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Original Article

Prevalence of Abnormal Thrombophilia Profile in Chronic Kidney Disease

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ABSTRACT

Objective: To determine the prevalence of altered thrombophilia in chronic kidney disease.

Study Design: Descriptive retrospective study

Place and duration of study: The study was conducted at Isra University hospital from June 2019 to December 2020

Material and Methods: 150 patients of stage 3, 4 and 5 of chronic kidney disease were enrolled in the study. Patients with stage 1 and 2 chronic kidney disease and on anticoagulation treatment were excluded from study. Stages of chronic kidney disease were classified according to KDIGO criteria. Thrombophilia screening for Antithrombin-III, protein C, protein S, Lupus anticoagulant and Activated Protein C was performed on coagulation analyzer. Findings were recorded and data were analyzed by SPSS version 25

Results: Fifty Seven out of 150 patients were positive for thrombophilia screening with Antithrombin-III deficiency in 28.3%, Protein C deficiency in 7.9%, Protein S deficiency in 3.3%, Lupus anticoagulant in 6.6% and activated Protein C resistance in 2.0%. Out of 43 Antithrombin-III deficient patients, 53.4% (n=23) were on hemodialysis. Out of 12 Protein C deficient patients, 58.3 %(n=7) were on hemodialysis. Out of 10 patients with lupus anticoagulant, 60% (n=6) were on hemodialysis and out of 3 patients with Activated Protein C resistance, 33.3% (n=1) were on hemodialysis.

Conclusion: In this study, Antithrombin-III deficiency was most common finding in CKD and thrombophilia was most common in stage 5 chronic kidney disease and lupus anticoagulant was common finding in relation to hemodialysis. More studies are needed to define true significance of thrombophilia screening in all stages of CKD patients.

Key words: Activated Protein C resistance, Anti thrombin-III, Chronic Kidney Disease, Lupus anticoagulant, Protein C, Protein S, Thrombophilia.

Introduction

Persistent kidney damage evaluated by estimated GFR and evident decrease in kidney function for more than three months is outlined as chronic kidney disease regardless of the source of damage[1]. Major determinants of kidney damage are hypertension, diabetes mellitus, renal stones, obesity and family history[2].

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Ongoing interstitial fibrosis, peritubular capillary loss with hypoxia, and deterioration of functioning nephrons due to atrophy of renal tubules is the final pathway of pathology of chronic kidney disease irrespective of the initial cause of kidney damage[3].

Hemodialysis and kidney transplantation are the specified treatment modalities for end-stage renal patients[4]. Patients on hemodialysis often experience thrombotic events. Thrombotic complications have been described in association with catheter malfunction and AV fistula in up to 25% of patients placed on hemodialysis. Arterial and venous thromboembolism, pulmonary embolism, or graft vessel thrombosis had been seen in approximately 8% of patients[5]. The contributing factors in thrombosis event mainly include low antithrombin level and enhanced thrombin formation, abnormalities of

platelets, protein C, protein S and reduced fibrinolytic activity[6]. Other risk factors of venous thrombosis in CKD patients are same as in normal populations such as bed rest, immobilization, obesity but the risk increases twofold in such patients[7].

Under normal physiological conditions, the coagulation pathway is well controlled. If any injury occurs in blood vessels, the coagulation response is not unrestricted but due to hemostatic derangement in patients with CKD, they are more vulnerable to hypercoagulable states[8,9].

Thromobophilia can be apparent as microvascular occlusion, venous thrombosis and acute rejection of allograft in renal transplant recipients[10]. Studies show that the rate of early graft loss due to venous thromboembolism was significantly elevated in patients with thrombophilia[11]. The patients with ESRD should therefore have an evaluation of their thrombophilia profile before undergoing renal transplantation and anticoagulation should be considered in hypercoagulable state[12,13].

Material and Methods

A retrospective study was conducted at Isra University hospital from March 2020 to December 2020. 150 patients with stage 3, 4 and 5 chronic kidney disease were included for thrombophilia screening. Informed consent was taken from patients prior to including them in the study. Patients on anticoagulation treatment and with stage 1 and 2 were excluded from the study due to issues of false positive results in thrombophilia profile. Chronic kidney disease was classified into stages according to KDIGO criteria.

Thrombophilia screening is performed by venous blood collected in 0.1-M buffered trisodium citrate (blood: citrate, 9:1). Platelet-poor plasma was produced by implementing two centrifugation steps (10 min at 3000 g). Platelet-poor plasma was then aliquoted and stored at −20°C until use.

Anti-thrombin-III, protein C, protein S, lupus anticoagulant, Activated protein c resistance levels were performed by coagulation analyzer and results were recorded.

Data was analyzed on statistical software SPSS version 25. Continuous variables such as age were presented as mean± SD. Categorical variables such as sex were given as numbers (percentages). P –value less than 0.05 will be considered as significant

Results

A total of 150 chronic disease patients participated in the study. The age range of patients was 17-60 years with mean age of 39.43± 9.7 years. Out of 150 patients, 64.5% (n=98) were male and 34.2% (n= 52) were female. 41.4% (n=63) were from urban area and 57.2% (n=87) were from rural area.

