

Association of Plasma Fibrinogen with Creatine Kinase-MB in Chronic Kidney Disease Patients - A Cross-Sectional Study

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Received: 25th Aug, 2026 | Revised: 1st Sep, 2026 | Accepted: 5th Sep, 2026 | Available Online: 17th Sep, 2026

ABSTRACT

Background: Chronic kidney disease (CKD) causes huge morbidity due to complications such as cardiovascular diseases (CVD). CVD is diagnosed based on the levels of Creatine Kinase (CK)-MB and Troponin-I and Troponin-T.

Objective: This study aimed to assess the association of fibrinogen with CK-MB in patients with CKD.

Methods: The observational cross-sectional study involved 40 CKD patients, of both genders, 30-70 years of age, recruited from the Department of Nephrology. Blood samples were collected for analysis of biomarkers. Ethics approval was obtained. All the patients provided written informed consent. Depending on the type of distribution, appropriate statistical tools were used. $p \leq 0.05$ was considered statistically significant. Statistical analysis was performed in SPSS software version 24.

Results: Among the participants, 32 (80%) were in CKD stage 5, while 8 (20%) were in stage 4. Plasma fibrinogen showed 411.2 ± 212.3 and 580.3 ± 202.7 in CKD stages 4 and 5 respectively with statistically significant p-value of 0.043. Fibrinogen showed a positive correlation with CK and creatinine (both $r=0.32$) and negative correlation with serum calcium ($r=-0.39$).

Conclusion: Fibrinogen levels were higher in CKD stage 5 and it showed correlated with creatinine kinase which is a known marker of cardiovascular disease. The nutritional status was low in stage 5 as indicated by lower total protein and albumin. This can cause low levels of enzymes such as CK and CK-MB. Hence, due to the limitations of CK, fibrinogen could be a potential marker in diagnosing CVD complications in CKD patients.

Keywords: Cardiovascular Disease, Chronic Kidney Disease, Fibrinogen, Platelets, Coronary Artery Calcification

How to cite this article: Sashank Sudhakar Sah¹ Sandhya Suresh² Keerthy Rethinam MS³ Santhi Silambanan^{4*}. Association of Plasma Fibrinogen with Creatine Kinase-MB in Chronic Kidney Disease Patients - A Cross-Sectional Study. Int J Drug Deliv Technol. 2026;16(83s):831-839. DOI: 10.25258/ijddt.16.83s.94.

Introduction

In chronic kidney disease (CKD), there is a progressive decline in kidney function, and an estimated glomerular filtration rate (eGFR) is less than 60 mL/min/1.73 m², which remains for at least three months.¹ At this stage, there is almost complete loss of kidney function, requiring dialysis or renal transplantation. Whatever may be the cause of renal injury, the last stage of CKD is always end-stage

renal disease (ESRD).¹ In 2012, Kidney Disease Improving Global Outcomes (KDIGO) classified CKD into six stages based on GFR as G1, G2, G3a, G3b, G4, and G5. (Graphical abstract) Depending upon the albumin excretion level in urine, each stage of CKD is further grouped as A1, A2, and A3.¹ The causes of CKD include diabetes mellitus, hypertension, obesity, glomerulonephritis,

tubulointerstitial nephritis, inherited diseases, polycystic kidney diseases, tumors, vasculitis, etc.² Diabetes mellitus causes a rapid decline in GFR and hypertensive patients, showed better outcomes by controlling blood pressure (BP) and albuminuria.¹ Various risk factors, such as old age, male gender, and non-White ethnicity, Asians (South Asians and Pacific Asians) may cause a rapid progression of CKD.¹

Among the general population, the prevalence of CKD is 8 - 16%.¹ CKD was prevalent in 26 million individuals in the United States (2016).² CKD also leads to various organ damage other than the kidney, such as the cardiovascular system, cognitive function, bone metabolism, etc.² CKD increase the risk for CVD thus, increasing morbidity and mortality.³ In CKD stages G4 and G5, approximately 40–50% of mortality is due to CVD.⁴ ESRD patients who are on maintenance hemodialysis (HD) are at risk for hemostatic alterations, which are due to increased activity of procoagulant factors and platelets and decreased activity of anticoagulants and fibrinolytic activity.⁵ (Graphical abstract) Hyperglycemia along with insulin resistance (IR) cause alterations number and functions of platelets, coagulation disorders and hypofibrinolysis, leading to the formation of fibrinolysis-resistant clots.⁶ The endothelial cell dysfunction along with hypercoagulability and thrombosis may increase the morbidity in diabetics.⁷ This study aimed to compare the levels of plasma fibrinogen with cardiac biomarkers in advanced stages of CKD.

Materials and Methods

The prospective cross-sectional study included 40 CKD patients of 30 –70 years of age, and belonging to both genders. The participants were recruited from the Department of Nephrology at Sri Ramachandra Institute of Higher Education and Research, between January 2025 to June 2025. All the patients were on regular HD. Patients with autoimmune diseases, cancer, liver and cardiac failures, and patients on drugs- analgesics, steroids, and anticancer were excluded. Blood samples were collected for analysis of plasma fibrinogen, renal parameters, electrolytes, CK, CK-MB, and peripheral blood cell counts. eGFR was calculated from serum creatinine levels using the CKD-EPI formula. Plasma fibrinogen was analysed by ELISA. Other parameters were analyzed by standard methods.

