International Journal of Advances in Medicine
Lokesh S et al. Int J Adv Med. 2016 Aug;3(3):559-563
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20162022

Research Article

A comparative study of platelet parameters in end stage renal disease patients undergoing haemodialysis and healthy individuals

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Received: 20 June 2016
Accepted: 25 June 2016

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ABSTRACT

Background: With the rising trend of diabetes mellitus and hypertension in developing countries like India, there is also a rise in chronic complications like end stage renal disease (ESRD). ESRD poses a huge financial burden on family and health care sector due to a high morbidity and mortality associated with it. Cardiovascular complications remain the most common cause of death among ESRD patients and those undergoing hemodialysis (HD). Hemodialysis patients behave in a distinct way that they are relatively more prone for bleeding than thrombotic manifestations. In recent days abnormalities in platelet parameters are found to be an effective tool in risk stratification of patients with chronic kidney disease (CKD) to develop coronary artery disease. Due to scarcity of literature especially from India, the present study was taken to find the association of various platelet parameters among hemodialysis patients. The aim was to study the platelet distribution width (PDW), mean platelet volume, platelet count, plateletcrit and platelet large cell ratio (PLCR) among ESRD patients undergoing maintenance hemodialysis and compare with healthy age and sex matched controls.
Methods: The present study was done on two groups. Group A (Cases) consisting of 40 ESRD patients receiving HD for more than 6 months, and group B (controls) consisting of 40 healthy controls from hospital staffs and healthy volunteers matched for age and sex.
Results: The mean values of platelet distribution width (PDW), mean platelet volume, platelet count, plateletcrit and platelet large cell ratio (PLCR) were found to be lower in cases when compared to healthy controls. PDW, platelet count and plateletcrit attained statistical significance, while others did not.
Conclusions: Abnormality in platelet parameter to assess CVD risk may be applicable in general population as well as in CKD patients, but its role in hemodialysis patient's further need to be evaluated.

Keywords: Chronic kidney disease, Hemodialysis, Coronary artery disease, Cerebrovascular disease, Platelet distribution width, Mean platelet volume, Platelet large cell ratio

INTRODUCTION

Haemodialysis (HD) remains an important form of renal replacement therapy (RRT) in end stage renal disease (ESRD) patients, in developing countries like India it still remains a primary modality of treatment due to growing numbers of ESRD and lack of adequate donors and transplantation centers. The principal cause of morbidity

and mortality in haemodialysis patients remains cardiovascular events. There are various factors predisposing for cardiovascular risk like worsening hypertension, uraemic toxins, oxidative stress, lipid abnormalities and inflammation.

Abnormalities in platelet parameters like mean platelet volume (MPV), platelet distribution width (PDW), platelet count, plateletcrit and platelet large cell ratio (PLCR) are studied extensively in patients with coronary artery disease (CAD) and cerebro vascular disease (CVD), both in general population as well as patients with risk factors like diabetes mellitus (DM), hypertension and chronic kidney disease (CKD).[1,2] The abnormal values are associated with increased risk of thrombotic events among patients with above said risk factors. Hemodialysis patients behave in a distinct way where they tend to develop higher bleeding manifestations than thrombotic complications when compared to other high risk patients. The present study was taken up to evaluate the platelet parameters among ESRD patients undergoing hemodialysis.

Even after an extensive literature search we could not find any previously published data from India that have evaluated abnormalities in platelet parameters among patients undergoing hemodialysis.

METHODS

The present study was done on 80 subjects, which included both male and female subjects in the age group of 30-60 years.

Group A (cases) included 40 patients with end stage renal dialysis (ESRD) undergoing intermittent haemodialysis for more than 6 months at Mahatma Gandhi Medical College and Research Institute (MGMCRI). All patients were undergoing three sessions of haemodialysis in a week with each lasting for 4 hours using bicarbonate buffer with a blood flow of 250 ml/min and dialysate flow of 500ml/min, with 1.6 m^2 surface area hollow fiber polysulfone membrane dialyzer.

Group B (controls) included 40 apparently healthy adult male and female volunteers with normal renal function who were employees of MGMCRI hospital, Puducherry, India and individuals who attended health checkups. Patients with septicaemia, past history coronary artery disease/cerebrovascular disease and patients receiving antiplatelet medications were excluded from the study.

This study was done in conformity with the declaration of Helsinki and it was approved by institutional human ethics committee of Mahatma Gandhi Medical College and Research Institute, Puducherry, India.

All the participants were interviewed and a full medical, substance abuse and occupational history and previous history of vascular events were taken. The duration of maintenance HD, presence of any co-morbidities, dietary history and current medication history was taken from participants of group A.

A pre-hemodialysis 5 ml of blood sample was withdrawn from participants of group A, and fasting levels of 5ml blood from participants of group B. The blood samples were processed by fully automated bidirectional analyser by hydrodynamic focusing and flow cytometry method.

