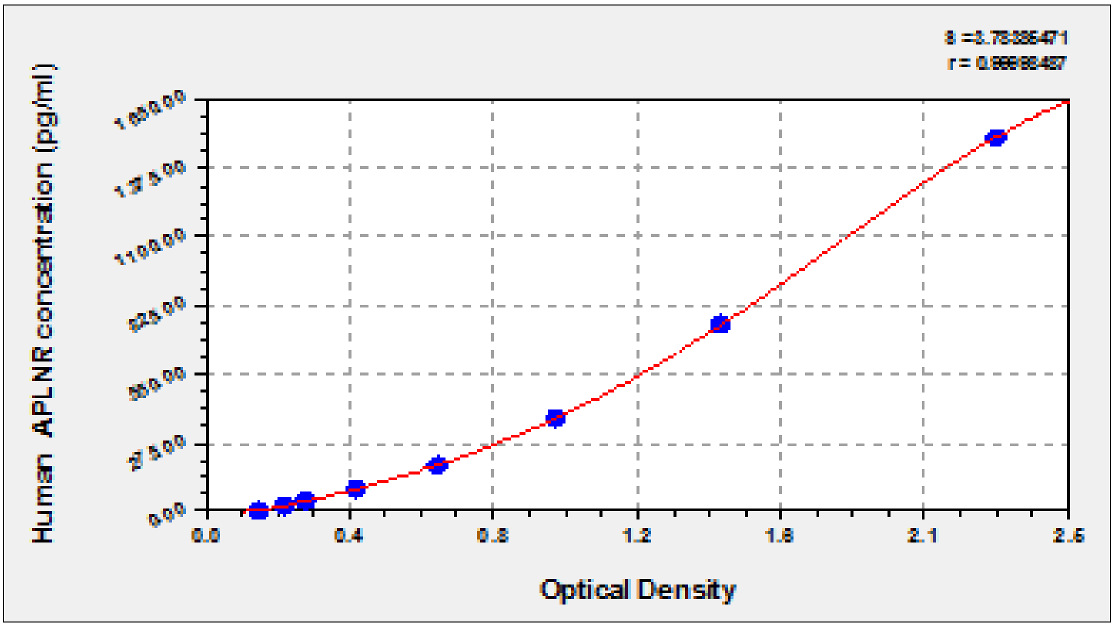

Fig 1: Calibration curve of serum Apelin was measured by enzyme-linked immunosorbent assay (ELISA)

B-urea, S-cr, S-UA, Ca+2, Na+2, K+, S-alb, T. Prot, were analyzed using an Automated Biochemical Analyzer (Dialab Autolyser) and a spectrophotometer (model 721). Various biochemical variables were measured to find the statistically significant correlations between the concentrations of the biochemical variables and the concentrations of apelin.

Statistical Analysis

Data were analyzed under the software spss version 19 on the test which applied is anova test and the means were compared by Duncan's multiple range test under the level of significantly 0.05.

Results

Results of Apelin Levels According to Age Groups (Patients & Control)

The study groups were divided into three subgroups according to their age including under or equal to 40, 41–55, and over 55 years. In Table 1 human serum Apelin display graduall decline with increasing age in patients and controls. Similar letters mean that there are no significant differences (p> 0.05). Different letters mean that there are significant differences between them (p< 0.05). Where the letter (a) means the highest significant differences mean, the letter (b) is the lowest significant differences mean, and the letter (c) is the lowest significant differences of a and b. M: male, F: female, St. Dev: Standard deviation, N: Number of patients, C.I: Confidence Interval for the difference between Means.

Table 1: Results of serum Apelin in the patients group and the control group depending on age groups

Apelin	Age	N	Mean	St. Dev	95% CI
Patient group	≤ 40	26	165.3 c	32.8	(128.8, 201.7)
	41-55	23	161.9 c	32.5	(123.1, 200.6)
	>55	21	153.2 c	30.7	(112.7, 193.8)
Control group	≤ 40	20	274.5 a	34.2	(232.9, 316.0)
	41-55	19	245.7 ab	31.9	(203.1, 288.3)
	>55	11	196.4 b	36.1	(140.4, 252.4)
F-Value = 5.91, P-Value = 0.01 St. Dev: Standard deviation, SE: Standard error					

Results of Apelin Levels According to Gender

The results were classified into two categories according to gender as male and female in the patients and control groups. The male-to-female ratio was 44:26 for patients and 23:27 for controls.