Ethics approval: Institutional ethics committee (IEC) approval was obtained (Ethics no. CSP/23/SEP/137/847, dated 10-11-2023). Written informed consent was obtained from all the participants included in the study.

Statistical analysis: The data obtained were subjected to a test for normal distribution. Continuous data were expressed as mean and standard deviation or median and interquartile range. Discrete variables were expressed as

frequency and percentage. Continuous variables compared using either the student ‘t’ test or the Mann-Whitney U test. Correlation among the variables was done by Spearman Correlation. $P \leq 0.05$ was considered statistically significant. The data were analyzed using the SPSS software version 24.

Results

The analysis of the data obtained from 40 CKD patients are shown in four tables and one figure. Table 1 shows the demographic details of the study participants. The mean age of the participants was 52.5 years and around 63% were males. Most of them were hypertensives, and a few were diabetics. Around 80% of them were in CKD stage 5, whereas 20% were in stage 4. (Table 1)

Table 1. Demographic details of the study participants

Variable	CKD patients (n=40)
Age (Year)	52.5 ± 11.7
Sex (n%)	
Male	25 (62.5)
Female	15 (27.5)
eGFR (mL/min)	7.15 ± 3.3
Occupation (n%)	
House wife	15 (27.5)
IT	4 (10)
Technician/ mechanic	9 (22.5)
Driver	2 (5)
Farmer	6 (15)
Business	4 (10)
Presenting complaints (n%)	
Routine dialysis	23 (57.5)
Pedal edema, ascites, dyspnea	17 (42.5)
Presence of metabolic conditions (n%)	
DM	10 (25)
HT	32 (80)
Anemia	17 (42.5)
Cerebrovascular disease	1 (2.5)
Cardiovascular disease	1 (2.5)
Thyroid disorder	1 (2.5)
BPH	1 (2.5)
Stage of CKD (n%)	
CKD 4	2 (5)
CKD 5	38 (95)

Note: IT: information technology, DM: diabetes mellitus, HT: hypertension, BPH: benign prostatic hypertrophy, eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease

Table 2 shows the comparison of biochemical variables according to the stage of CKD. Plasma

fibrinogen showed 411.2 ± 212.3 and 580.3 ± 202.7 in CKD stages 4 and 5 respectively with statistically p-value of 0.043. BUN, creatinine and uric acid were significantly higher in CKD stage 5 with p-values 0.023, 0.010 and 0.011 respectively. Serum calcium was significantly lower in CKD stage 5 ($p < 0.001$). Total protein and serum albumin were statistically decreased in CKD stage 5 with p-values 0.017 and < 0.001 respectively. (Table 2)

Table 2. Comparison of variables among CKD stages 4 and 5

Variable	CKD stage 4 (n=8)	CKD stage 5 (n=32)	p-value
Age (year)	46.0 $\pm$ 19.8	52.8 $\pm$ 11.5	0.20
eGFR (mL/min)	5 $\pm$ 0.5	4.5 $\pm$ 0.7	0.06
Hb (g/dL)	7.4 $\pm$ 3.8	8.9 $\pm$ 2.2	0.14
RBC (X $10^6/\text{mm}^3$)	2.6 $\pm$ 1.1	3.1 $\pm$ 0.8	0.15
WBC (X $10^3/\text{mm}^3$)	6.9 $\pm$ 1.6	8.3 $\pm$ 2.8	0.18
Platelets (X $10^5/\text{mm}^3$)	2.5 $\pm$ 0.1	2.4 $\pm$ 0.7	0.69
CK (U/L)	51.0 $\pm$ 9.9	61.1 $\pm$ 54.3	0.60
CK-MB (U/L)	11.8 $\pm$ 5.4	13.5 $\pm$ 5.8	0.45
Fibrinogen (mg/dL)	411.2 $\pm$ 212.3	580.3 $\pm$ 202.7	0.043*
BUN (mg/dL)	49.2 $\pm$ 15.1	69.5 $\pm$ 24.6	0.023*
Creatinine (mg/dL)	8.7 $\pm$ 2.8	11.1 $\pm$ 2.1	0.010*
Uric acid (mg/dL)	6.3 $\pm$ 0.1	8.4 $\pm$ 2.2	0.011*
Calcium (mg/dL)	8.1 $\pm$ 1.2	7.2 $\pm$ 0.1	<0.001**
Phosphorus (mg/dL)	6.1 $\pm$ 3.2	7.1 $\pm$ 4.9	0.58
Total protein (g/dL)	7.6 $\pm$ 0.1	6.8 $\pm$ 0.9	0.017*
Albumin (g/dL)	4.6 $\pm$ 0.1	3.7 $\pm$ 0.6	<0.001**

Note: Hb: hemoglobin, RBC: Red blood cell; WBC: white blood cell; CK: creatine kinase; eGFR: estimated glomerular filtration rate; Mann-Whitney U test was used. $p \leq 0.05$ was considered statistically significant. *: p-value significant **: p-value highly significant

