Original Article

Impact of Haemodialysis on Coagulation Profile in Chronic Kidney Disease

Veena Raja[1]*, Shivashekar Ganapathy[1], Suresh Kumar Karthikean[2] and Pradhiksha Das Prakash[2]

[1]Department of Pathology, SRM Medical College Hospital and Research Centre, SRM IST, Potheri, Chengalpattu - 603203
[2]Department of Forensic Medicine, ACS Medical College and Hospital, Chennai - 600077

ABSTRACT

Background: Chronic kidney disease (CKD) with its high prevalence, morbidity and mortality is an important public health problem. Considering the nature of the haemodialysis process, it has a considerable impact on the coagulation profile. To find out the variations in Platelet count, Prothrombin time (PT), International Normalised Ratio (INR) and Activated Partial Thromboplastin Time (aPTT) before and after haemodialysis patients.

Materials and Methods: This prospective observational study of Coagulation profile and platelet count in pre and post hemodialysis patients with chronic renal failure was conducted on 150 CKD patients in the Department of Pathology, SRM Medical College Hospital & Research Centre. p value <0.05 was considered to be statistically significant.

Results: In this study, there was significant reduction in platelet count from mean 2.29 cells/cu.mm in pre dialysis to 2.03 cell/cu.mm in post dialysis. There was a significant prolongation in both PT and aPTT values in post dialysis

Conclusion: These findings expose CKD patients to higher risk of bleeding disorders, which may have a role in increasing the rate of patient mortality and morbidity. In the light of this study, there is a need for nephrologist to monitor the coagulation profile and platelet count of CKD patients on dialysis, and treat any derangements in the same, so as to improve outcome for these patients.

Keywords: Chronic Kidney Disease, Coagulation Profile, Hemodialysis, Bleeding Disorders, Thrombocytopenia

Introduction

Chronic kidney disease (CKD) is a global health problem, with a very high cost of care and a great burden particularly in developing countries like India. The Kidney Disease Outcomes Quality Initiative describes 5 stages of CKD, with the Stage 5 being End Stage Renal Disease (ESRD) which is characterized by progressive, irreversible deterioration in the renal function and the body failing to maintain fluid and electrolyte balance resulting in uraemia[1]. In CKD both bleeding and thrombotic complications are observed mainly because of disturbed balance between pro and anti-haemostatic factors, leading to high morbidity and mortality[2]. Due to the high cost and difficulty in finding a compatible organ donor associated with transplantation, dialysis remains as one of the most common modalities of RRT worldwide[3].

Haemodialysis (HD) results in alterations of platelet function and changes in both coagulation and fibrinolytic systems. Platelets have been well-known to interact with dialysis membranes since the 1970's; dialysis membranes have been shown to cause platelet adhesion, aggregation, and activation[4]. Thrombotic events result from variations in vessel wall integrity, platelet activation

and reduced blood flow into the fistula used to access the vessel. Hypercoagulability states are associated with cerebral spill, cardiac disease and pulmonary embolism. Both PT (Prothrombin time) and aPTT (activated Partial Thromboplastin time) tend to increase post dialysis. In cases where fistulas of polytetrafluorethylene (PTFE) is used, increased coagulation has a risk for thrombus formation in vascular access for dialysis [5]. The aim of the study is to find out the variations in platelet count, PT, International Normalised Ratio (INR) and aPTT before and after HD. The present study might help the clinicians to initiate proper precautions before and after the dialysis procedures.

Materials & Methods

This prospective observational study of coagulation profile and platelet count in pre and post hemodialysis patients with chronic renal failure was conducted in the Department of Pathology in collaboration with the Department of Nephrology, SRM Medical College Hospital & Research Centre and approved by our Institutional Ethical Committee. A total of 150 patients diagnosed as CKD and subjected for hemodialysis were included in this study. An informed consent was obtained from all the subjects. Hematological
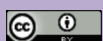
changes were assessed before and after dialysis, by taking into account the parameters such as platelet count, PT, INR and aPTT. Patients of all age group and gender diagnosed as Chronic Kidney Disease in the Department of Nephrology and initiated for renal replacement therapy in the form of hemodialysis were included in this study.

Patients suffering from muscular atrophy, malignancy, inherited or acquired blood diseases, hepatitis or other liver diseases, infection, acute or chronic inflammation, connective tissues diseases, dehydration, or recent haemorrhagic episode were excluded from this study.

