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Impact of Hemodialysis on Gasdermin D and Vanin 1 Among Patients With Chronic Kidney Disease

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ABSTRACT

Chronic kidney disease is a progressive disorder defined by structural and functional abnormalities in the kidneys, irreversible renal function impairment. An estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1·73 m², an albumin creatinine ratio (ACR) of ≥ 30 mg/g, or indicators of damage to the kidneys, like albuminuria, hematuria, or abnormalities found through laboratory tests or imaging, that persist for at least three months. The aim of this study was to investigate the impact of hemodialysis on Gasdermin D and Vanin 1 among patients with chronic kidney disease CKD. The study included 30 control samples and 60 patients with CKD who underwent regular hemodialysis in dialysis centers in Baquba Teaching Hospital and Baladruz General Hospital (30 sample pre dialysis and 30 sample post dialysis). (5 ml) of the blood sample were collected, to determine biochemical markers Gasdermin D and Vanin 1 by using an Enzyme Immunoassay (ELISA) kit. The current study showed a significant increase in all the measured parameters in patients with CKD when compared to control group. the highest levels of Gasdermin D in the pre-dialysis group (1.93 ± 0.40 ng/ml), post-dialysis (1.25 ± 0.24 ng/ml), and the lowest levels in the control group (0.75 ± 0.34 ng/ml) with (p-value <0.001). And Vanin 1 the pre-dialysis group had significantly elevated levels (1162.02 ± 147.61 ng/L) compared to post-dialysis (841.36 ± 131.16 ng/L) and control groups (524.58 ± 165.79 ng/L). blood urea in the pre-dialysis group (92.96 ± 17.58 mg/dl), post-dialysis group (47.61 ± 7.40 mg/dl) and the control group (26.97 ± 5.21 mg/dl) (p<0.001). And Serum creatinine pre-dialysis levels (6.64 ± 1.76 mg/dl), post-dialysis levels (3.26 ± 0.85 mg/dl) and control levels (0.71 ± 0.11 mg/dl) (p<0.001). Whereas The pre-dialysis group (4.58 ± 0.93 mg/dl), post-dialysis group (2.83 ± 0.79 mg/dl), and the control group (4.11 ± 0.98 mg/dl)..

1. INTRODUCTION

Chronic kidney disease is a progressive disorder defined by structural and functional abnormalities in the kidneys caused by a variety of factors that result in progressive, irreversible renal function impairment. A decrease in kidney function, an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1·73 m², an albumin creatinine ratio (ACR) of ≥ 30 mg/g, or indicators of damage to the kidneys, like albuminuria, hematuria, or abnormalities found through laboratory tests or imaging, that persist for at least three months.(1,2) The prevalence of chronic kidney disease (CKD) ranges from 8 to 16 % worldwide.(3) In the United States, females were more likely than males to suffer from chronic kidney disease (CKD) between 2017 and 2020 (15.4% vs. 12.6%).(4) Diabetes and hypertension are the most frequent causes of chronic kidney disease (CKD) in developed nations.(5) Chronic kidney disease, CKD, has risen in the last three decades to become one of the leading causes of death for the global patient population. This illness ranked 13th among the leading causes of mortality in 2016. With 850 million people suffering from kidney illnesses, chronic kidney disease (CKD) is currently regarded as a top public priority worldwide.(6)

(GSDMD) is the effector of pyroptosis (inflammatory programmed cell death), plays an important role in the controlled rupture of the plasma membrane, which can result in cell death, release of cytokines, or both.(7) GSDMD-N creates a transmembrane pore, releasing cytokines such IL-1β and IL-18, disrupting ion and water control, leading to pyroptosis.(8) Pyroptosis is an essential pathogenic mechanism behind kidney cell destruction in chronic kidney disease (CKD).It is a controlled kind of cell death brought on by high inflammatory levels from cell infections.(9)

Vanin-1 is a protein that exists in the kidney's proximal tubule brush boundaries.(10)The tissues with the highest levels of Vnn1 basal expression are those with high CoA turnover, like the kidney and liver, but not the heart or muscles.(11)vanin1 hydrolyzes pantetheine to produce the cysteamine and pantothenic acid (vitamin B5). Vanin-1 causes cellular stress by producing cysteamine.(12) cysteamine is known to disrupt redox equilibrium by decreasing the replenishment of cellular anti-oxidative glutathione reserves.(13)

2. METHODOLOGY

Patient and methods

This is a cross-sectional, hospital-based study, the agreement of attendance to Baquba Teaching Hospital and Baladruz General Hospital that approved by Diyala health Department, to collect the samples from the patients. This study was done from the period from the 20th September 2024 to the end of February 2025. The study included 30 control samples and 60 patients with CKD who underwent regular hemodialysis and their age were between 18 to 64 years. They were clinically diagnosed by nephrologist as ESRD patients (on hemodialysis). They were classified into three groups:

Group 1: with chronic kidney disease (ESRD). (30 sample pre dialysis).