Table 3 shows showed that the females were in the higher age group with a median age of 59 years, compared to males who had a median age of 49 years. eGFR was markedly decreased in females with median value of 4mL/min compared to males (8mL/min) which was statistically significant ($p=0.016$). Haemoglobin showed a statistically significant decrease in levels in females compared to males ($p=0.001$). RBC, WBC, and platelets did not show any significant difference among the genders. Serum CK, and CK-MB, and fibrinogen did not show statistically significant differences across the genders. Serum total calcium levels were significantly lower in females compared to males ($p=0.046$). (Table 3)

Table 3. Comparison of variables among genders of CKD patients

Variable	CKD males (n=25)	CKD females (n=15)	p-value
Age (year)	49 (41 – 49)	59 (46 – 62)	0.18
eGFR (mL/min)	8 (5 - 10)	4 (4 - 9)	0.016**
Hb (g/dL)	9.4 (8.2 – 10.1)	7.6 (6.8 – 8.2)	0.001**
RBC (X $10^6/\text{mm}^3$)	2.9 (2.74 – 3.49)	2.8 (2.69 – 3.21)	0.19
WBC (X $10^3/\text{mm}^3$)	8.4 (6.1 – 9.6)	8.1 (6.1 – 9.6)	0.72
Platelets (X $10^5/\text{mm}^3$)	2.4 (1.7 – 2.6)	2.4 (1.9 – 2.5)	0.43
CK (U/L)	46 (25 – 77.5)	44 (34 – 74)	0.70
CK-MB (U/L)	10.2 (8 – 16.8)	15 (11 – 19.6)	0.11
Fibrinogen (mg/dL)	374.5 (250.8 – 447)	368.1 (315.3 – 492.3)	0.81
BUN (mg/dL)	43 (38.5 – 58)	46 (36 – 72)	0.32
Creatinine (mg/dL)	9.3 (6.55 – 11.3)	9.9 (5.6 – 10.2)	0.77
Uric acid (mg/dL)	7.6 (6.7 – 8.8)	8.5 (6.6 – 10.1)	0.65
Calcium (mg/dL)	8.0 (7.3 – 8.9)	6.9 (6.5 – 8.0)	0.046*
Phosphorus (mg/dL)	5.2 (3.4 – 8.4)	5.6 (3.9 – 10.3)	0.92
Total protein (g/dL)	6.9 (6.4 – 7.5)	7.2 (5.7 – 7.6)	0.87
Albumin (g/dL)	3.8 (3.2 – 4.2)	4.0 (3.2 – 4.2)	0.84
Globulin (g/dL)	3.3 (2.4 – 3.7)	3.1 (2.4 – 3.4)	0.56

Note: Hb: hemoglobin, RBC: Red blood cell; WBC: white blood cell; CK: creatine kinase; eGFR: estimated glomerular filtration rate; Mann-Whitney

*U test was used. $p \leq 0.05$ was considered statistically significant. *: p -value significant; **: p -value highly significant*

Table 4 shows a comparison of variables among diabetic and nondiabetic CKD patients. Among the study participants, 10 (25%) were diabetics, and 30 (75%) were nondiabetics. CK was significantly elevated in diabetics compared to nondiabetics ($p=0.049$). CK-MB and fibrinogen did not show a statistically significant difference among the groups. In both groups, serum sodium was in the lower limit of the biological reference interval, more so in diabetics ($p=0.049$). Serum potassium was in the upper limit of the biological reference interval, but more prominent in diabetics compared to nondiabetics ($p=0.032$). (Table 4)

Table 4. Comparison of variables among diabetic and nondiabetic CKD patients

Variable	CKD with DM (n=10)	CKD without DM (n=30)	p-value
Age (year)	59 (49 – 68)	55 (41 – 59)	0.10
eGFR (mL/min)	8.5 (4 – 9)	6 (4 – 9)	0.60
Hb (g/dL)	7.8 (7.6 – 9.5)	8.5 (7.6 – 10.1)	0.26
RBC (X $10^6/\text{mm}^3$)	3.0 (2.8 – 3.4)	2.8 (2.5 – 3.3)	0.32
WBC (X $10^3/\text{mm}^3$)	7.4 (5.9 – 10.4)	8.0 (6.1 – 9.4)	0.95
Platelets (X $10^5/\text{mm}^3$)	2.5 (1.8 – 3.1)	2.45 (1.9 – 3.5)	0.51
CK (U/L)	71 (36 – 107)	44 (25 – 60)	0.049*
CK-MB (U/L)	14 (10.2 – 19.8)	11 (8 – 18)	0.36
Fibrinogen (mg/dL)	371.3 (317.6 – 408.7)	370.9 (278.8 – 450.0)	0.96
BUN (mg/dL)	46 (38 – 63)	45 (39 – 58)	0.98
Creatinine (mg/dL)	7.3 (5.3 – 9.8)	9.6 (6.7 – 11.8)	0.13
Uric acid (mg/dL)	8.7 (7 – 10.2)	7.5 (6.4 – 8.7)	0.46
Calcium (mg/dL)	7.5 (6.4 – 8.9)	8.25 (7.2 – 8.8)	0.28
Phosphorus (mg/dL)	5.6 (3.5 – 10.2)	5.2 (3.3 – 10.5)	0.96
Total protein (g/dL)	7 (6.4 – 7.6)	7 (5.8 – 7.6)	0.69
Albumin (g/dL)	4 (3.5 – 4.2)	3.8 (3.2 – 4.2)	0.44
Globulin (g/dL)	2.8 (2.5 – 3.7)	3.2 (2.4 – 3.5)	0.83