Clinical history of Age, Gender, Cause of the disease, Duration of hemodialysis and associated co-morbid illness (diabetes, hypertension) were recorded.

The parameters assessed for each case included:

a. **Platelet count:** Under aseptic precautions, two millilitres of venous blood were obtained by routine phlebotomy procedure from renal failure patients before and after hemodialysis within 2hours. The samples were collected in an Ethylene Diamine Tetra Acetic Acid (EDTA) vacutainer and analysed within 2 hours for platelet count using Sysmex XT 1800i (automated haematology analyser).

b. **PT & aPTT:** 2.7ml venous blood before dialysis and after dialysis within 2 hours was collected in vacutainer containing anticoagulant of 3.2% trisodium citrate (0.3ml). The international sensitivity index (ISI) of the reagent used was 0.95, where the PT of the control sample was calculated to be 13 seconds & aPTT of the control sample was calculated to be 31 seconds using semiautomated analyser (Stago START 4). The International Normalised Ratio (INR) was calculated according to the chart provided by the reagent supplier (Hemosil).

Statistical Analysis

Statistical analysis was done using SPSS software 17.0. Chi square test was used for the comparison between two proportions. p value <0.05 was considered to be statistically significant.

Results

In present study, out of 150 CKD patients, 104 (69.3%) were males and 46 (30.7%) were females. The total number of cases were compared between males and females and was not statistically significant (Table 1).

The most common primary etiology for ESRD leading to dialysis was patient suffering from hypertension 46% followed by diabetes 30.7%. The other causes included chronic glomerulonephritis (8.7%), Adult Polycystic Kidney Disease (APCKD, 1.3%), renal calculi (3.3%), drug induced (2%), Ig A nephropathy (2%), lupus nephritis (2%), sea food allergy (0.7%) and Chronic tubulointerstitial disease (3.3%, Table 2).

The platelet count ranges from 69,000-7,05,000/mm^3 and 56,000 – 6,50,000/mm^3 in pre dialysis and post dialysis respectively. There was significant reduction in platelet count from mean 2.29/mm^3 to 2.03/mm^3 in post dialysis when compared to pre dialysis value. This value was statistically significant with a p value of 0.0001 (Table 3).

In this study, among pre dialysis a normal platelet count was noted in 85.3%, mild thrombocytopenia in 10.7% and moderate thrombocytopenia in 4%. Normal platelet count was present in 70%, cases with mild thrombocytopenia was increased to 22% in post dialysis when compared with pre dialysis and cases with moderate thrombocytopenia was increased to 8% when compared with pre dialysis values which was statistically significant (Table 4).

There was significant prolongation of prothrombin time from mean 15.99 sec and mean INR 1.21 to a mean value of 22.01 sec and mean INR 1.65 in post dialysis when compared to pre dialysis. There was statistically significant prolongation of aPTT in post dialysis with mean of 47.73 sec when compared to pre dialysis value with mean of 40.31sec (Table 5).

Table 1: Age and gender distribution of CKD patients.

Age group	Female (n=46)		Male (n=104)		Chi Square & p value
	N	%	N	%	
21 – 30	3	6.5%	4	3.8%	x^2= 3.382 p= 0.496
31 – 40	7	15.3%	12	11.5%	
41 – 50	11	23.9%	17	16.4%	
51 – 60	14	30.4%	33	31.8%	
>60	11	23.9%	38	36.5%	

Table 2: Causes of ESRD leading to dialysis.

Causes of CKD	No. of cases(n=150)	Percentage of patients
Hypertensive nephrosclerosis	69	46%
Diabetic nephropathy	46	30.7%
Chronic glomerulonephritis	13	8.7%
APCKD	2	1.3%
Renal calculi	5	3.3%
Drug induced	3	2%
Ig A nephropathy	3	2%
Lupus nephritis	3	2%
Sea food allergy	1	0.7%
Chronic Tubulointerstitial diseases	5	3.3%

Table 3: Platelet count in pre and post dialysis values of CKD patients

Period	Platelet count(/mm^3)		Paired T test	p value
	Mean	Standard error of mean	14.352	0.0001
Pre dialysis	229260.00	8439.37		
Post dialysis	203760.00	7653.97		

Table 4: Grading of platelet count in pre and post dialysis values of CKD patients

Grading of platelet count	Pre dialysis		Post dialysis		Chi square & p value
	Cases	%	Cases	%	
Normal platelet count	128	85.3%	105	70%	x^2= 10.17 & p=0.006
Mild thrombocytopenia	16	10.7%	33	22%	
Moderate thrombocytopenia	6	4%	12	8%	

Table 5: Mean PT, INR & aPTT in pre and post dialysis values of CKD patients.

