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Original Article

The Prognostic Role of Apelin in the Assessment of Cardiac Outcomes in Patients with Chronic Kidney Disease: A Case-Control Study

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Abstract *- Chronic kidney disease is a complicated, multifaceted disorder with multiple complications. Limited studies have assessed the potential role of Apelin in the assessment of cardiac outcomes in patients with chronic kidney disease. Herein, we performed a prospective case-control study including 70 patients with CKD. Patients on chronic dialysis were excluded. Laboratory examinations, including serum Apelin levels, were performed. Moreover, the patients were monitored for 18 months. The mean value of apelin was lower in CKD patients than in the control group (378.86 pg/ml compared to 663.93 pg/ml, p<0.0001). Cardiovascular complications were more frequent in CKD patients than in the control group (38.6% as compared to 6.7%, respectively, p=0.017). Furthermore, serum apelin levels were lower in patients with CVD complications (317.3 ± 73.9 pg/ml, compared to 417.5 ±51.3 pg/ml, p<0.001). Multivariate regression analysis revealed that only Apelin levels were a significant predictor of CVD complications with a negative correlation (Odds ratio 0.96, 95%CI [0.95-0.99], p=0.001) Subsequently, we found that only apelin had a significant correlation with the occurrence of cardiovascular complications in patients with CKD. The lower the levels of apelin, the higher the incidence of cardiovascular complications.*

Keywords *- Apelin, Chronic Kidney Disease, Cardiovascular disease, Prognosis.*

1. Introduction

Chronic kidney disease (CKD) is a complicated and multifaceted disease. It causes disruption in renal function and progression toward end-stage kidney disease (ESKD). Furthermore, patients with CKD frequently have cardiovascular disease (CVD), and worsening of renal function has been associated with CVD progression [1]

Even though CKD is a public health concern that imposes a massive clinical and economic liability due to its complications, awareness of it is very low. Only 6% of the general population knows its risk, and 10% of the population at high risk are aware of their CKD status [1]. Additionally, CKD patients screening and detection in primary care centers is subpar, as it falls between 6-50% of the cases, and it depends on the speciality of the primary care, stage of the disease, and experience [1]

ESKD patients' mortality rate is notably higher compared to the general population. The main cause of this disparity is CVDs, which are responsible for 40-60% of these deaths [2].

Cardiovascular complications are common comorbidities that might worsen during the progression of renal dysfunction. This is due to the alignment of multiple risk factors, including the accumulation of nitrogenous waste products, disruption of lipid metabolism, disruption of vasodilation and vasoconstriction mechanisms, and direct damage of the cardiomyocytes. Furthermore, conventional risk factors such as hypertension, diabetes, and lower physical activity. Arteriosclerosis is frequently observed in patients with CKD in addition to other risk factors that are specifically associated with CKD, such as anemia, malnutrition, proteinuria, hyperparathyroidism, water and electrolytes retention, and lastly, the accumulation of some substances such as homocysteine [3].

Left ventricular hypertrophy (LVH) is one of the main cardiac complications of CKD. It is mostly seen in peritoneal dialysis patients and represents a major cause of heart failure and sudden cardiac arrest [2 - 4]. Up to 40% of patients with ESKD develop congestive heart failure that results from diastolic dysfunction [4].

Due to the high prevalence of CKD and its late diagnosis due to the silent clinical presentation, and because of the lack of screening tools, serious complications may develop, mainly cardiovascular complications. This happens before a detectable increase in typical alarming biomarkers occurs (creatinine - lipid profile - hypertension), which highlights the necessity to search for new biomarkers with high specificity to predict CVD progression in the context of CKD.

Numerous laboratory markers were suggested for the screening of CVD in the context of CKD progression, including the Apelin. It is a peptide with recently explained pathophysiological effects. It was described in 1998 as a selective APJ internal ligand [5 -6]. APJ is a G-coupled membrane receptor that has a close homology with the angiotensin receptor 1 (AT-1), although Apelin and angiotensin do not share their receptors [7]. APJ receptors were discovered in the endothelial cells of cardiac, renal, pulmonary, and coronary arteries in addition to the smooth muscle cells of vascular walls [8]. Pre-Apelin is mainly secreted by the central nervous system, kidneys, heart, lungs, and adipose tissue [9].