*Note: Hb: hemoglobin, RBC: Red blood cell; WBC: white blood cell; CK: creatine kinase; eGFR: estimated glomerular filtration rate; Mann-Whitney U test was used. $p \leq 0.05$ was considered statistically significant. *: p -value significant*

Fibrinogen showed a positive correlation with CK and creatinine ($r=0.32$) and negative correlation with serum calcium ($r=-0.39$). Platelets showed positive correlation with uric acid and phosphorus. Fibrinogen showed negative correlation with calcium, CK-MB with albumin, total protein with BUN and creatinine, uric acid with calcium and albumin. (Table 5)

Table 5. Spearman Correlation among the variables

	RB C	Hb	TC	PL T	C K	C K-M B	FI B	BU N	Cr ea t	U A	Ca	P	TP
H b	0.19												
T C	-0.11	-0.06											
P LT	-0.06	-0.29*	0.48*										
C K	0.08	-0.11	0.08	0.08									
C K-M B	-0.39*	-0.01	0.21	-0.24	0.32*								
FI B	-0.09	-0.15	0.17	-0.24	0.32*	0.01							
B U N	-0.10	-0.06	0.12	0.19	0.08	0.23	0.18						
Cr ea t	-0.18	-0.22	0.00	0.00	0.06	0.12	0.32*	0.18					
U A	-0.03	-0.19	0.26	0.22*	0.34*	0.20	0.05	0.13	0.16				
Ca	0.35*	0.47*	-0.09	-0.19	-0.21	-0.15	-0.39*	-0.39*	-0.19*	-0.60*			
P	-0.13	-0.37*	0.23	0.32*	0.19	0.07	0.14	0.15	0.04	0.26	-0.47*		
T P	0.42*	-0.02	-0.02	0.23	-0.18	-0.10	-0.20	-0.66*	-0.35*	-0.09	0.13	-0.05	

Al	0.1	-	0.4	-	0.4	-	0.3	0.2	0.4	0.1	-	0.4
b	5	0.0	5*	0.1	0.0	4*	0	1	6*	7	1	9*
	3		*	4	3	*	09		*		7	*

Note: Pink coloured cells: Significant positive correlation; Blue coloured cells: significant negative correlation. *: p-value significant; **: p-value highly significant

Discussion

Early stages of CKD are asymptomatic, and clinical features become evident only when the disease progresses to stage 4 and beyond.² GFR progressively decreases as a normal physiological phenomenon beginning around the third to fourth decade of life, with the rate of decline accelerating notably beyond the seventh decade. The concurrent presence of comorbid conditions, abnormal urinary albumin excretion, and raised blood pressure may support the likelihood of disease-mediated pathological changes within the kidney.⁸ In the present study, the mean age of the participants was 52.5 years. Among the study participants, 62.5% were males and 37.5% were females. Around 80% of them were in CKD stage 5, whereas 20% were in stage 4. (Table 1)

Among the study participants, 25% were diabetics and 75% were nondiabetics. (Table 2) Females were in the higher age group with a median age of 59 years, compared to males with a median age was 49 years. eGFR was markedly decreased in females with median value of 4mL/min compared to males (8mL/min) (p=0.016). (Table 3) In the present study, BUN, creatinine and uric acid were significantly higher in CKD stage 5 with p-values 0.023, 0.010 and 0.011 respectively. (Table 2) According to Vodičar J et al., 2018, serum creatinine is a critical marker in predicting survival in HD patients. In ESRD patients, serum creatinine in addition to being a uremic marker, also predicts nutritional status, muscle mass, and survival. ESRD patients have sarcopenia, with lower creatine phosphate stored in the skeletal muscle.⁹ Few patients despite showing a decrease in serum creatinine levels by 1 mg/dL, exhibited high mortality rates, probably due to sarcopenia.¹⁰ (Graphical abstract) Uric acid was higher in the diabetics than in the nondiabetics. (Table 4) The prevalence of gout increases from 1 - 2% (adults with normal kidney function) to 32% (adults with stage 4 CKD).¹¹ Whereas, the prevalence of hyperuricemia also increases from 11% in normal individuals to 80% in CKD stage 4 patients.¹²

In the present study, serum calcium was significantly lower in CKD stage 5 (p<0.001) (Table 2) and they were significantly lower in females compared to males (p=0.046). (Table 3) Serum total calcium was much lower in diabetics compared to nondiabetics. (Table 4) According to Kumar S et al., 2020, the biological reference interval for serum total calcium and phosphorus are 8.8-10.2 mg/dL, and 2.1-5.6

mg/dL, respectively. In their study, 55.7% CKD patients had serum calcium less than 8.8mg/dL, whereas 44.3% patients had normal calcium levels. In 41.4% CKD patients, serum phosphorus was more than 5.6mg/dL and 58.6% individuals serum phosphorus within normal limits.¹³ (Graphical abstract)