Parameters	Pre dialysis (n=150)	Post dialysis (n=150)	Paired T test	p value
PT	15.99 ± 0.43	22.01 ± 0.47	-35.208	0.0001
INR	1.21 ± 0.03	1.65 ± 0.03	-35.109	0.0001
aPTT	40.31 ± 1.91	47.73 ± 1.91	-49.483	0.0001

Table 6: Platelet, PT and aPTT in post dialysis compared to pre dialysis with previous studies.

Study	Year	Cases	Platelet	PT	aPTT
Pahim et al [2]	2017	160	Increased	No change	Increased
Mandi et al [14]	2016	30	Increased	Decreased	Decreased
Alghythan et al [11]	2012	100	Decreased	Increased	Increased
Khan et al [12]	2015	100	Decreased	Increased	Increased
Present study	2018	150	Decreased	Increased	Increased

Discussion

HD is the most common modality for renal replacement treatment in India where near normal kidney function is attained in CKD patients with the use of HD machine. There is an averse improvement in the life expectancy of CKD patients on HD over a long period of time and thus the need to interpret hematological comorbidity associated with CKD[6]. Among 150 patients undergoing HD and enrolled for the study, 104(69.3%) were males with the maximum age of >60years and 46(30.7%) were females, the maximum number of patients were from the age group 51-60 years. This could be explained due to the cause that most of the patients were identified with hypertensive nephrosclerosis followed by diabetic nephropathy which is prevalent above 50years[7]. Similar findings were reported in studies conducted by Gautam et al[3] and Hakim et al[4] where CKD patients were above 50years of age.

Hemodialysis decreases the percentage of RNA-rich platelets through elimination of the younger and more active platelets and worsen the thrombocytopenia present in uremic patients[8]. Some of the activation and aggregation of platelets during dialysis may be due to exposure of blood to the roller pump segment of the dialysis tubing or to microbubbles and does not depend on exposure to the dialyzer membrane per se. With regard to dialyzer membranes, platelet activation seems to be reduced with reused dialyzers and with synthetic versus cellulosic membranes. The platelet count decreases during dialysis, but this decrease is usually small, tends to be maximal at 15–30min into dialysis, and mostly resolves by the end of dialysis[9]. Unfractionated heparin (heparin) is the most commonly used anticoagulant for HD. It is well-known that heparin can cause immune-mediated thrombocytopenia due to immunoglobulin antibody formation against the complex of platelet factor 4 (PF4) and heparin (HIT antibodies). Heparin may also contribute to HD associated platelet activation, thrombocytopenia, and increased PF4 release from platelets during a heparin dialytic session[10].

From the present study we found that there was a marked significant change in the coagulation profile among CKD population. Platelet count decreased among the post dialysis when compared with the pre dialysis value. In this study, there was significant reduction in platelet count from mean 2.29 cells/cu.mm in pre dialysis to 2.03 cell/cu.mm in post dialysis. The percentage of cases towards thrombocytopenia increased after dialysis when compared to pre dialysis. Normal platelet count was present only in 70%, cases with mild thrombocytopenia was increased to 22% in post dialysis when compared with pre dialysis and cases with moderate thrombocytopenia was increased to 8% when compared with pre dialysis. In spite of adequate

heparin anticoagulation, platelets have been known to interact with dialysis membranes and have been shown to cause platelet adhesion, aggregation and activation [4]. These results were compared with the study done by Alghythan et al and Khan et al in which there were similar findings as in our study[11,12].

In our study there was a significant prolongation in both PT and aPTT values (Table 5). Prothrombin time was increased in post dialysis when compared with pre dialysis values. There was significant prolongation of prothrombin time from mean 15.99 sec in pre dialysis to mean 22.01 sec in post dialysis. This is due to regular heparin dosage administered during the process of dialysis[13]. There was also prolongation of aPTT in post dialysis with mean 47.73 sec compared to pre dialysis mean of 40.31 sec.The reason for increase in aPTT level is due to anticoagulant (heparin) usage in HD which binds to the enzyme inhibitor antithrombin III. This results in the inactivation of thrombin and other proteases involved in blood clotting particularly FXa [11]. Alghythan et al[11] and Khan et al[12] showed similar results where, PT and aPTT increased after dialysis as shown in Table 6. Mandi et al [14], observed PT and aPTT decreased following dialysis, which was in contrast with the present study.