Group 2: with chronic kidney disease (ESRD). (30 sample post dialysis).

Group 3: control (30 sample).

An interview was carried out with these patients using questionnaire form designed by the investigator including their name, age, gender, etc.

The blood samples were drawn from the vein. (5 ml) of the blood sample were collected and allowed to clot at room temperature (25 ˚C) for 30 minutes. After that centrifugation was done at (4000) rpm for 10 minutes to separate the serum.

Biochemical analysis. Gasdermin D and Vanin 1 were determined using an Enzyme Immunoassay (ELISA) kit. Blood urea, serum creatinine and serum uric acid were measured colorimetrically using commercially available kits on a fully auto analyzer of Clinical Biochemistry Laboratory.

Data analysis was performed using (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). Data are presented as mean ± standard deviation (SD) for normally distributed variables. Paired t-tests were used to compare pre- and post-dialysis parameters within the same group of patients, and using (ANOVA) followed by Tukey's post hoc test for multiple comparisons. with P-value <0.05 considered significant. The diagnostic performance of novel biomarkers was evaluated using Receiver Operating Characteristic (ROC) curve analysis, with calculation of Area Under the Curve (AUC), sensitivity, specificity, and optimal cutoff values

3. RESULTS:

Table -1 Demographic and Clinical Characteristics of the Study Groups (N=60)

Characteristic	CKD (n=30)	Control (n=30)	P-value
Age (years)*	47.07 ± 13.04	42.70 ± 9.14	0.186†
Gender			
Female	18 (60%)	14 (46.7%)	0.3047‡
Male	12 (40%)	16 (53.3%)	
Total	30 (50%)	30 (50%)	
Chi-square value			1.054
Contingency coefficient			0.131

***Data presented as mean ± SD †Independent t-test ‡Chi-square test**

Table -2 Analysis of Novel Biomarkers Across Study Groups

Biomarker	Pre-dialysis (n=30)	Post-dialysis (n=30)	Control (n=30)	F-value	p-value	Post-hoc significance
Gasdermin D (ng/ml)	1.93 ± 0.40	1.25 ± 0.24	0.75 ± 0.34	92.11	<0.001	Pre > Post > Control
Vanin 1 (ng/L)	1162.02 ± 147.61	841.36 ± 131.16	524.58 ± 165.79	132.94	<0.001	Pre > Post > Control

This study exhibited the highest levels of Gasdermin D in the pre-dialysis group (1.93 ± 0.40 ng/ml), followed by post-dialysis (1.25 ± 0.24 ng/ml), and the lowest levels in the control group (0.75 ± 0.34 ng/ml). The percent reduction of 35.2%

post-dialysis (Table 4-3). And Vanin 1 followed a similar pattern. The pre-dialysis group had significantly elevated levels (1162.02 ± 147.61 ng/L) compared to post-dialysis (841.36 ± 131.16 ng/L) and control groups (524.58 ± 165.79 ng/L). The observed reduction of 27.6% post-dialysis

Table -3 Comparison of Traditional Biochemical Parameters Among Study Groups

Parameter	Pre-dialysis (n=30)	Post-dialysis (n=30)	Control (n=30)	F-value	p-value	Post-hoc significance
Blood Urea (mg/dl) *	92.96 ± 17.58	47.61 ± 7.40	26.97 ± 5.21	253.52	<0.001	Pre > Post > Control
Serum Creatinine (mg/dl)	6.64 ± 1.76	3.26 ± 0.85	0.71 ± 0.11	200.22	<0.001	Pre > Post > Control
Serum Uric Acid (mg/dl)	4.58 ± 0.93	2.83 ± 0.79	4.11 ± 0.98	29.26	<0.001	Pre = Control > Post