CKD patients are prone for cardiovascular calcification (CVC) which can increase the risk of cardiovascular death. In CVC, there is a deposition of calcium-phosphate crystals in the arterial walls and cardiac valves. The vascular smooth muscle cells (VSMCs), macrophages, endothelial cells, and interstitial cells in the blood vessels are involved in the calcification process.¹⁴ The osteochondrogenic differentiation is mediated through transcription factors such as Runx2, osterix, and Msx2.¹⁵ Various mechanisms involved in the vascular calcification include apoptosis, extracellular matrix degradation, synthesis and secretion of abnormal matrix vesicles, increased oxidative stress, cellular senescence, mitochondrial dysfunction, endoplasmic reticulum stress, autophagy, and acquisition of osteogenic microRNA profiles in the extracellular vesicles.¹⁶ There is an imbalance between calcification promoters and inhibitors. In CKD, calcification inducers, such as altered calcium and phosphorus levels, oxidative stress, inflammatory cytokines, and uremic toxins are highly prevalent and calcification inhibitors such as fetuin-A, albumin, ionized magnesium, and vitamin K-dependent anticalcification proteins are decreased.¹⁷ Hyperphosphatemia enhances the differentiation of VSMC into bone or cartilage cells. Calcium causes apoptosis and release of vesicles in VSMC. Coronary artery calcium (CAC) score assists in categorizing the risk of CVD in asymptomatic CKD patients.¹⁸ Hence, it is better to maintain serum calcium levels around 9 mg/dL and phosphorus around 4.5mg/dL to delay CKD progression.¹⁹

In the present study, the mean Hb, RBC count, WBC count, and platelets were 8.8g/dL, 3.1 million cells/mm³, 8200 cells/mm³, and 2.4 lakh cells/mm³ respectively. There were no significant differences among the stages of CKD. (Table 2) Only Hb showed a statistically significant decrease in females compared to males (p=0.001). (Table 3) There were no significant alteration in blood cell markers based due to diabetes mellitus. (Table 4). Anemia of CKD is normocytic normochromic, and it is due to decreased erythropoietin production in the kidneys, abnormal iron metabolism, and reduced red blood cell survival due to accumulation of uremic toxins.²⁰ In HD patients, the target Hb is 10 - 11.5 g/dL. According to the World Health Organization (WHO), the biological reference interval of Hb is 13 - 18 and 12 - 16 g/dL in adult men and non-pregnant women, respectively.²¹ The normal reference interval of RBC count is 4.6 - 6.2 and 4.2 - 5.4 million cells/ μ L in adult men and women,

respectively.²¹ According to Tahir U et al., 2025, there is a decrease in Hb levels from stages 3 to 5. The prevalence of anemia in CKD stages 3, 4 and 5 are 38, 68 and 92.3%, respectively. The RBC count declined from mean value of 4.04, and 3.38 in CKD stages 3 and 5 respectively.²² In the present study, both Hb and RBC count were below the biological reference intervals. In the same study, platelet counts declined from stage 3 to stage 5. The prevalence of thrombocytopenia increased from 14 to 34.3% across stages. Thrombocytopenia is due to reduced thrombopoietin production, impaired maturation, and increased destruction of platelets.²² The present study aligns with this study with the mean platelet count among the participants was 2.4 lakhs/mL. Platelets showed positive correlation with uric acid and phosphorus. (Table 5)

The males had higher platelet levels compared to females. (Table 3) Tahir et al., 2025, found that the WBC count increased with CKD progression. The altered WBC count infers that there is inflammatory background in CKD.²² In the present study, the WBC was higher in stage 5 compared to stage 4 which was statistically not significant. Total protein and serum albumin were statistically decreased in CKD stage 5 with p-values 0.017 and <0.001 respectively. (Table 2) Total protein was negatively correlated with BUN and creatinine. (Table 5) Albumin being a negative acute phase reactant, decreases during inflammatory conditions.

CVD is the leading cause of morbidity and mortality in CKD patients, having a 20-fold higher risk of cardiovascular events compared to the general population.²³ The association of CVD with CKD is multifactorial, involving both traditional and non-traditional risk factors.²⁴ Furthermore uremic toxins, anemia, and disturbances in mineral metabolism contribute to cardiovascular complications.²⁵ Elevated blood pressure (BP) accelerates the progression of kidney damage, and reduced kidney function leads to increased BP due to sodium and fluid retention and activation of the renin-angiotensin-aldosterone system (RAAS).²⁶ (Graphical abstract) Dyslipidemia in CKD is characterized by high levels of triglycerides and low levels of high-density lipoprotein (HDL) cholesterol, which contribute to atherogenesis.²⁷ Moreover, CKD is associated with chronic inflammation and oxidative stress, both of which are key contributors to atherosclerosis and adverse cardiovascular events.²³ Disturbances in calcium, phosphate, parathyroid hormone, and vitamin D metabolism lead to vascular calcification.²⁸ Uremic toxins, such as indoxyl sulfate and p-cresyl sulfate, get accumulated in CKD contributing to CVD.²⁹