In Table 2, serum Apelin concentrations were higher in males than in females pg/mL; P >0.05) in patients group and in control group. In addition, when comparing male and female in the patient group, there was no significant difference, as well as in the control group (p>0.05), but there was a significant difference when comparing male in the patient group with the male in the control group, and the same results with the comparing of female (p<0.05).

Table 2: Results of serum Apelin in the patients group and the control group depending on gender

Apelin	Gender	N	Mean	St. Dev	95% CI
Patient grop	M	44	169.0 b	31.1	(140.8, 197.2)
	F	26	146.2 b	35.5	(109.5, 182.9)
Control group	M	23	258.2 a	31.2	(219.2, 297.2)
	F	27	236.3 a	37.5	(200.30, 272.23)
F-Value = 8.59, P-Value = 0.01					

Results of Blood Urea and Serum Creatinine Levels in patients with renal failure and the control group

As shown in Tables 3, the results found that B-urea and S-cr levels were significantly higher in the patients group than in the control group (p=0.0008 and p=0.0007, respectively).

Table 3: Results of Blood Urea and Serum Creatinine Levels in patients with renal failure and the control group

Study groups	Mean ± SD	
	Blood Urea	Serum creatinine
Patient group	178.6 ±50.0	9.15±2.860
Control group	28.2 ±5.45	0.778±0.156
P. value	0.0008	0.0007

Results of Electrolyte Levels in patients with renal failure and the control group

As shown in Tables 4, the results found that sodium levels were significantly lower in the patients group than in the control group (p=0.0002). Potassium levels were significantly higher in the patients group than in the control group p=0.0007. The results found that S-alb levels were significantly lower in the patient group than in the control group and the total protein levels were significantly higher in the patient group than in the control group (p=0.0008).

Table 4: Results of Electrolyte Levels in patients with renal failure and the control group

Study groups	Mean ± SD					
	Serum sodium	Serum K	Albumin	Total protein	Uric acid	Calicum
Patient group	134.10 ±9.63	5.321 ±0.725	3.710±0.628	6.892±0.747	7.01±1.99	1.95 ±0.892
Control group	140.03 ±5.07	4.309±0.727	4.076±0.479	6.610±0.660	4.34 ±1.21	8.62 ±0.614
P. value	0.0002	0.0004	0.0007	0.0008	0.0008	0.0004

Results of eGFR levels and their relationship to Apelin levels

As shown in Table 5, the results found that eGFR was lower in the patient group than in the control group (p= 0.00001).

Table 5: Results of eGFR levels in the patient group and the control group

Study groups	Mean ± SD
	eGFR
Patient group	7.41 ±3.17
Control group	113.4 ±16.0
P. value	0.00001

Table 6: The R-values and P-values of correlations among the Apelin and study variables in control group

Variables	B.Urea	S.Creat	eGFR	S.UA	Calicum	Alb	T.Prot	Sodium	Potassium
S.Creat	0.653 0.000								
eGFR	-0.566 0.000	-0.740 0.000							
S.UA	0.267 0.025	0.335 0.005	0.284 0.017						
Ca	-0.517 0.000	-0.615 0.000	0.543 0.000	0.321 0.007					
Alb	0.116 0.338	0.145 0.233	-0.198 0.101	-0.038 0.754	-0.146 0.227				
Sodium	-0.322 0.007	-0.522 0.000	0.399 0.001	-0.022 0.856	0.417 0.000	-0.038 0.752	0.023 0.852		
Potassium	0.374 0.001	0.552 0.000	-0.535 0.000	0.052 0.670	-0.334 0.005	0.309 0.009	0.264 0.027	-0.281 0.018	
Apelin	-0.441 0.000	-0.434 0.000	0.465 0.000	-0.293 0.014	0.389 0.001	-0.305 0.010	-0.109 0.367	0.177 0.142	-0.395 0.001

Discussion

Therefore, Apelin might be a biomarker for the risk of worsening renal function. This result was consistent with other results which showed that Apelin concentrations were significantly reduced in patients with renal disease when compared to controls [12].