TABLE-1: Relationship of thrombophilia screening to CKD stages

	n =150 (%)	Stage 3 n =46 (%)	Stage 4 n = 44 (%)	Stage 5 n =60 (%)	p-value by Chi-square test
Anti-thrombin deficiency	**Yes** 43(28.6)	7 (15.2)	10 (27.7)	26 (43.3)	0.001
	No 107 (71.3)	39 (84.7)	34 (77.2)	34 (56.6)	
Protein C deficiency	**Yes** 12 (8.0)	1 (2.17)	3 (6.8)	8 (13.3)	0.034
	No 138 (92.0)	45 (97.8)	41 (93.1)	52 (86.6)	
Protein S deficiency	**Yes** 5 (3.3)	1 (2.17)	1 (2.2)	3 (5.0)	0.407
	No 145 (96.6)	45 (97.8)	43 (97.7)	57 (95.0)	
Lupus Anticoagulant	**Yes** 10 (6.6)	1 (2.17)	2 (4.5)	7 (11.6)	0.048
	No 140 (93.3)	45 (97.8)	42 (95.4)	53 (88.3)	
Activated Protein C resistance	**Yes** 3 (2.0)	0 (0.0)	0 (0.00)	3 (5.0)	0.058
	No 147 (98.0)	46 (100)	44 (100)	57 (95.0)	

TABLE-2: Relationship of thrombophilia screening to hemodialysis

	n (%)	Hemodialysis	without hemodialysis	p-value
Anti-thrombin Deficiency	**Yes** 43 (28.6)	23 (53.4)	20 (46.5)	0.000
	No 107 (71.3)	11 (10.2)	96 (89.7)	
Protein C deficiency	**Yes** 12 (8.0)	7 (58.3)	5 (41.6)	0.002
	No 138 (92.0)	27 (19.5)	111 (80.4)	
Protein S deficiency	**Yes** 5 (3.3)	0 (0.0)	5 (100)	0.221
	No 145 (96.6)	34 (23.4)	111 (76.5)	
Lupus anticoagulant	**Yes** 10(6.6)	6 (60.0)	4 (40.0)	0.003
	No 140 (93.3)	28(20.0)	112 (80.0)	
Activated protein C resistance	**Yes** 3 (2.0)	1 (33.3)	2 (66.6)	0.658
	No 147 (98.0)	33 (22.4)	114 (77.5)	

Discussion

Patient with chronic renal disease has high prevalence of systemic inflammation and diffuse endothelial damage. As a result of this damage, endothelium modulates the coagulation cascade by inhibiting activated coagulation factors such as factor V and VIII through protein C and S pathway[14].

In our study, 64.5% male presented with CKD which is similar to study conducted by Chang PY in which male were 56.14%[15]. Gender is important in terms of maintaining hemoglobin levels, renal replacement therapy and renal transplant outcome[16].

In this study, we found that 41.4% CKD patients were from urban area and 57.2% were from rural area which in contrast to the other study done in 2002, 74% were from urban area and 26% from rural area[17]. CKD due to unknown etiology and renal stones are the major cause of renal failure in rural area while diabetes mellitus and hypertension are the leading cause of renal failure in urban areas.

In this study, we demonstrated that abnormal thrombophilia profile was seen in 37.5% in which most common deficiency was Antithrombin III i.e. 28.3% which is quite high as compare to other study conducted by Shoaib M which showed 5% antithrombin-III deficiency[18]. Another study by Silva, R 2013 showed 53% abnormal thrombophilia profile and 11% antithrombin-III deficiency in patient prior to renal transplant[19]. On vascular endothelium, antithrombin-III has both anticoagulant and anti-inflammatory action. Low anti thrombin III in chronic kidney disease is mainly due severe proteinuria which in result causes further renal damage[20].

In our study, 7.9% and 3.3% showed deficiency of protein C and protein S while lupus anticoagulant was seen in 6.6% in comparison to study by Ghisdal L in which 12.1% and 3.7% showed protein C and protein S deficiency and lupus anticoagulant was seen 37.7% [21].In our study, lupus anticoagulant was common finding in patient with hemodialysis which is similar to the other study in which lupus anticoagulant was seen in 69.8% which were on hemodialysis[22]

In our study, abnormal thrombophilia was more common in stage 5 CKD. The risk of thromboembolism increases with increasing impaired kidney function. In end stage renal disease, risk of thromboembolism increases by about 5.5 times. Thrombophilia screening is important for candidate waiting for renal transplant because renal transplantation is a major surgical procedure and risk of thromboembolism is high during and after procedure

Conclusion

Thrombophilia screening in chronic kidney disease aids the physician to start appropriate anticoagulation at appropriate time. More studies are needed to define true significance of thrombophilia screening in all stages of CKD patients.

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A. Conception/Study/Designing/Planning
B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion