

## Plasma Fibrinogen Level, Homeostatic Alterations And Nitric Oxide Levels in Chronic Renal Disease

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### Abstract:

**Background and objectives:** Recent studies have elucidated the alterations in hemostatic profile in chronic renal disease. This study aims at evaluating the changes in the hemostatic profile in stage III and IV patients of chronic renal disease. **Material and methods:** This case-control study included chronic renal failure patients of stages III, IV and an equal number of matched healthy volunteers. Serum Urea, Creatinine, plasma fibrinogen, bleeding time, prothrombin time, APTT, platelet count, D-Dimer and nitric oxide were estimated in all the patients.

**Results:** a significantly increase plasma fibrinogen level

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### I. Introduction

Chronic renal disease (CKD) is a worldwide health problem associated with prothrombic tendency and bleeding diathesis [1]. Platelet dysfunction, prolonged bleeding time is the other vascular dysfunctions associated with hyperuremic status of CKD [2]. Thrombosis in glomerular arteries and alterations in platelet count are often observed in CKD. Platelets directly contribute to the disease progression in CKD by causing autoimmune deposition in the glomerular apparatus thus, deranging their filtering ability [3]. The platelet dysfunction in CKD is due to intrinsic abnormalities and endothelial dysfunction of the vascular system. The normal physiological response of platelets such as recruitment, aggregation, adhesion to damaged vascular wall is impaired in CKD [4]. Various studies have suggested the association of platelet dysfunction and coagulation abnormalities in CKD [4, 5]. Hypercoagulopathy, impaired fibrinolytic activity predisposing to a thromboembolic phenomenon is observed in renal diseases [5]. The vascular entrance for dialysis in Stage III and IV CKD patients is often affected by thrombosis. Studies reveal upto 60% Of CKD patients with central venous catheter are affected by thrombosis [6]. Altered haemostasis, perioperative bleeding, hypercoagulable state, vascular dysfunction is often found in CKD patients [6,7].

One of the important regulators of hemostasis, vascular endothelial function and renal tubular function is nitric oxide (NO). NO produced in the kidney is responsible for hemostasis, vascular function, sodium excretion and maintenance of arterial blood pressure [7, 8 and 9]. Hence, this study was designed to estimate the Serum Urea, Creatinine, plasma fibrinogen, bleeding time, prothrombin time, APTT, platelet count, D-Dimer and nitric oxide in CKD patients and healthy volunteers. We also aimed to find the association of NO with the above parameters of coagulopathy.

### II. Material and Methods

This case-control study was conducted in the Department of Biochemistry, SCB Medical College during August 2015 to September 2016. We included stage III and stage IV CKD patients undergoing dialysis in the Department of Nephrology, SCB Medical College. The staging was done as per the estimated glomerular filtration rate. The study included three groups: group-1 included age and sex matched healthy volunteers; group-2 included stage III CKD patients; group-3 included stage IV CKD patients. In each group 50 numbers of individuals were included. All patients on antiplatelet therapy, septicemia, and other vascular or bleeding disorders were excluded. Fasting venous blood samples were collected and plasma was used within two hours for estimation of prothrombin time, activated partial thromboplastin time, fibrinogen level and D.dimer. A complete blood cell count (CBC), hemoglobin levels and Erythrocyte sedimentation rates were also done. All the data is represented as mean  $\pm$  standard deviation. The statistical analysis was done by SPSS version 19. An one way ANOVA was done to compare the data and Pearson's correlation analysis was used to establish the relation between the parameters. A p value  $< 0.05$  was considered significant.

### III. Results

The present study included 100 cases of chronic kidney diseases, 50 for stage III and 50 for stage-IV. There were 35 males and 15 females in stage III and 40 males and 10 females in stage IV. In stage III CKD 8

out of 50 patients, had a plasma D.dimer level less than 250 ng/ ml. 32 patients had value 250-500 ng/ml and 4 patients had value in the range of 500-1000 ng/ml. we observed that in stage IV, 6 patients out of 50 had D.dimer level in the range of 250-500 ng/ml. 42patients had 500-1000ng/ml and 2 patients had D.dimer level between 1000-2000ng/ml. Table 1 shows the comparison of the biochemical parameters. We observed significant difference in the plasma fibrinogen levels in the pataients and controls. There was significantly higher level in stage IV CKD pateints. Plasma D- Dimer level was also high in the CKD patients. Plasma nitric acid level was also low in the CKD patients. A significantly lower hemoglobin level, lower RBC, WBC and platelet count was seen in these patients.We observed a significant correlation between the plasma fibrinogen level and nitric oxide level.

**Table 1.** Comparison of the biochemical parameters

Biochemical parameters	Controls	Stage III CKD PATIENTS	STAGE IV CKD PATIENTS
Plasma fibrinogen level (mg%)	152 ± 6.3	268 ± 5.4 <sup>a</sup>	374 ± 5.6 <sup>b,c</sup>
D-Dimer level (ng/ml)	98.1 ± 2.2	200 ± 6.54 <sup>a</sup>	244 ± 6.73 <sup>b,c</sup>
Prothrombin time (sec)	12	12.64±1.66	13.2±0.9
International normalized ratio (INR)	1.1	1.5	1.8
Activated partial thromboplastin time (APTT) (sec)	28	32	38
Platelet count/μL	25x10 <sup>4</sup>	15 x10 <sup>4a</sup>	12 x10 <sup>4b,c</sup>
WBC count/μL	10,000	7,500 <sup>a</sup>	7000 <sup>b,c</sup>
RBC count million cell /μL	5.8	5.2 <sup>a</sup>	4.5 <sup>b,c</sup>
Hemoglobin (g/dl)	14.8	10.6 <sup>a</sup>	10.2 <sup>b,c</sup>
Plasma nitric oxide level (μM/L)	18.6 ± 1.6	24.56 ± 4.2 <sup>a</sup>	39.32 ± 6.8 <sup>b,c</sup>

A depicts a significant difference between stage III CKD patients and controls; b depicts a significant difference between stage IV CKD patients and controls; c depicts a significant difference between stage IV CKD patients and stage III CKD patients.

**Table 2:** Correlation of plasma nitric oxide with plasma fibrinogen

	Plasma fibrinogen	
Plasma nitric oxide level	R= -0.568	p value 0.002

#### IV. Discussions

The present study revealed a s high plasma fibrinogen and D- dimer level in the CKD patients as compared to controls suggesting a hypercoagulable state in these patients. This finding is in congruence with previous studies [10, 11and 12]. We observed a lower platelet, WBC count in the patients [12, 13, 14]. A possible cause for the decrease in cell count could be defective and lowered thrombopoietic activity [15]. These findings explain the common finding of bleeding diathesis in CKD patients and requirement of monitoring and treatment of coagulation disorders in CKD patients[16, 17]. We observed the nitric oxide which correlated with the plasma fibrinogen level suggesting an inflammatory state, endothelial dysfunction and vascular complications[18, 19].

#### V. Conclusion

In conclusion we suggest all the patients of chronic kidney disease should be screened for bleeding tendency, coagulation disorders to avoid vascular complications. We recommened further evaluation with genetic and molecular markers to elucidate the cause of vascular complications in CKD.

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