These results also agreed with those found by Doğan *et al*., (2018) [13] who reported that the group of peritoneal dialysis patients had lower levels of Apelinthan the control group, but the difference was not statistically significant. Other results indicated that the Apelin and APJ expression in skeletal muscle was transiently elevated during early stages of CKD and then decreased during later stages. The results obtained were classified into three groups according to the age category, (≤40 years), (41–55 years), and (>55 years) groups. Gender groups were divided into female and male categories. The male to female ratio within the study group was 67:53. In general, the results revealed that men aged 55 years and older were most affected by renal dysfunction. Amin and his colleagues also noted that CKD affects men more frequently than women. CKD most severely affects people between 40 and 60 years [14]. Karadag *et al*., (2014) [15] found an inverse relationship between age and the Apelin levels in peritoneal dialysis patients. Age and gender effects were common and have been demonstrated to interact frequently. The Apelin levels tended to decline more gradually in women than in men, although both men and women tended to do so. Apelin and age were shown to be negatively correlated [13]. Jawad *et al*., (2017) [1] found that the risk of kidney failure increases with age in both men and women. The results revealed that the B-urea and S-cr levels were significantly higher in the patients group than in the control group.

As kidney function declines, a metabolic byproduct called urea can also accumulate. Liu and his team's study found that urea levels were significantly elevated in both men and women and were influenced by age and gender [16]. As a result, urea concentration measurements are combined with S-cr concentration measurements to estimate renal function. The elevated S-cr levels are a symptom of kidney disease or decreased kidney function. If the kidneys are damaged for any reason, the blood level of S-cr increases because the kidneys cannot remove S-cr properly. Abnormally high S-cr levels therefore serve as a warning sign of potential renal damage or failure [17]. Similar to this, Amin *et al*., (2014) [14] observed that predialysis B-urea and S-cr levels were significantly higher than the normal range in the CKD patients. The current study results showed that serum Apelin showed significant negative correlations with B-urea ($r = -0.441$, $p < 0.0001$) and S-cr ($r = -0.434$, $p < 0.0001$), The current results are consistent with those found by Humaish *et al*. (2016) (18) who investigated the relationship between the Apelin levels and the B-urea and S-cr levels. The predominant extracellular cation is sodium, although the kidneys maintain control of retained sodium in the body, with excess excreted in the urine and finely controlled by tubular reabsorption. After initial glomerular filtration, approximately 60% of the filtered sodium and bicarbonate were recovered in the proximal tubules. The small amount of about 25% of it was reabsorbed with chloride in the henle loop of the renal tubules and the remaining 75% was reabsorbed in the distal tubules where it competed with potassium and hydrogen ions for absorption under the control of aldosterone [17].

The major intracellular cation is potassium. In exchange for potassium, sodium that has diffused into the cell is vigorously excreted. In addition to its function in intracellular osmolarity, potassium is also required for several enzymatic processes, myocardial regulation, and transmission of nerve impulses. The most reliable electrolyte indicator of renal failure is serum potassium. In renal failure, plasma potassium increases due to a combination of decreased filtration and decreased potassium production in the distal tubules. The most serious and fatal side effect of renal failure is hyperkalemia [17]. In this study, 120 blood samples from the ESRD patients diagnosed with renal dysfunction were examined and a good record of electrolytes, including sodium and potassium, was examined., the results revealed that sodium levels were significantly lower and potassium levels were significantly higher in the patients group than in the control group. The above results were consistent with those found by El-Ishaq *et al*., (2021) [17]. The most common electrolyte problem is hyponatremia. Dilution disease is a category of illness classified together with hyponatremia. Major causes of dilutional disease include renal failure, syndrome of inappropriate antidiuretic hormone secretion, and other reasons. Hyponatremia results from inadequate excretion of water from the glomeruli due to the decreased glomerular filtration rate (renal failure). This means that the body cannot excrete the ingested water. However, this often happens when the filtration rate drops significantly to 20-

30% of the normal rate. CRF with variable urine output was another obvious cause of potassium imbalance. Decreased potassium excretion in patients with CRF was the main cause of hyperkalemia [19]. GFR is an important factor in assessing renal function. This test measures the amount of S-cr in the blood and calculates a renal function score to determine how well the kidneys are functioning. eGFR is primarily used in clinical settings to assess renal function. Participants are considered to have ESRD using the eGFR calculation if their GFR is less than 15 ml/min [20].