In the present study, plasma fibrinogen showed 411.2 ± 212.3 and 580.3 ± 202.7 in CKD stages 4 and 5 respectively with statistically significant p-value of 0.043. (Table 2) as well as across the genders. (Table 3) There was significant difference

in total CK between diabetic and non-diabetic individuals ($p=0.049$). However, CK-MB and fibrinogen did not show statistically significant difference between diabetics and non-diabetics. (Table 4) Fibrinogen was positively correlated with CK and creatinine and negatively correlated with calcium. CK-MB showed negative correlation with serum calcium. (Table 5)

Lin LH et al., 2022, identified an independent association between fibrinogen to albumin ratio (FAR) and CVD prevalence, with FAR also correlating significantly with CVD. Prior studies have reported inverse associations between eGFR and fibrinogen, and positive associations with serum albumin, while both elevated fibrinogen and reduced albumin have been tied to atherosclerotic disease and death in CKD.³⁰ The risk of coronary events increased with increasing fibrinogen plasma concentrations, independent of LDL-c levels. A higher plasma fibrinogen concentration has a similar effect on cardiovascular risk similar to smoking cigarette, obesity, arterial hypertension, and diabetes. Fibrinogen is an acute phase protein, synthesized primarily by the liver under the influence of proinflammatory cytokine, interleukin-6 (IL-6). The production of fibrinogen is also increased by glucocorticosteroids.³¹ Fibrinogen influences atherogenesis after getting converted to fibrin and its degradation products, which are atherogenic in nature. It can also favor lipid deposition in the arteries, thereby initiating inflammation in the endothelium.³² Endothelial microparticles (EMPs) are derived from the endothelium and are released into the circulation even before the onset of significant endothelial damage. This is evident much earlier than the release of vascular markers from the damage subsequent to inflammatory or oxidative damage.³³ (Graphical abstract)

Myocardial infarction and stroke are associated with thromboembolism, especially in diabetics. Diabetics form dense clots with only small pores, which cannot undergo fibrinolysis easily. These clots are more prone for thrombotic episodes. The thrombus consists of fibrin fibres, and network of neutrophil extracellular traps (NETs), NET secretion takes place during the immediate phase of inflammation and they provide a scaffold-like structure for thrombus growth, activate coagulation pathways and platelets. Also, they block the inhibitors of the coagulation pathway. Fibrin along with NETs makes the thrombus stronger, which are resistant to fibrinolysis.³⁴

Fibrinogen directs RBCs along with macrophages to the wound site, thereby increasing viscosity, increasing the size, and stability of thrombus. This interferes with generation of plasmin and increasing clot stability, and decreasing fibrinolysis; thus, contribute to CVD.³⁵ The activity of protein C is decreased in ESRD patients on HD, thus increasing

coagulation tendency and increased thrombotic risk.²⁹ Hence, measurement of fibrinogen could help in reducing mortality due to cardiovascular complications in CKD patients.³⁶

Limitations:

The sample size was small, hence the distribution of patients across the stages of CKD, genders, and associated comorbidities could not be analyzed effectively. Intake of diet, drugs, and other illnesses was not included. Healthy controls were not included. Further larger studies are required.

Conclusion:

Serum fibrinogen levels were higher in CKD stage 5 compared stage 4. Fibrinogen levels correlated positively with creatine kinase and creatinine and negatively with calcium. Creatine kinase was elevated in diabetics compared to nondiabetics. Since the levels of CK and CK-MB could be influenced by the nutritional status of CKD patients, plasma fibrinogen could be a potential biomarker to diagnose cardiovascular complications in CKD patients, thus reducing morbidity and mortality. Further studies are needed to confirm the findings obtained in this study.

Declarations:

Ethics statement

All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was undertaken in a tertiary care centre (SRIHER). Institutional ethics committee (IEC) approval was obtained before sample collection for the conduct of the study. Ethics no. CSP/23/SEP/137/847, dated 10-11-2023. Written informed consent was obtained from all the study participants

Funding: RICERCA – UG students by SRIHER received by Mr. Sashank Sudhakar Sah

Acknowledgments: The authors wish to thank the management of Sri Ramachandra Institute of Higher Education and Research (SRIHER) for providing the required infrastructure to conduct the research.

Use of AI tools: No Artificial Intelligence (AI) tools were used in the writing of this manuscript.

Conflict of interest: The authors declare no conflict of interest.

Data Sharing Statement: All the data are available in the manuscript.

Authors' contributions: Conceptualization: Sashank SS, Sandhya S, Santhi S; Methodology: Sashank SS, Sandhya S, Santhi S; Formal analysis: Sashank SS, Santhi S; Investigation: Sashank SS, Sandhya S, Keerthy RMS, Santhi S; Resources: Sashank SS, Sandhya S; Data curation: Sashank SS, Sandhya S; Writing- original draft: Sashank SS, Sandhya, Keerthy RMS, Santhi; Writing- Review & editing Supervision: Sashank SS, Sandhya S, Keerthy RMS, Santhi S; Project administration:

Sashank SS, Sandhya S, Keerthy RMS, Santhi S; Funding acquisition: Sashank SS. All the authors have contributed equally to writing the final manuscript.