Test results in Table (2) show that the blood urea levels were significantly elevated in the pre-dialysis group (92.96 ± 17.58 mg/dl) compared to the post-dialysis group (47.61 ± 7.40 mg/dl) and the control group (26.97 ± 5.21 mg/dl) (p<0.001). The reduction in blood urea levels post-dialysis by 48.8%. And Serum creatinine levels exhibited a similar trend, with pre-dialysis levels (6.64 ± 1.76 mg/dl) being markedly higher than post-dialysis levels (3.26 ± 0.85 mg/dl) and control levels (0.71 ± 0.11 mg/dl) (p<0.001). Hemodialysis resulted in a 50.9% reduction in serum creatinine. While the Serum uric acid levels demonstrated significant differences among the groups (p<0.001). The pre-dialysis group showed elevated levels (4.58 ± 0.93 mg/dl) compared to the post-dialysis group (2.83 ± 0.79 mg/dl), and the control group exhibited levels (4.11 ± 0.98 mg/dl).

Table -4 Pearson correlation coefficient: subject="pre dialysis"

		Gasdermin D	Vanin 1	B. urea	S. creatinine	S. uric acid
Gasdermin D (ng/ml)	r	1.00				
	p					
Vanin 1 (ng/L)	r	0.55	1.00			
	p	0.00				
B. urea (mg/dl)	r	0.27	0.11	1.00		
	p	0.15	0.55			
S. creatinine (mg/dl)	r	0.14	0.17	0.50	1.00	
	p	0.45	0.37	0.00		
S. uric acid (mg/dl)	r	0.14	0.18	0.11	0.00	1.00
	p	0.45	0.35	0.57	1.00	
Age (year)	r	-0.24	-0.11	0.08	-0.13	0.71
	p	0.20	0.57	0.66	0.51	<0.0001

The analysis revealed a significant positive correlation between the novel biomarkers Gasdermin D and Vanin 1 (r = 0.545, p = 0.0018). Traditional renal markers, serum creatinine demonstrated a significant positive correlation with blood urea (r = 0.504, p = 0.0045)

Table -5 Pearson correlation coefficient: " post-dialysis patients "

		Gasdermin D	Vanin 1	B. urea	S. creatinine	S. uric acid
Gasdermin D (ng/ml)	r	1				
	p					
Vanin 1 (ng/L)	r	0.399	1			
	p	0.029				

B. urea (mg/dl)	r	0.067	-0.198	1		
	p	0.7231	0.2944			
S. creatinin (mg/dl)	r	-0.007	-0.014	0.354	1	
	p	0.9701	0.9395	0.0547		
S. uric acid (mg/dl)	r	0.455	0.063	0.162	-0.139	1
	p	0.0115	0.7428	0.3912	0.4643	
Age (year)	r	-0.234	-0.174	0.029	-0.159	0.523
	p	0.2125	0.3588	0.8776	0.4022	0.003

The correlation between Gasdermin D and Vanin 1 remained significant but decreased in strength post-dialysis ($r = 0.399$, $p = 0.0290$). Gasdermin D showed a new significant positive correlation with serum uric acid post-dialysis ($r = 0.455$, $p = 0.0115$). The correlation between serum creatinine and blood urea became marginally significant post-dialysis ($r = 0.354$, $p = 0.0547$),

Table -6 Diagnostic Performance of Novel Biomarkers in CKD

Parameter	AUC	SE	95% CI	Optimal Cutoff	Sens	Spec
Gasdermin D ng/ml	0.996	0.00437	0.932 to 1.000	>1.261	100	93.33
Vanin 1ng/L	1.000	0.000	0.940 to 1.000	>723.517	100	100

Vanin 1 demonstrated exceptional diagnostic accuracy with an Area Under the Curve (AUC) of 1.000 (SE = 0.000, 95% CI: 0.940-1.000). At the optimal cutoff value of >723.517 ng/L, Vanin 1 achieved perfect discrimination between CKD patients and healthy controls, showing both 100% sensitivity and 100% specificity. Similarly, Gasdermin D exhibited excellent diagnostic performance with an AUC of 0.996 (SE = 0.00437, 95% CI: 0.932-1.000). Using an optimal cutoff value of >1.261 ng/ml, Gasdermin D achieved 100% sensitivity and 93.33% specificity

