

Coagulation Profile and Platelet Indices in Diabetes with Chronic Kidney Disease on Haemodialysis

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ABSTRACT

Introduction: Bleeding and thrombotic complications are high possibility in CKD. The present study was conducted to evaluate the platelets indices in patients on haemodialysis having Type 2 diabetes with CKD as compared to diabetic patients without CKD.

Material and methods: 100 patients of ckd with diabetes and 100 patients of diabetes without ckd were studied over a period of seven months. The coagulation profile and platelet indices were compared. The coagulation profile and platelet indices were also compared in ckd patients before and after dialysis.

Results: Increase in platelet indices mainly MPV and Platelet Distribution Width (PDW) with significant p-value 0.003 and 0.005 respectively in study group. PT and APTT both were increased in study group with significant p-value of 0.003. Platelet count improved but MPV and PDW values were slightly decreased with p-value < 0.005. PT showed not much difference whereas APTT values were higher compare to post dialysis with p-value<0.007.

Conclusion: Basic coagulation profile like PT and APTT and MPV can predict long term complications of diabetic platelets on haemodialysis and these should be monitored in CKD patients.

Keywords: Diabetes, CKD (Chronic Kidney Disease), Dialysis

INTRODUCTION

Chronic Kidney Disease in India is an important public health problem. CKD and non communicable diseases are ignored in the face of persistent challenges for resources of communicable diseases and high infant and maternal mortality rate.¹ The main contributing factor for high prevalence of CKD in India are hypertension and diabetes mellitus. By 2030, India is expected to have the world's largest population of patients with diabetes. Because of challenges in access to care, over 50% of patients with advanced CKD are first seen when the eGFR is 15 ml/min per 1.73 m².² End Stage Renal Disease (ESRD) is a last stage of diabetic nephropathy, a microvascular complication of the disease.³ Hemodialysis (HD) was introduced in India in 1962, transplantation was introduced in 1971, and peritoneal dialysis (PD) was introduced in 1991. Up to 2017, there are over 130,000 patients receiving dialysis, and the number is increasing by about 232 per million population, a reflection of increasing longevity in general. HD is the most common modality followed by transplantation, and PD is a distant third. India is estimated to have about 120,000 patients on HD. Early diagnosis of CKD made by screening those with

diabetes, hypertension, autoimmune diseases, or family history of CKD must become a priority. The Indian Society of Nephrology has made education modules for community physicians with helpful algorithms regarding CKD management and timely nephrology referral. It is hoped that this translates into most patients with CKD being managed appropriately by primary care and family physicians, with appropriate referral to nephrologists when needed. Subsequent follow-up of these patients should continue to be under their primary care physician, with only periodic visits to the nephrologist until advanced stages of CKD are reached and advanced care, like RRT, becomes necessary. India has unique situations and challenges that influence early diagnosis and management of CKD.

Various defects in primary hemostasis have been described in uremia. These include abnormalities in platelet number, dense granule content, concentration of intracellular ADP, serotonin and cyclic AMP, release of platelet α granules, calcium ion mobilization, arachidonic acid metabolism, cyclooxygenase activity, GPIIb/IIIa binding, platelet aggregation and adhesion, vWF activity, prostaglandin I₂ and nitric oxide production by the vessel wall, and altered blood rheology due to anemia. The bleeding and thrombotic complications are observed in CKD due to disturbed balance between pro and anti haemostatic factors, leading to high morbidity and mortality.⁴ Diabetes mellitus is associated with increased complications due to variety of abnormalities reported in diabetic platelets.⁵ These diabetic platelets, in response to stimulating agents can exhibit increased adhesiveness and exaggerated aggregation phenomenon.⁶ In Western population various studies have proven on platelet activation and its association with diabetes, however very limited studies on Asian Indian populations.⁷ Hence, it is necessary to commence such studies for future prospective. Substantial activation of diabetic platelets can occur in