Apelin has a major role in the physiology of cardiac and vascular functions. It serves as a vasodilator and thus reduces blood pressure [10]. However, Apelin may cause vasoconstriction in dysfunctional endothelium [11]. It also has a positive inotropic effect on myocardial contractility [12]. Additionally, Apelin inhibits ADH secretion [13], and it acts as a vasodilator of afferent and efferent arterioles in the glomerulus of the kidney [14-15-16].

Moreover, calcium and phosphate disorders, in addition to arterial calcification, play a major role in the development of cardiovascular diseases in CKD patients. A study suggested that Apelin might prevent the calcification of arteries through the inhibition of osteo-differentiation of the smooth muscle cells, which is the first step in vascular wall calcification [17]. Furthermore, there is little data on Apelin's role in CVD risk in patients with CKD. Therefore, we aimed in our study to assess the role of serum apelin as a predictor of CVD progression in patients with CKD.

2. Methods

Ethical approval was provided by the ethical committee of Tishreen University Hospital (TUH) on 5th January 2019. Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-In-Chief of this journal on request. This study was carried out in accordance with the Declaration of Helsinki.

We performed a prospective case-control study. The subjects of the sample were obtained from the Department of Nephrology at Tishreen University. The sample size was 70 patients with CKD (stages 2,3,4). All were classified based on GFR (Stage 2 with GFR between 60-89 l/min, stage 3a with GFR between 45-59 l/min, stage 3b with GFR of 30-44 l/min, and stage 4 with GFR between 15-29 l/min). We included 15 healthy controls from the outpatient clinic of the University Hospital to be the control group. The inclusion criteria were age > 17 years and confirmed diagnosis of CKD (stages 2 to 4). Exclusion criteria included chronic dialysis, pregnancy, patients suffering from cancer, and autoimmune diseases. Written informed consent was obtained from all patients and controls.

Data regarding the renal and cardiac status of CKD patients, in addition to the GFR results, were obtained from patient records from the Department of Nephrology of Tishreen University at the beginning of the study. Body height, weight, and body mass index (BMI) were measured. Three blood pressure measurements were taken by an experienced nurse according to standard protocols while the patient was seated and after having at least 5 minutes of rest. A questionnaire was handed out that included the name, gender, and past medical history. It also included if the patients had a cardiac disease before the development of CKD or throughout the progression of CKD. Participants were asked if they were previously diagnosed or if their doctor or any other medical specialist informed them of having coronary artery disease (heart attack, angina, heart failure, coronary bypass surgery, or any other interventions). Then, the patients were examined by a cardiologist, followed by complementary tests such as ECG and echocardiogram. The same was applied to the control group. The questionnaire also included whether the patients were taking any medication. The cause of kidney disease and the family/genetic history were also collected.

The blood samples were obtained from the patients in the laboratory of Tishreen University after 10 hours fasting period. Later, blood examinations for triglycerides, cholesterol, and fasting blood glucose were performed. After that, the plasma samples were stored at -80 Celsius until the blood Apelin test was done. Before conducting the Apelin blood test, the samples were taken out of the refrigerator and left at room temperature before commencing the test that follows the competitive enzyme immunoassay method. Apelin Lab-Kit: Shanghai Biological (China Cat.No: YHB0362Hu) was used with a reference range for measurement of [Assay Range: 10pg/ml-4000pg/ml]

The patients were followed for 18 months, starting from 25th July 2021 to 12th December 2022. They were continually observed with cardiovascular examinations by cardiologists of Tishreen University in addition to having their general and renal functions checked during weekly visits. The study was conducted according to the STROCSS guidelines [18], and ethical approval was obtained in accordance with the Helsinki declaration.

Statistical analysis was performed using IBM SPSS V22 (IBM Corporation, Armonk, NY, USA). Data are expressed as percentages for categorical variables and as mean ± standard deviation (SD) or median ± interquartile range (IQR) for continuous variables. Continuous variables were compared using Students T and Mann Whitney U tests as appropriate. Differences between multiple groups with a normal distribution were compared by one-way ANOVA. Within-group differences were analyzed using repeated measures ANOVA or paired t-test. If no normal distribution was found, ANOVA on ranks (Kruskal-Wallis) was performed, and the Wilcoxon signed-rank test was used for within-group comparisons. Comparisons of categorical variables between groups were performed by Pearson's X^2 test for expected frequencies <5 by Fisher's exact test. Furthermore, a logistic regression analysis was performed to look for independent predictors of cardiovascular complications in patients with CKD. A p-value of <0.05 was considered to be significant.