The results showed that eGFR was lower in the patients group than in the control group (p= 0.00001). A strong risk factor for the development of ESRD and progression of renal disease includes decreased eGFR [21]. The mean Apelin level was significantly positively correlated with the levels of eGFR. These results are similar to those of earlier studies [22]. S-alb is the protein that is most prevalent in plasma, accounts for about half of the T-Prot composition of serum. It frequently serves as a clinical biomarker. Majoni *et al*., (2020) [23] demonstrated that an albumin level was associated with yearly decreases in eGFR and renal outcome. Another study found that lower renal function in older adults was independently and significantly correlated with lower S-alb levels (Lang *et al*., 2018) [24]. The kidneys play an important role in the control of the S.UA levels. Kidney function can be affected by abnormal uric acid levels. When uric acid levels in the blood reach pathological levels, renal tubules are damaged and can lead to oxidative stress, endothelial dysfunction and intrarenal inflammation (Wang *et al*., 2022) [25]. According to a study by Joo *et al*., (2020) [26], there was a substantial negative correlation between the high S.UA levels and renal function in the Korean population, suggesting that the S.UA levels may be involved in the development of kidney disease. The current study showed that the serum calcium levels were significantly lower in the patients group than in the control group. Major alterations in CKD include calcium, phosphate, PTH, and Vit.D hormonal systems. Mostly occurs in severe CKD, especially in ESRD (Cannata-Andía *et al*., 2021) [27].

Conclusion

Chronic kidney disease is a leading cause of morbidity and mortality worldwide. CKD may result in the need for dialysis or a kidney transplant. To provide further information on the relationship between the hormone apelin and biochemical markers in patients with ESRD, the association of the serum Apelin levels with this condition was investigated in this study. This observational study included 50 healthy controls and 70 patients with progressive ESRD. Data were collected from a specific hospital dialysis clinic during a 6-month study period.

This study demonstrated that apelin is decreased in ESRD and may serve as a biomarker for possible deterioration of renal function. In general, the results revealed that Apelin levels were the lowest (lower in women than in men) and age ≥55 years had the most adverse effect on both men and women with respect to renal impairment. This required government intervention to address the social causes of kidney failure. B-urea, S.cr, potassium, T-Prot, and S.UA were all significantly higher in the ESRD patients, whereas the S.alb, sodium, calcium, and Vit.D levels were significantly lower. Therefore, this study may be an important step towards reliable detection, diagnosis and counseling of ESRD. The ESRD patients are more likely to have dyslipidemia than healthy people. Therefore, it is important to examine the lipid profile of the ESRD patients.

Significant negative correlations were found between serum Apelin and B-urea, S.cr, S.alb, potassium and S.UA. İn addition, there were positive correlations between Apelin and eGFR, Vit.D, and calcium. These findings indicate that Apelin levels may be a useful diagnostic or predictive factor in determining the severity and onset of CKD. However, further studies are needed to precisely clarify this relationship.

Ethical Approval: This study was conducted under ethical approval from the Ethical Committee at the College of Medicine / Tikrit University No. 78/241 dated 22/12/2023. The consent of the participants/guardians was obtained before enrolling in the study and drawing blood samples from patients.

References

1. Jawad AK, Okab AA. Assessment of Risk Factors among Renal Failure Patients in Baghdad Teaching Hospital. Iraqi National Journal of Nursing Specialties, 2017, 30(2).
2. Ghelichi-Ghojogh M, Fararouei M, Seif M, Pakfetrat M. Chronic kidney disease and its health-related factors: a case-control study. BMC Nephrology,2022:23(1):1-7.
3. Moazzeni SS, Arani RH, Hasheminia M, Tohidi M, Azizi F, Hadaegh F. High incidence of chronic kidney disease among Iranian diabetic adults: using CKD-EPI and MDRD equations for estimated glomerular filtration rate. Diabetes & Metabolism Journal,2021:45(5):684-97.
4. Hu G, Wang Z, Zhang R, Sun W, Chen X. The role of apelin/apelin receptor in energy metabolism and water homeostasis: a comprehensive narrative review. Frontiers in Physiology,2021:12:632886.
5. Kimura K, Hosoya T, Uchida S, Inaba M, Makino H, Maruyama S, *et al*. Febuxostat therapy for patients with stage 3 CKD and asymptomatic hyperuricemia: a randomized trial. American Journal of Kidney Diseases,2018:72(6):798-810.
6. Forbes A, Gallagher H. Chronic kidney disease in adults: assessment and management. Clinical Medicine,2020:20(2):128.
7. Zhang Y, Jiang W, Sun W, Guo W, Xia B, Shen X, *et al*. Neuroprotective Roles of Apelin-13 in Neurological Diseases. Neurochemical Research,2023:1-15.
8. Nyimanu D, Chapman FA, Gallacher PJ, Kuc RE, Williams TL, Newby DE, *et al*. Apelin is expressed throughout the human kidney, is elevated in chronic kidney disease & associates independently with decline in kidney function. British Journal of Clinical Pharmacology,2022:88(12):5295-306.
9. Kuba K, Sato T, Imai Y, Yamaguchi T. Apelin and Elabela/Toddler: double ligands for APJ/Apelin receptor in heart development, physiology, and pathology. Peptides,2019:111:62-70.
10. Murali S, Aradhyam GK. Structure–function relationship and physiological role of apelin and its G protein coupled receptor. Biophysical Reviews,2023:1-17.