References

1. Murton M, Goff-Leggett D, Bobrowska A, Garcia Sanchez JJ, James G, Wittbrodt E, et al. Burden of Chronic Kidney Disease by KDIGO Categories of Glomerular Filtration Rate and Albuminuria: A Systematic Review. *Adv Ther* 2021;38(1):180-200. doi: 10.1007/s12325-020-01568-8.
2. Vaidya SR, Aeddula NR. Chronic Kidney Disease. [Updated 2024 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535404/>
3. Li Y, Jiang R, Ouyang C, Wang J, Yu Q, Lu J, et al. Chronic kidney disease is associated with increased risk of sudden cardiac death. *Nat Commun* 2025;16(1):9180. doi: 10.1038/s41467-025-64254-9.
4. Yu AS, Pak KJ, Zhou H, Shaw SF, Shi J, Broder BI, et al. All-Cause and Cardiovascular-Related Mortality in CKD Patients With and Without Heart Failure: A Population-Based Cohort Study in Kaiser Permanente Southern California. *Kidney Med*. 2023;5(5):100624. doi: 10.1016/j.xkme.2023.100624.
5. Parul F, Ratnani T, Subramani S, Bhatia H, Ashmawy RE, Nair N, et al. Anticoagulation in Patients with End-Stage Renal Disease: A Critical Review. *Healthcare (Basel)* 2025;13(12):1373. doi: 10.3390/healthcare13121373.
6. Li X, Weber NC, Cohn DM, Hollmann MW, DeVries JH, Hermanides J, et al. Effects of Hyperglycemia and Diabetes Mellitus on Coagulation and Hemostasis. *J Clin Med* 2021;10(11):2419. doi: 10.3390/jcm10112419.
7. Valencia I, Lumpuy-Castillo J, Magalhaes G, Sánchez-Ferrer CF, Lorenzo Ó, Peiró C. Mechanisms of endothelial activation, hypercoagulation and thrombosis in COVID-19: a link with diabetes mellitus. *Cardiovasc Diabetol* 2024;23(1):75. doi: 10.1186/s12933-023-02097-8.
8. Noronha IL, Santa-Catharina GP, Andrade L, Coelho VA, Jacob-Filho W, Elias RM. Glomerular filtration in the aging population. *Front Med (Lausanne)* 2022;9:769329. doi: 10.3389/fmed.2022.769329.
9. Vodičar J, Pajek J, Hadžić V, Bučar Pajek M. Relation of Lean Body Mass and Muscle Performance to Serum Creatinine Concentration in Hemodialysis Patients. *Biomed Res Int* 2018;2018:4816536. doi: 10.1155/2018/4816536