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| Investigations | Prior dialysis | Post dialysis | p value |
|-------------------------------------|----------------|---------------|---------|
| PT | 17.54±3.34 | 17.48±2.26 | 0.875 |
| PT-INR | 1.95±0.98 | 1.94±0.88 | 0.67 |
| APTT | 40.78±21.9 | 45.87±26.8 | 0.007 |
| Platelet count (10 ³ µL) | 182.55±456.25 | 187.85±642.53 | 0.276 |
| Mean Platelet Volume | 9.84±2.39 | 8.96±2.91 | <0.005 |

Table-1: Comparison between Pre Haemodialysis and Post Haemodialysis

course of haemodialysis which may be due to exposure of blood to the roller pump segment and microbubbles in the haemodialyser. Hence, dialysis membranes quality plays a vital role in platelets activation.⁸

Many studies from different parts of the world revealed that diabetes is a key factor for mortality in ESRD patients. Thus, this study was conducted to evaluate the platelets indices in patients on haemodialysis having Type 2 diabetes with CKD as compared to diabetic patients without CKD. Bleeding and thrombotic complications are high possibility, so we also assess the basic coagulation profile and platelet indices.

MATERIAL AND METHODS

This prospective study was conducted in the tertiary care centres of sitapur and shahjahanpur districts of Uttar Pradesh (India) between august 2018 to february 2019 for the period of seven months. Two groups of patients were taken. The first group (study group) consisting of 100 patients with Type 2 diabetes with CKD on haemodialysis. Diagnosis of CKD was according to National Kidney Foundation, KDOQI CKD guidelines 2002.⁹ The control group consists of 100 patients of Type 2 diabetes without CKD. Diagnosis of Type 2 diabetes was based on the WHO criteria- Fasting plasma glucose \geq 126 mg/dL and 2 hour post glucose \geq 200 mg/dL. Blood urea and serum creatinine were normal. Informed consent was taken from all patients (both study and control groups) and Institutional ethical committee permission was taken before the study. Patients of septicemia, infection, malignancy, primary haemostatic disorders, on antiplatelet agents (except aspirin) such as clopidogrel, dipyridamole or non-steroidal anti-inflammatory drugs and age less than 18 years were excluded from the study. As we have to see the effect of haemodialysis on haematological and coagulation profile, two samples were collected. Samples were collected from the patients before and after the haemodialysis. 5 ml of venous blood was collected in 2 different test tubes containing sodium citrate for coagulation profile (PT, APTT) and EDTA for complete blood counts. For control group 5 ml of venous blood was collected in two different test tubes containing sodium citrate for coagulation profile (PT, APTT) and EDTA for complete blood counts. RBC, WBC and platelet indices were estimated automatically by the ALERE H560 coulter method using EDTA anticoagulant blood samples. PT, APTT values were measured automatically on STAGOSTART 4 instruments using 3.2% sodium citrate anticoagulant blood samples.

STATISTICAL ANALYSIS

The data were analysed using SPSS version 22. For the

qualitative variables, Chi-square test was performed. Independent t-test was used to test the difference between means.

RESULTS

100 patients were considered in the case study group with Type 2 diabetes with CKD (82 male and 18 female) and 100 patients having diabetes without CKD (82 male and 18 female) as control group. Male predominance was seen in both groups. Age was homogeneous in both the groups, mean age ranged from 55.52±6.729 years.

Comparison between Study Group and Control Group

The red blood cells and leukocyte counts showed no statistical difference between the groups. Haemoglobin was slightly lowered in study group (mean 7.98±2.01) than controls (mean 11.2±1.45). Haematocrit value showed mild reduction in study group (mean 24.5±6.54) than controls (mean 29.12±3.59) and p-value less than 0.0005.

There was an increase in platelet indices mainly MPV and Platelet Distribution Width (PDW) with significant p-value 0.003 and 0.005 respectively in study group. PT and APTT both were increased in study group with significant p-value of 0.003.