3. Results

The study included 85 participants that were classified as follows: 12 patients (14.12%) with CKD stage2, 20 patients (23.53%) with CKD stage 3a, 16 patients (18.82%) with CKD stage 3b, 22 patients (25.88%) with CKD stage 25.88%, and 15 healthy participants (17.65%) as the control group. Out of the patients group (n=70), there were 43 males (61.43%) and 27 females (38.57%) with an approximate male-to-female ratio of 2:1. In the control group (n=15), there were 8 males (53.33%) and 7 females (46.67%).

In Table 1 depicts comparisons between the studied variables among CKD patients and the control group. We found that the average GFR was lower in CKD patients than in the control group, being 42.06 ml/min/1.73 m^2 compared to 122.4 ml/min/1.73 $m^{2,}$ respectively (p<0.0001). We also found that the average Apelin values were lower in CKD patients than in the control group, being 378.86 compared to 663.93 (p<0.0001). On the other hand, the average systolic and diastolic blood pressures were higher in CKD patients than that of the control group. The distribution of age, height, weight, cholesterol and triglyceride levels didn't differ between the study and control group (statistical significance higher than 5%) (Table1).

Table 1. Comparisons between the studied variables among CKD patients and the control group

	Control(N=15)				CDK (N=70)				
	Mean	SD	Min	Max	Mean	SD	Min	Max	p-value
Age	53.27	8.11	42	70	53.80	10.18	17	80	0.8497
Height	165.13	6.09	155	175	163.87	6.49	152	177	0.4921
Weight	87.20	14.05	60	110	84.54	14.19	60	125	0.5116
BMI, kg/m2	31.83	3.81	24.34	38.97	31.39	4.22	22.3	39.92	0.7074
GFR ml /min / 1.73 m2	122.40	2.44	120	126	42.06	18.83	15	82	<0.0001
DBP	79.27	9.29	68	95	83.14	5.82	70	95	0.0402
SBP	120.20	7.64	110	135	128.17	5.24	120	145	<0.0001
Cholesterol	172.00	30.21	100	215	188.20	32.50	135	300	0.08
TG	137.60	26.18	100	199	142.69	20.68	110	250	0.4126
Ngal ng/ml	70.13	77.49	46	350	293.36	174.76	106	600	<0.0001
Smda mg/dl	9.80	6.00	5	30	48.80	60.63	16	540	0.0153
Apline	663.93	157.5	400	1000	378.86	77.93	240	550	<0.0001

Table 2 depicts CVD complications among the participants of this research. CVD incidence rate was higher among CKD patients than that of the control group (nearly 39% compared to approximately 7%, and this difference was statistically significant p=0.017).

Also, myocardial infarction (MI) and LVH were the most common CVD complications among CKD patients. Also depicts CVD distribution according to the stage of CKD. We noticed an increased incidence rate of CVDs along the progression of CKD.

Table 3 depicts the related factors to CVD occurrence in CKD patients. We noticed a significant statistical correlation between GFR, systolic and diastolic BP, cholesterol and Apelin from one side and CVD in CKD patients on the other side.

Systolic and diastolic BP, cholesterol and triglyceride levels were higher in CKD patients who developed CVD complications than in CKD patients who didn't develop any CVD complications.

Table 2. CVD complications among the participants

		Control(N=15)		CDK (N=70)		
		n	%	n	%	
Cardiac complication	No	14	93.33	43	61.43	p-value 0.017
	Yes	1	6.67	27	38.57	
Type of Cardiac complication	Myocardial infarction	1		11		
	LVH	0		10		
	Atrial fibrillation	0		1		
	Cardiac Failure	0		3		
	CVA	0		3		
	angina pectoris	0		4		
	Aggravation	0		2		

CVD distribution according to the stage of CKD	N	n	%	p-value
Control	15	1	6.67	0.027
CDK stage 2	12	2	16.67	
CDK stage 3a	20	7	35	
CDK stage 3b	16	6	37.5	
CDK stage 4	22	12	54.55	

Regarding Apelin, the average Apelin level in CKD patients who developed CVDs was lower than in CKD patients who didn't develop any CVDs. Table 3 depicts the multivariate analysis results, with the consideration of variable factors. Only Apelin was statistically significant with respect to CVD incidence in CKD patients. The multivariate analysis showed that the CVD incidence rate decreased by 4% for each increase in Apelin by 1 unit.