The SPSS, version 19 software tool was used for the data processing. All the values were expressed as mean±standard deviation unless otherwise indicated. The differences in the mean values between the groups were analyzed by using the Student's t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

In the present study we had 80 participants. The gender distribution was predominantly male in both groups. There was a significant difference in blood urea nitrogen, serum creatinine, SBP and DBP among group A and group B (Table 1).

Table 1: Baseline characters among cases and controls.

Parameters	Group A Cases	Group B Controls
Total number (N)	40	40
Sex		
Male	33	32
Female	07	08
Age	48.30±10.95 years	48.18±9.73 years
Addictions	Nil	Nil
Comorbidities		
Diabetes mellitus	40	Nil
Hypertension	35	Nil
Systolic blood pressure (SBP)	156.25±22.15 mm Hg	121.38±7.97 mmHg
Diastolic blood pressure (DBP)	93.75±13.90 mmHg	75.06±5.768 mmHg
Blood urea nitrogen (BUN)	53.75±17.75 mg/dl	12.12±3.33 mg/dl
Serum creatinine	10.07±2.77 mg/dl	0.79±0.13 mg/dl

Diabetes and hypertension was the common co-morbidities found in cases. The mean values of platelet distribution width (PDW), platelet count and plateletcrit was found to be 13.51±2.08 fL Vs 14.99±2.57 fL, 2.30±0.74 lakh/cumm Vs 2.80±1.17 lakh/cumm and 0.25±0.83% Vs 0.34±0.15% among cases and controls which was found to be statistically significant with a p-value of 0.006, 0.025 and 0.002 respectively (Table 2).

Table 2: Mean values of platelet indices among cases and controls.

Platelet indices	References	Cases	Control	P-value
PDW	9.6-15.2 fL	13.51± 2.08	14.99± 2.57	O.006
MPV	6.5-12.0 fL	11.37±1.26	11.43±1.22	0.809
PLT count	1.5-4.5 lakh/cumm	2.30±0.74	2.80±1.17	0.025
PLCR	19.7-42.4%	35.70± 7.45	37.95±7.63	0.187
plateletcrit	0.19-0.39%	0.25±0.83	0.34±0.15	0.002

The average values of mean platelet volume (MPV) and platelet large cell ratio (PLCR) among cases and controls was found to be 11.37±1.26 fL vs 11.43±1.22 fL (p=0.809) and 35.70±7.45 % vs 37.95±7.63 % (p=0.187) respectively, which was not found to be statistically significant (Table 2).

DISCUSSION

The mean level of PDW was found to be significantly lower among cases as compared to controls, which was found to be statistically significant with p value of 0.006 (Table 2, 3). M. Schrool et al observed a post haemodialysis decline in PDW as compared to pre haemodialsis levels which was found to be significant.[3,4] They also observed a post haemodialysis decline of PDW by 11%. Out of 40 cases, 09 (22.5%) had higher levels of PDW as compared to 16 (40%) in controls, the levels were significantly lower in cases as compared to controls. Mehmet Koroglu et al in their study found that there was no significant variation in PDW between dialysis and CKD patients.[5] PDW increase during platelet activation and thereby can predict activation of coagulation more efficiently in general population.[6] There are limited data to support its role on HD patients.

Table 3: Mean levels of platelet distribution width among cases and controls.

PDW	Cases (%)	Controls (%)	P-value
9.6-15.2 fL	31 (77.5)	24 (60)	0.091
> 15.2 fL	09 (22.5)	16 (40)	

Table 4: Mean platelet volume among cases and controls.

MPV	Cases (%)	Controls (%)	P-value
6.5-12.0 fL	28 (70)	29 (72.5)	0.805
> 12.0fl	12 (30)	11 (27.5)	

Mean platelet volume (MPV) reflects the average platelet size and it tends to be larger when body produce more numbers of platelets. In this study the MPV among cases was 11.37±1.26 fL as compared to 11.43±1.22 fL in control group (Table 2, 4), which was not found to be statistically significant (p=0.809).

Berssman JD et al in their study observed hyperdestructive causes to be the common cause of high MPV with low platelet count, thalassemia to be the commonest cause of high MPV with normal platelet count, myeloproliferative disorders and inflammation to be the commonest cause of high MPV with increased platelet count.[7] They also observed that MPV was low in patients with chronic renal failure independent of platelet count, an observation similar to this study.