Comparison between Pre Haemodialysis and Post Haemodialysis Sessions

The red blood cells and leukocyte counts showed no changes in study group between pre and post haemodialysis sessions. There was improvement in haemoglobin levels and haematocrit readings in study group post haemodialysis sessions. Platelet count improved but MPV is slightly decreased with p-value < 0.005. PT showed not much difference whereas APTT values were higher compare to post dialysis with p-value < 0.007 (table-1).

DISCUSSION

Diabetes is a metabolic syndrome characterized by chronic hyperglycaemia resulting in endothelial dysfunctions and vascular complications predominantly affecting organs like kidneys, peripheral nervous system and ocular organ.¹⁰⁻¹² Various mechanisms contribute to platelet dysfunction, affecting the adhesion, activation and aggregation. Hyperglycaemia affects calcium homeostasis and ultimately leads to cytoskeleton abnormalities and increased secretion of pro-aggregant factors.¹³⁻¹⁶ The most common sites of bleeding in uremic patients are from puncture sites, mucosal and serosal surfaces (epistaxis, gastrointestinal and genitourinary bleeds, hemorrhagic pericarditis and pleuritis), and subdural hematomas.¹⁷ CKD patients have risk factors for injury to all these sites – frequent venepuncture; increased

prevalence of peptic ulcers, angiodysplasia, mesenteric ischemia and diverticulosis; glomerular disease, acquired cystic, and polycystic kidney disease; pleural and pericardial inflammation; hypertension and head trauma due to falls. The risk is compounded by age, anticoagulation, antiplatelet agents, and anemia. Likewise, post kidney biopsy bleeds have been linked to hypertension, the gauge of the biopsy needle, depth of needle insertion, number of needle passes, and degree of arteriosclerosis in the biopsy tissue rather than BT.¹⁸ Uremic hemostatic abnormalities, though clinically insignificant in themselves, acquire importance when superimposed on this conglomeration of pathologies. We therefore suggest that greater attention be paid to these risk factors, which are far more likely to cause bleeding in uremic patients than primary or secondary hemostatic abnormalities. In the present study, the MPV was significantly higher in diabetics CKD patients than control groups who were known diabetics like other studies.^{11,15} The increased MPV are reflected by large circulating platelets and is an independent risk factor for complications in diabetics.¹⁵ Many studies have suggested that patients with diabetes have increased MPV when compared with non diabetic and, among the diabetics, those with vascular complications presented higher MPV values.^{15,19-22} Some studies showed that MPV was significantly higher in diabetics patients with vascular complications than in diabetics without complications, as in present study.^{22,23}

Hyperglycaemia is associated with hypercoagulable state, which can lead to long term complications.^{24,25,26} Alterations in MPV, were reflected by poor glycaemic control which may be due to osmotic effect caused from increased glucose levels and its metabolites in blood.¹⁵

In our study, coagulation parameters were prolonged in patients than control. Monitoring PT and APTT levels help in determining the risk of development of bleeding complications.^{11,27}

In the present study, the effect of haemodialysis was studied by comparing the pre haemodialysis and post haemodialysis coagulation and platelet indices in study group. Studies have shown that dialysis partially corrects platelet dysfunction associated with CKD, but does not eliminate the risk of haemorrhage. Platelet-dependent fibrin clot formation, which is defective in these patients, improves with haemodialysis. This may contribute to the improved platelet function seen after dialysis.^{37,38} In this present study platelet count and other platelet indices were improved, similar findings seen in other studies.^{11,28,29} In our study, there was decrease in haemoglobin and haematocrit values in patients before haemodialysis session compared to controls. These values were increased in patients after haemodialysis. Renal system fails to sustain production of erythropoietin in CKD which leads to chronic anaemia.³⁰ No significant difference in platelet count in patients before and after haemodialysis. This finding was seen in study done by Bilgin A et al., also.³¹ This study had many limitations also as long term complications were not studied, sample size is small and effect of insulin and oral hypoglycemic agents could not

studied.

CONCLUSION

Mean platelet volume (MPV) is an important prognostic marker in assessing the complications of diabetes. Basic coagulation profile like PT and APTT and MPV can predict long term complications of diabetic platelets on haemodialysis and these should be monitored in CKD patients.

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