Table 3. The related factors to CVD occurrence in CKD patients

	No (N=43)		Yes (N=27)		
	Mean	SD	Mean	SD	p-value
Age	53.02	9.06	55.04	11.82	0.4245
Weight	84.53	14.78	84.56	13.47	0.9953
BMI, kg/m2	30.91	4.35	32.14	3.97	0.2387
GFR ml /min / 1.73 m2	46.86	18.85	34.41	16.37	0.0062
DBP	81.72	5.55	85.41	5.61	0.0089
SBP	126.84	4.99	130.30	5.00	0.0062
Cholestrol	179.28	26.67	202.41	36.23	0.0031
TG	136.53	13.08	152.48	26.39	0.0013
Apline	417.53	51.27	317.26	73.87	<0.0001

multivariate analysis results	Odds Ratio	[95% Conf. Interval]		p-value
Age	0.89	0.77	1.02	0.103
Height	0.83	0.26	2.61	0.744
Weight	1.06	0.36	3.15	0.919
BMI, kg/m2	0.89	0.05	17.10	0.94
GFR ml /min / 1.73 m2	1.11	0.96	1.29	0.176
DBP	1.11	0.90	1.37	0.343
SBP	1.14	0.92	1.41	0.216
Cholestrol	1.02	0.98	1.07	0.349
TG	1.05	0.96	1.14	0.29
Apline	0.96	0.95	0.99	0.001

Therefore, we studied Apelin's diagnostic ability in predicting CVD progression in patients with CKD. This is done by calculating a sensitivity value and specificity. Lastly, the best value of Apelin in diagnosing CVD in CKD patients was identified. Table 4 depicts the diagnostic value of Apelin. The analysis revealed that a value of Apelin of 330 or less has the best diagnostic value with a 74% sensitivity and a 100% specificity (Table 4).