Limitations of The Study

Follow up of patients more than one dialysis visit could not be done due to the irregular visit of the patients for the dialysis procedure.

The state of morbidity and mortality of the patients could not be assessed as most of the patients were discharged after dialysis procedure.

Conclusion

Hypertensive nephrosclerosis is the most common cause of CKD. This may be an indicator of lack of blood pressure control in hypertensive patients. Post dialysis values of platelet count were found to be decreased than pre dialysis values. Coagulation studies like prothrombin time and activated partial thromboplastin time were prolonged after hemodialysis. These findings expose CKD patients to higher risk of bleeding disorders, which may have a role in increasing the rate of patient mortality and morbidity. Therefore, monitoring of coagulation parameters (prothrombin and activated partial thromboplastin time) may help the clinicians to determine the risk of development of bleeding complications.

Declaration

Ethical Approval: Approved by Institutional Ethical committee

Funding

None

Competing Interest

None declared

References

1. Habib A, Ahmad R, Rehman S. Hematological changes in patients of chronic renal failure and the effect of hemodialysis on these parameters. Int J Res Med Sci. 2017;5(11):4998–5003

2. Pahim H, Megalamane S. Platelet Indices and Basic Coagulation Profile of Type 2 Diabetic Patients undergoing Haemodialysis in Rural Population. J Clin Diagnostic Res. 2017;11(10):9–12

3. Gautam R, Patil PM. Hematological Changes in Pre and Post Hemodialysis in Patients With Chronic Renal Failure. J Evid Based Med Health. 2018;5(25):1914–9

4. Hakim YAH, Abbas AA, Khalil A, Hameeda T, Mustafa IA. The Effect of Hemodialysis on Hemoglobin Concentration, Platelets count and White Blood Cells Count in End Stage Renal Failure. Int J Med Res Heal Sci. 2016;5(5):22–35

5. Jalal DI, Chonchol M, Targher G. Disorders of hemostasis associated with chronic kidney disease. Semin Thromb Hemost. 2010;36(1):34–40

6. Chakravarti A, Ukey A, Bajaj P, Saragade P. A Study of Hematological Profile in Patients of Chronic Renal Failure Undergoing Hemodialysis at a Tertiary Health Care Institute. MVP J Med Sci. 2017;4:107–12

7. Kovesdy CP, Alrifai A, Gosmanova EO, Lu JL, Canada RB, Wall BM, et al. Age and outcomes associated with BP in patients with incident CKD. Clin J Am Soc Nephrol. 2016;11(5):821–31

8. Pandian J, Amitkumar K, Swaminathan A. Assessment of impact of hemodialysis on hematological parameters among patients with chronic kidney disease. Comp Clin Path. 2017;26(1):213–8

9. Daugirdas JT, Bernardo AA. Hemodialysis effect on platelet count and function and hemodialysis-associated thrombocytopenia. Kidney Int. 2012;82(2):147–57

10. Matsuo T, Wanaka K. Heparin-Induced Thrombocytopenia and Hemodialysis. J Blood Disord Transfus. 2011, S2

11. Abdullah Khader Alghythan and Abbas H. Alsaeed. Hematological changes before and after hemodialysis. Sci Res Essays. 2012;7(4):490–7

12. Khan MZ, Akhtar SZ, Pervez SN, Khan MS, Malik A. Coagulation profile in pre and post hemodialysis. Int J Applied Res. 2015;7(1):33–6

13. Khalid A, Zafar L. Effect of Haemodialysis on Mean Prothrombin Time and Activated Partial Thromboplastin Time in Patients of End Stage Renal Disease. J Rawalpindi Med Col. 2015;19(3):247–9.

14. Mandi SP, Ghosh K, Chakraborty S, Pal M, Koley S, Comparative study of standard coagulation profile in non-dialyzed and post-dialyzed patients suffering from chronic kidney disease. Journal of Drug Delivery & Therapeutics. 2016;6(3):78-83.

*Corresponding author:
Dr. Veena Raja, 902, B-Block, 8th Floor, Gate no. 35, SRM Medical Staff Quarters, SRM IST, Potheri – 603203, Chengalpattu District, Tamilnadu
Phone: +91 9600385030
Email: drveenaraja88@gmail.com