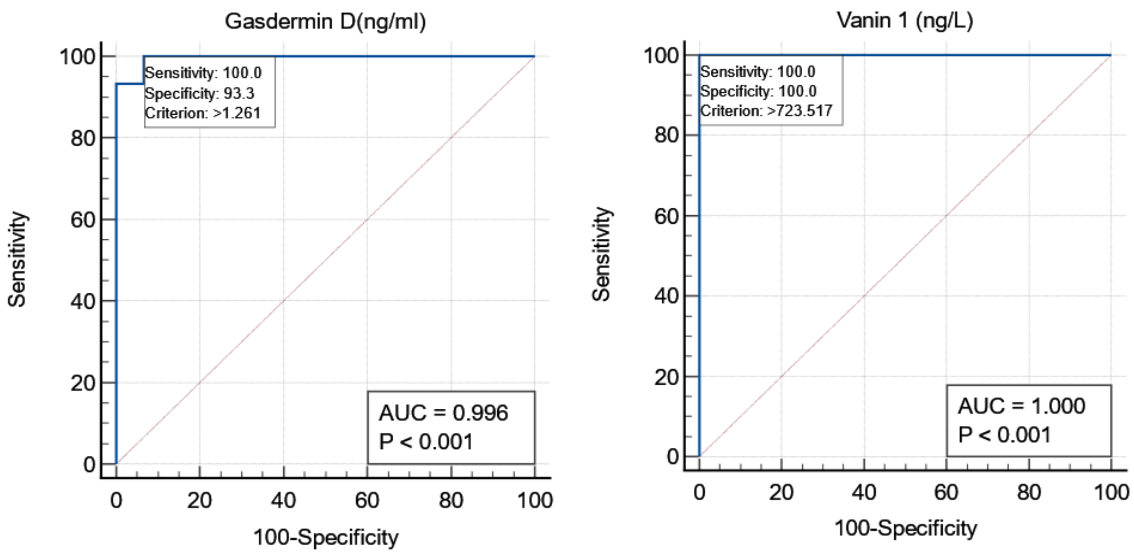

Figure -1 ROC Curve Analysis of Novel Biomarkers for CKD Diagnosis. The markers distinguish between pre-dialysis patient from control

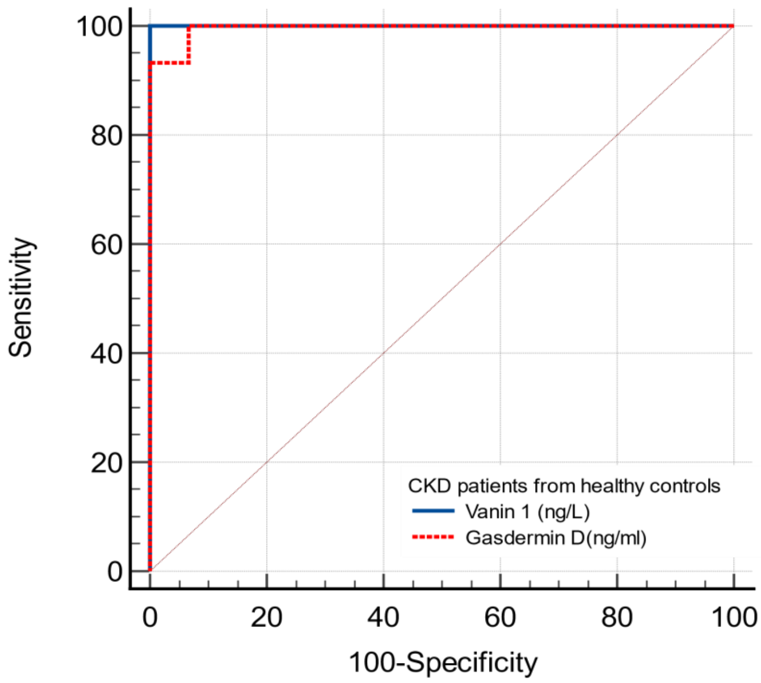

Figure -2 comparison of Curve Analysis of Novel Biomarkers for CKD Diagnosis

4. DISCUSSION:

The present study investigated the impact of hemodialysis on novel biomarkers, Gasdermin D and Vanin 1, in chronic kidney disease patients. the findings revealed several significant observations regarding both traditional renal parameters and these novel biomarkers.