Table 4. diagnostic value of Apelin

Apelin value	Sensitivity	95% CI	Specificity	95% CI	+PV	95% CI	-PV	95% CI
<240	0	0.0 - 12.8	100	91.8 - 100.0			61.4	61.4 - 61.4
≤240	7.41	0.9 - 24.3	100	91.8 - 100.0	100		63.2	60.7 - 65.7
≤244	11.11	2.4 - 29.2	100	91.8 - 100.0	100		64.2	61.1 - 67.2
≤249	14.81	4.2 - 33.7	100	91.8 - 100.0	100		65.2	61.5 - 68.6
≤250	22.22	8.6 - 42.3	100	91.8 - 100.0	100		67.2	62.6 - 71.5
≤255	25.93	11.1 - 46.3	100	91.8 - 100.0	100		68.3	63.2 - 72.9
≤280	29.63	13.8 - 50.2	100	91.8 - 100.0	100		69.4	63.9 - 74.3
≤289	33.33	16.5 - 54.0	100	91.8 - 100.0	100		70.5	64.7 - 75.7
≤290	37.04	19.4 - 57.6	100	91.8 - 100.0	100		71.7	65.4 - 77.2
≤299	40.74	22.4 - 61.2	100	91.8 - 100.0	100		72.9	66.3 - 78.6
≤300	62.96	42.4 - 80.6	100	91.8 - 100.0	100		81.1	72.4 - 87.5
≤315	66.67	46.0 - 83.5	100	91.8 - 100.0	100		82.7	73.7 - 89.1
≤320	70.37	49.8 - 86.2	100	91.8 - 100.0	100		84.3	75.0 - 90.6
≤330	74.07	53.7 - 88.9	100	91.8 - 100.0	100		86	76.5 - 92.1
≤340	74.07	53.7 - 88.9	95.35	84.2 - 99.4	90.9	71.7 - 97.5	85.4	75.5 - 91.7
≤345	74.07	53.7 - 88.9	93.02	80.9 - 98.5	87	68.6 - 95.3	85.1	75.0 - 91.6
≤350	77.78	57.7 - 91.4	86.05	72.1 - 94.7	77.8	61.9 - 88.3	86	75.1 - 92.7
≤355	81.48	61.9 - 93.7	86.05	72.1 - 94.7	78.6	63.1 - 88.7	88.1	76.9 - 94.3
≤359	81.48	61.9 - 93.7	83.72	69.3 - 93.2	75.9	60.9 - 86.4	87.8	76.3 - 94.1
≤360	85.19	66.3 - 95.8	83.72	69.3 - 93.2	76.7	62.1 - 86.8	90	78.3 - 95.7
≤367	85.19	66.3 - 95.8	81.4	66.6 - 91.6	74.2	60.1 - 84.6	89.7	77.8 - 95.6
≤370	85.19	66.3 - 95.8	76.74	61.4 - 88.2	69.7	56.7 - 80.2	89.2	76.7 - 95.4
≤378	85.19	66.3 - 95.8	74.42	58.8 - 86.5	67.6	55.1 - 78.1	88.9	76.1 - 95.3
≤389	85.19	66.3 - 95.8	69.77	53.9 - 82.8	63.9	52.2 - 74.1	88.2	74.8 - 95.0
≤390	88.89	70.8 - 97.6	69.77	53.9 - 82.8	64.9	53.5 - 74.8	90.9	77.2 - 96.7
≤399	88.89	70.8 - 97.6	62.79	46.7 - 77.0	60	49.9 - 69.3	90	75.1 - 96.4
≤400	88.89	70.8 - 97.6	41.86	27.0 - 57.9	49	41.9 - 56.1	85.7	66.1 - 94.9
≤430	88.89	70.8 - 97.6	39.53	25.0 - 55.6	48	41.2 - 54.9	85	64.7 - 94.6
≤440	88.89	70.8 - 97.6	37.21	23.0 - 53.3	47.1	40.5 - 53.7	84.2	63.1 - 94.3
≤450	92.59	75.7 - 99.1	23.26	11.8 - 38.6	43.1	38.4 - 48.0	83.3	54.2 - 95.5
≤455	92.59	75.7 - 99.1	20.93	10.0 - 36.0	42.4	37.9 - 47.0	81.8	51.2 - 95.1
≤460	96.3	81.0 - 99.9	18.6	8.4 - 33.4	42.6	38.7 - 46.6	88.9	51.4 - 98.4
≤466	96.3	81.0 - 99.9	16.28	6.8 - 30.7	41.9	38.3 - 45.7	87.5	47.7 - 98.2
≤490	96.3	81.0 - 99.9	13.95	5.3 - 27.9	41.3	37.9 - 44.7	85.7	43.3 - 97.9
≤495	96.3	81.0 - 99.9	11.63	3.9 - 25.1	40.6	37.5 - 43.8	83.3	38.2 - 97.6
≤500	96.3	81.0 - 99.9	6.98	1.5 - 19.1	39.4	36.8 - 42.1	75	24.7 - 96.5
≤505	96.3	81.0 - 99.9	4.65	0.6 - 15.8	38.8	36.5 - 41.2	66.7	16.0 - 95.5
≤509	96.3	81.0 - 99.9	2.33	0.06 - 12.3	38.2	36.2 - 40.3	50	6.1 - 93.9
≤510	96.3	81.0 - 99.9	0	0.0 - 8.2	37.7	36.0 - 39.4	0	
≤550	100	87.2 - 100.0	0	0.0 - 8.2	38.6	38.6 - 38.6		

Table 5. Summary table

Estimated specificity at a fixed sensitivity			
Sensitivity	Specificity	95% CI	Criterion
80	86.05	17.85 to 100.00	≤353
90	33.02	0.00 to 88.37	≤443
95	19.42	0.00 to 79.07	≤458.25
97.5	0	0.00 to 20.17	≤523
99	0	0.00 to 18.79	≤539.2
Estimated sensitivity at a fixed specificity			
Specificity	Sensitivity	95% CI	Criterion
80	85.19	65.93 to 96.30	≤367.9
90	75.68	51.85 to 88.89	≤347.17
95	74.07	51.85 to 86.30	≤340.75
97.5	74.07	0.00 to 0.00	≤335.375
99	74.07	0.00 to 0.00	≤332.15
Relationship between apekin and CVD Complications		Cardiac disease	Total
		No	Yes
Epline test	≤330 (+)	0	20
	>330 (-)	43	7
	Total 43		27

correlation of the researched biomarkers with CKD stages	Control		CDK stage 2		CDK stage 3a		CDK stage 3b				CDK stage 4			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p-value			
GFR ml /min / 1.73 m2	122.40	2.44	71.50	6.10	51.85	4.84	37.19				4.74	20.64	4.74	<0.0001
Apelin	663.93	157.51	486.67	30.86	383.20	62.78	357.00				51.59	332.00	68.31	<0.0001