In this study out of 40 cases studied, 12 (30%) had MPV of >12.0 fL as compared to 11 (27.5%) control population which was not found to be significant. Pal R et al observed that the MPV was significantly higher among patients with acute coronary syndrome than in patients presenting with non-cardiac chest pain.[1] Similar high MPV was also observed by Murat SN et al in CAD patients and they concluded MPV to be a marker of coronary atherosclerosis.[2] R.Pal et al and Muran SN et al did not include patients with CKD in their study.[1,2] Koroglu M et al observed a high MPV in CKD patients and concluded that MPV can be used as a biomarker to estimate atherosclerosis risk in CKD patients and patients on hemodialysis.[5]

This study have conflicting reports on implication of MPV as a predictor of atherosclerosis in hemodialysis patients as compared to the general population, a low MPV observed in this study probably may be due to platelet aggregation and activation when it comes in contact with the semipermeable membrane of the dialyzer.[8,9] The observation in this study of low MPV among hemodialysis patients limits its role as a predictor of atherosclerosis in patients on chronic hemodialysis when compared to general population.

In this study the average platelet count was found to be 2.30±0.74 lakh/cumm among cases as compared to 2.80±1.17 lakhs/cumm among controls (Table 2, 5), which was found to be statistically significant (p=0.025). None of our cases and controls had thrombocytopenia, whereas 2 (5%) cases had platelet counts of >4.5 lakhs/cumm as compared to 4 (10%) among control group (p=0.675). Alghythan AK et al observed that the mean platelet count in pre HD patients was $199.19\pm56.74x10^3$ as compared to controls with a platelet count of $262.32\pm48.00x10^3$ which was statistically significant (p<0.001).[10]

Table 5: Mean platelet count among cases and controls.

PLT count	Cases (%)	Controls (%)	P-value
1.5-4.5 lakh/cumm	38(95)	36(90)	0.675
> 4.5 lakh/cumm	2(5)	4(10)	

They also observed further fall of platelet count to 176.86±56.08x10^3 after hemodialysis. Schoorl et al observed that chronic hemodialysis patients had lower range of platelet counts within the reference limits, they also witnessed a drop of 13% after the first passage of blood along the dialysis membrane at t=1 min after starting hemodialysis.[3,4] The probable cause for a low normal platelet counts among chronic hemodialysis patient is likely to be due to platelet degranulation due to platelet activation and adherence in the dialyzer.

The mean plateletcrit among cases was 0.25±0.83% as compared to 0.34±0.15% among controls which was found to be significantly lower (p=0.002) (Table 2,6). Out of 40 cases, 12 (30%) patients had a high plateletcrit as compared to 11 (27.5%) in control group, which was not statistically significant. Koroglu M et al, in their study found that patients on hemodialysis had relatively lower plateletcrit as compared to controls.[5] They also observed that CKD patients had much higher values of plateletcrit when compared to controls as well as hemodialysis patients, which was found to be statistically significant. A higher plateletcrit in CKD patients was attributed to chronic inflammation which probably may increase the risk of atherosclerosis. The use of plateletcrit as a biomarker for atherosclerosis in hemodialysis patients remains controversial and mandates further larger studies to support its use.

Table 6: Mean plateletcrit among cases and controls.

Plateletcrit	Cases (%)	Controls (%)	P-value
0.19-0.39%	28(70)	29(72.5)	0.805
>0.39%	12(30)	11(27.5)	

Table 7: Mean platelet to large cell ratio among cases and controls.

PLCR	Cases (%)	Controls (%)	P value
19.7-42.4%	33(82.5)	30(75)	0.412
>42.4%	7(17.5)	10(25)	

The mean platelet large cell ratio (PLCR) among cases was found to be 35.70±7.45% as compared to 37.95±7.63% in control group which was not found to be significant (p=0.187) (Table 2,8). Out of 40 cases, 7 (17.5%) cases and 10 (25%) controls were found to have higher levels of PLCR which again was not significant (p=0.412). Schoorl M et al, in his study observed a similar lower mean PLCR of 29.0±7.4% and further a 6% decline from the baseline value at t=150 min of hemodialysis.[3,4] PLCR falls significantly in thrombocytosis while it rises in thrombocytopenia.[11]

CONCLUSIONS

The platelet parameters are extensively studied in association with coronary artery disease, cerebrovascular disease, chronic kidney disease, obesity etc, and it is found to be a reliable predictor of underlying inflammation and severity of atherosclerosis. But its use in hemodialysis patients appears to be controversial as all these parameters are lesser than that observed in control population, thus rising suspicion on its clinical utility in this subset of patients. Further studies with larger sample size are required to delineate its role in hemodialysis patients especially involving Indian patients.

ACKNOWLEDGEMENTS

Authors are thankful to Shri M.K.Rajagopalan, Chairman Sri Balaji Vidyapeeth University for his help and support. They also acknowledge the support and cooperation from the patients and healthy controls enrolled in the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Lokesh S, Siva RG, Kadavanu TM, Hemachandar R, Kumar A, Tiwari SR, Lakshmi A, Ezhumalai G. A comparative study of platelet parameters in end stage renal disease patients undergoing haemodialysis and healthy individuals. Int J Adv Med 2016;3:559-63.