(Table-1) the demographic analysis demonstrated well-matched study groups, with no significant differences in age and gender distribution between CKD on dialysis, and control groups. This demographic homogeneity strengthens the reliability of the study's comparative analyses and minimizes potential confounding factors in the interpretation of biomarker levels.

(Table-2) a key finding of our study was the significant elevation of both novel biomarkers in CKD patients compared to healthy controls. Gasdermin D levels were markedly higher in pre-dialysis patients (1.93 ± 0.40 ng/ml) compared to controls (0.75 ± 0.34 ng/ml), with a significant reduction following hemodialysis (1.25 ± 0.24 ng/ml, $p<0.001$). The current results agree with the study (Zhang X et al)(14) that suggested Patients with ESKD had noticeably higher serum GSDMD levels and associated with complication of CKD such as Vascular calcification (VC) is an important risk factor for cardiovascular disease. GSDMD plays an important role in the initiation and progression of several inflammatory disorders

Similarly, Vanin 1 showed elevated levels in pre-dialysis patients (1162.02 ± 147.61 ng/L) with significant reduction post-dialysis (841.36 ± 131.16 ng/L, $p<0.001$). The current results agree with the study (Piko N et al)(15) that suggested increased concentration of biomarkers of oxidative stress in hemodialysis patients (HD), and the Vanin 1 pathway plays an important role in increased oxidative stress by increasing cystamine, which reduces glutathione stores.

These patterns suggest potential roles for both markers in reflecting disease severity and monitoring treatment response.

(Table-3) traditional renal function parameters showed expected patterns consistent with established knowledge. Blood urea and serum creatinine levels were significantly elevated in pre-dialysis patients compared to controls, this study is agree with previous studies (16,17) which confirms hemodialysis patients have higher levels of urea and creatinine compared to the control group, with substantial reductions post-dialysis (48.8% and 50.9% respectively, $p<0.001$). These findings confirm the effectiveness of the hemodialysis procedure in removing uremic toxins and validate our study methodology, our results are consistent with previous studies (Zhang et al)(18) that have shown that dialysis significantly reduces blood urea and creatinine levels.

Serum uric acid levels demonstrated significant differences among the groups ($p<0.001$). The pre-dialysis group showed elevated levels (4.58 ± 0.93 mg/dl) compared to the post-dialysis group (2.83 ± 0.79 mg/dl), the current results agree with the study (Arenas M et al)(19) that suggested the Serum uric acid levels were significantly lowered with HD replacement therapy. a post-hoc significance of Pre = Control > Post. The substantial reduction in uric acid levels post-dialysis reflects the hemodialysis impact on reducing uric acid, though pre-dialysis levels suggest hyperuricemia associated with CKD.

In the (table-4) the analysis revealed a significant positive correlation between the novel biomarkers Gasdermin D and Vanin 1 ($r = 0.545$, $p = 0.0018$), suggesting these markers may share common pathophysiological pathways in CKD patients prior to hemodialysis.

Neither Gasdermin D nor Vanin 1 showed significant correlations with traditional renal markers (blood urea, serum creatinine, and uric acid; all $p > 0.05$). This suggests these novel biomarkers might reflect different aspects of renal pathophysiology compared to conventional markers.

In the (table-5) show the correlation between Gasdermin D and Vanin 1 remained significant but decreased in strength post-dialysis ($r = 0.399$, $p = 0.0290$) compared to pre-dialysis values (pre-dialysis: $r = 0.545$). This maintained correlation, albeit weaker, suggests these biomarkers continue to share common biological pathways even after hemodialysis intervention. The current study provided a Gasdermin D showed a new significant positive correlation with serum uric acid post-dialysis ($r = 0.455$, $p = 0.0115$), a relationship that was not observed in the pre-dialysis state.

In (table-6) ROC curve analysis revealed outstanding diagnostic accuracy, with Vanin 1 achieving perfect discrimination (AUC=1.000, 95% CI: 0.940-1.000) at an optimal cutoff of >723.517 ng/L. Gasdermin D similarly demonstrated excellent diagnostic capability (AUC=0.996, 95% CI: 0.932-1.000) with an optimal cutoff of >1.261 ng/ml. The weak correlations observed between these novel biomarkers and traditional parameters suggest they may provide independent diagnostic information, potentially capturing different aspects of CKD pathophysiology.

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