Table 5 shows how the specificity and sensitivity values are affected by the changes in Apelin values. With increased sensitivity (increased Apelin value), the specificity value decreases. (Sensitivity=20/27 probability of positive test in patients who developed CVD complications. Specificity=43/43 probability of normal test result (-) in patients who didn't develop CVD complication. +PV=20/20 probability of CVD complication occurrence if Apelin value was lower than 330 (+test).-PV=43/50 probability of no CVD complication occurrence if the Apelin value is normal (-test) (Table 5. The relationship between Apelin and CVD complication is demonstrated in Table 5, which also represents the correlation of the researched biomarkers with CKD stages. We found that the GFR and Apelin values decreased with the progression of the disease.

4. Discussion

In this study, we evaluated the correlation of Apelin levels with the development of CVD complications in the context of CKD in a homogenous group of CKD patients with different stages, with none being at the dialysis stage. Keeping in consideration the typical cardiovascular risk factors (BP values and plasma lipid levels). To our knowledge, this is the first study from Syria.

We found that the average Apelin was lower in CKD patients than in the control group. This is similar to a previous study by El-Shehaby et al [19] that revealed the strong relationship between the Apelin levels and the stage of CKD as its values decrease with the progression of kidney failure. Hence, it seems that the worse the renal function is, the lower the apelin levels get.

The incidence of CVD complications in CKD patients is higher than that of the control group. MI and LVH were the most common CVD complications among CKD patients along the progression of the disease. These results were also highlighted in previous studies by Granata et al. and Zoccali et al. [3, 20]. The average systolic and diastolic BP, GFR, triglyceride, and cholesterol levels were all higher in CKD patients who developed CVD complications than in patients with CKD who didn't develop CVD complications.

Regarding Apelin, the average Apelin in CKD patients who developed CVD complications was lower than the average Apelin in CKD patients who didn't develop CVD complications.

The multivariate analysis results showed that Apelin was the only independent predictor of CVD complications in CKD patients. Similar findings were published by Ana Paula Silva et al. From all the variables that were analyzed in CKD patients, Apelin was one of the major biomarkers of CVD-related deaths. Also, it was noted that the lower the Apelin value got, the higher the risk of developing CVD and the longer the hospitalization period was [21]. The increased rate of CVD in CKD patients is well known, and multiple studies have tried to investigate the relationship in search of biomarkers for predicting CVD in the context of CKD. A study done by Malyszko et al. and his colleagues [22] that looked into the relationship between Apelin levels and cardiac ischemic disease development in CKD patients reported that Apelin levels in CKD patients with cardiac ischemic diseases were lower than in CKD patients without cardiac ischemic diseases. They assumed this correlation was evidence of the positive effect of the mentioned muscle contractility in the previous studies [12, 23-25]. After that, we studied the Apelin value's role in the diagnosis of CVD complications and tried to determine the best Apelin value for the diagnosis of CVD complications in CKD patients. This is what distinguishes our research from the other studies. The analysis showed that the Apelin value of 330 or less is the best value for the prediction of prognosis, with a 74% sensitivity and a 100% specificity.

We also investigated the association between the biomarkers of the study and the stage of CKD and found a decrease in GFR and Apelin with the progression of the disease, marking an early failure. Furthermore, we found that Apelin had a significant association with CVD incidence in CKD patients. Apelin levels were negatively correlated with the known CV risk factors and positively correlated with eGFR. This fact underlines the possible preventive role of Apelin in the context of CVD and renal disease. These results elucidate that Apelin levels may have an important clinical role as a biomarker of CVD progression.

Limitations of the study included the limited number of patients due to the short period of the study, in addition to the inability to conduct molecular studies that were unavailable at our department at the time of the study. However, with detailed clinical and laboratory examinations, we managed to perform the first study that highlights a promising prognostic role for Apelin in Syrian patients suffering from chronic kidney disease with its devastating cardiac comorbidities.

5. Conclusion

In our study, serum Apelin demonstrated a promising predictive marker for the progression of cardiovascular disease in CKD patients. Our results revealed that lower Apelin levels were correlated with an increased incidence of cardiovascular complications and a worse prognosis.

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Abbreviations

CKD: Chronic Kidney Disease.
CVD: Cardiovascular Disease.
LVH: Left Ventricular Hypertrophy.
BP: Blood Pressure.
BMI: Body Mass Index.
GFR: Glomerular Filtration Rate

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