10. McDonnell T, Phillips T, Kalra PA, Fraser SDS, Banks RE, Vuilleumier N, et al. Associations of Creatinine Muscle Index with markers of sarcopenia and mortality in chronic kidney disease: A prospective cohort study. *PLoS Med* 206;23(2): e1004775. doi: 10.1371/journal.pmed.1004775
11. Johnson RJ, Lozada LG, Lanaspa MA, Piani F, Borghi C. Uric acid and chronic kidney disease: still more to do. *Kidney Int Rep* 2023;8(2):229-39. doi: 10.1016/j.ekir.2022.11.016
12. Johnson RJ, Sanchez Lozada LG, Lanaspa MA, Piani F, Borghi C. Uric Acid and Chronic Kidney Disease: Still More to Do. *Kidney Int Rep* 2022;8(2):229-39. doi: 10.1016/j.ekir.2022.11.016.
13. Kumar S, Jha PR, Bavishi N, Pathak KJ. Study of evaluation and correlation of calcium and phosphorus in chronic kidney disease with reference to parathyroid hormone. *Int. J. Adv Med* 2020;7(3):397. doi: 10.18203/2349-3933.ijam20200484
14. Chen S, Tang R, Liu B. Current Understanding of Cardiovascular Calcification in Patients with Chronic Kidney Disease. *Int J Mol Sci* 2024;25(18):10225. doi: 10.3390/ijms251810225
15. Dube P, DeRiso A, Patel M, Battepati D, Khatib-Shahidi B, Sharma H, et al. Vascular Calcification in Chronic Kidney Disease: Diversity in the Vessel Wall. *Biomedicines* 2021;9(4):404. doi: 10.3390/biomedicines9040404.
16. Lee SJ, Lee IK, Jeon JH. Vascular Calcification-New Insights Into Its Mechanism. *Int J Mol Sci* 2020;21(8):2685. doi: 10.3390/ijms21082685.
17. Yamada S, Nakano T. Role of Chronic Kidney Disease (CKD)-Mineral and Bone Disorder (MBD) in the Pathogenesis of Cardiovascular Disease in CKD. *J Atheroscler Thromb* 2023;30(8):835-50. doi: 10.5551/jat.RV22006.
18. Abass NM, Yousef AM, Sabet EA, Kamal YM, El-Rashidy MH. Study of serum calcium and phosphorus levels in chronic kidney disease patients with acute coronary syndrome. *Egypt J Intern Med* 2024;36(1):59. doi: 10.1186/s43162-024-00325-5
19. Tsuchiya K, Akihisa T. The Importance of Phosphate Control in Chronic Kidney Disease. *Nutrients* 2021;13(5):1670. doi: 10.3390/nu13051670
20. Guideline on haemoglobin cutoffs to define anaemia in individuals and populations [Internet]. Geneva: World Health Organization; 2024. PMID: 38530913
21. Gulati G, Uppal G, Gong J. Unreliable Automated Complete Blood Count Results: Causes, Recognition, and Resolution. *Ann Lab Med* 2022;42(5):515-30. doi: 10.3343/alm.2022.42.5.515
22. Tahir U, Akram H, Mahmood R, Nisar Z, Iqbal HZ, Gulfeshan AS, et al. Hematological Indices and Abnormalities in Chronic Kidney Disease and Their Associations with Disease Severity. *Cureus* 2025;17(10):e94222. doi: 10.7759/cureus.94222
23. Samal AK, Lenka DN. Cardiovascular outcomes in patients with chronic kidney disease: an observational cohort study. *Eur J Cardiovasc Med* 2024;14:533-40. doi: 10.61336/ejcm/24-4-68
24. Yellapantula B, Jhunjunwala KD, Bhrushundi M, Sharma R. Prevalence of Cardiovascular Disease in Patients with Chronic Kidney Disease and End-Stage Renal Disease in India: A Cross-Sectional Study. *J Pharm Bioallied Sci* 2025;17(Suppl 1):S630-S633. doi: 10.4103/jpbs.jpbs_1457_24.
25. Lu Y, Meng L, Wang X, Zhang Y, Zhang C, Zhang M. The Non-Traditional Cardiovascular Culprits in Chronic Kidney Disease: Mineral Imbalance and Uremic Toxin Accumulation. *Int J Mol Sci* 2025;26(16):7938. doi: 10.3390/ijms26167938.
26. Kaur J, Rout P. Physiology, Renin Angiotensin System. [Updated 2026 Feb 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470410/>
27. Lacount S, Tannock LR. Dyslipidemia in Chronic Kidney Disease. [Updated 2025 Apr 30]. In: Feingold KR, Adler RA, Ahmed SF, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK305899/>
28. Siracusa C, Carabetta N, Morano MB, Manica M, Strangio A, Sabatino J, et al. Understanding Vascular Calcification in Chronic Kidney Disease: Pathogenesis and Therapeutic Implications. *Int J Mol Sci* 2024;25(23):13096. doi: 10.3390/ijms252313096.
29. El Chamieh C, Liabeuf S, Massy Z. Uremic Toxins and Cardiovascular Risk in Chronic Kidney Disease: What Have We Learned Recently beyond the Past Findings? *Toxins (Basel)* 2022;14(4):280. doi: 10.3390/toxins14040280.
30. Lin LH, Liu H, Jin DH, Zou J, Xie YX, Qiu H, et al. Fibrinogen-to-albumin ratio is related to the severity of coronary artery disease in chronic kidney disease patients undergoing coronary angiography. *Nefrologia* 2022;42(6):696-703. doi: 10.1016/j.nefro.2021.05.007
31. Surma S, Banach M. Fibrinogen and Atherosclerotic Cardiovascular Diseases-Review of the Literature and Clinical Studies.

- Int J Mol Sci* 2021;23(1):193. doi: 10.3390/ijms23010193.
32. Vilar R, Fish RJ, Casini A, Neerman-Arbez M. Fibrin(ogen) in human disease: both friend and foe. *Haematologica* 2020;105(2):284-96. doi: 10.3324/haematol.2019.236901.
 33. Silambanan S, Hermes RS, Bhaskar E, Gayathri S. Endothelial Microparticle as an early Marker of Endothelial Dysfunction in Patients with Essential Hypertension: A Pilot Study. *Indian J Clin Biochem.* 2020;35(2):245-50. doi: 10.1007/s12291-019-00861-w.
 34. de Vries JJ, Hoppenbrouwers T, Martinez-Torres C, Majied R, Özcan B, van Hoek M, et al. Effects of Diabetes Mellitus on Fibrin Clot Structure and Mechanics in a Model of Acute Neutrophil Extracellular Traps (NETs) Formation. *Int J Mol Sci* 2020;21(19):7107. doi: 10.3390/ijms21197107.
 35. Nencini F, Giurranna E, Borghi S, Taddei N, Fiorillo C, Becatti M. Fibrinogen Oxidation and Thrombosis: Shaping Structure and Function. *Antioxidants (Basel)*. 2025;14(4):390. doi: 10.3390/antiox14040390.
 36. Saeed Z, Sirolli V, Bonomini M, Gallina S, Renda G. Hallmarks for Thrombotic and Hemorrhagic Risks in Chronic Kidney Disease Patients. *Int J Mol Sci* 2024;25(16):8705. doi: 10.3390/ijms25168705.