11. Huang Z, Wu L, Chen L. Apelin/APJ system: a novel potential therapy target for kidney disease. Journal of Cellular Physiology,2018:233(5):3892-900.
12. Mahmood IS, Sarhat ER. Effects of chronic renal failure and hemodialysis on serum levels of apelin and ghrelin. Biochemical & Cellular Archives,2022:22(1).
13. Doğan İ, Kahvecioglu S, Eser B, Kayadibi H, Yayar O, Doğan T, *et al*. Significance of apelin-13 for inflammation and cardiac morphology in peritoneal dialysis patients. Turkish Nephrology Dialysis and Transplantation Journal,2018:27(2).
14. Amin N, Mahmood RT, Asad MJ, Zafar M, Raja AM. Evaluating urea and creatinine levels in chronic renal failure pre and post dialysis: a prospective study. Journal of Cardiovascular Disease,2014:2(2):1-4.
15. Karadag S, Ozturk S, Gursu M, Gurdal A, Basinoglu F, Yigit S, *et al*. The relationship between apelin and cardiac parameters in patients on peritoneal dialysis: is there a new cardiac marker? BMC Nephrology,2014:15(1):1-7.
16. Liu Q, Wang Y, Chen Z, Guo X, Lv Y. Age- and sex-specific reference intervals for blood urea nitrogen in Chinese general population. Scientific Reports,2021:11(1):10058.
17. El-Ishaq A, Garba AM, Emanuel DD. Assessment of Electrolytes, Urea and Creatinine in Patients with Renal Impairment Attending Yobe State Specialist Hospital Damaturu. Sumerianz Journal of Medical and Healthcare,2021:4(2):114-22.
18. Humaish MJ, AL-Samarrai AMH, AL-Samarrai NI. Study the relationship between apelin and some biochemical parameters in patients with kidney diseases. Tikrit Journal of Pure Science,2016:21(7):110-8.
19. Zsom L, Zsom M, Salim SA, Fülöp T. Estimated glomerular filtration rate in chronic kidney disease: a critical review of estimate-based predictions of individual outcomes in kidney disease. Toxins,2022:14(2):127.
20. Ammirati AL. Chronic kidney disease. Revista da Associação Médica Brasileira,2020:66:s03-9.
21. Cheng T, Wang X, Han Y, Hao J, Hu H, Hao L. The level of serum albumin is associated with renal prognosis and renal function decline in patients with chronic kidney disease. BMC Nephrology,2023:24(1):1-17.
22. Dawood A, Abdelraof M, El Ghobashy Y. The relationship between serum apelin level and different grades of diabetic nephropathy in type 2 diabetic patients. Egyptian Journal of Obesity, Diabetes and Endocrinology,2017:3(1):32.
23. Majoni SW, Barzi F, Hoy W, MacIsaac RJ, Cass A, Maple-Brown L, *et al*. Baseline liver function tests and full blood count indices and their association with progression of chronic kidney disease and renal outcomes in Aboriginal and Torres Strait Islander people: the eGFR follow-up study. BMC Nephrology,2020:21:1-10.
24. Lang J, Katz R, Ix JH, Gutierrez OM, Peralta CA, Parikh CR, *et al*. Association of serum albumin levels with kidney function decline and incident chronic kidney disease in elders. Nephrology Dialysis Transplantation,2018:33(6):986-92.
25. Wang M, Lin X, Yang X, Yang Y. Research progress on related mechanisms of uric acid activating NLRP3 inflammasome in chronic kidney disease. Renal Failure,2022:44(1):615-24.
26. Joo HJ, Kim GR, Choi DW, Joo JH, Park EC. Uric acid level and kidney function: A cross-sectional study of the Korean national health and nutrition examination survey (2016–2017). Scientific Reports,2020:10(1):1-11.
27. Cannata-Andía JB, Martín-Carro B, Martín-Vírgala J, Rodríguez-Carrio J, Bande-Fernández JJ, Alonso-Montes C, *et al*. Chronic kidney disease—mineral and bone disorders: pathogenesis and management. Calcified Tissue International,2021:108:410-22.