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RESEARCH ARTICLE

COMPARATIVE STUDY OF STANDARD COAGULATION PROFILE IN NON-DIALYZED AND POST-DIALYZED PATIENTS SUFFERING FROM CHRONIC KIDNEY DISEASE

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ABSTRACT

Aims and Objectives: This comparative cross sectional study assessed whether there was any subtle change in the standard coagulation profile of chronic kidney disease (CKD) patients who needed no dialysis or who were dialysis candidates but had not yet started dialysis. Aim of this study was to find out any correlation between patients' coagulation parameters and their degree of uremia.
Materials and Methods: A total 30 CKD patients were carefully selected and assigned to three groups after excluding patients who were predisposed to bleeding diathesis. Group A—10 CKD patients on the verge of hemodialysis (HD); Group B-10 CKD patients who were clinically and biochemically stable and on renal replacement therapy in the form of HD; and Group C-10 CKD patients who were in the early stages of standard medical treatment. A coagulation profile study was done for all three groups using nonparametric statistical analysis.
Results and Discussion: Significant thrombocytopenia and prolongation of prothrombin time (PT) were present in (Group A), whereas no significant coagulation abnormality was noted in the other two groups. A significant correlation was found between uremia (creatinine clearance) and platelet count, P time, and APTT in Group B and Group C patients and with bleeding time in patients stable with conservative management (Group C).
Conclusion: The study shows coagulation parameters are progressively affected with the progress of renal disease and that dialysis has an important impact on coagulopathy in CKD. But the coagulation parameters showed no statistically significant correlation with degree of uremia.
Key Words: Chronic Kidney Disease, Coagulation Profile, Hemodialysis, Uremia

INTRODUCTION:

Chronic kidney disease (CKD) is a condition characterized by permanent and significant loss of the glomeruler filtration rate (GFR) [1]. With reduction of the GFR, renal function deteriorates progressively and uremia develops. Uremia is characterized by very high blood urea and creatinine levels and accumulation of metabolic waste product. Irrespective of the cause, the eventual impact of chronic renal parenchymal disease is reflected in alteration of function of virtually every organ system in the body. Coagulopathy is one of these effects. The association of altered hemostasis and uremia has long been recognized and is one of the leading causes of morbidity and mortality[2]. The haemostatic defect in uremia often is complex and multifactorial, including thrombocytopenia, platelet aggregation defects or dysfunction, and coagulation abnormalities. With renal replacement therapy, one can treat uremia and improve CKD patients' quality of life. It would be a great advantage to know whether correction of the biochemical abnormality lessens the risk of severe haemorrhagic complications, but this has yet to be confirmed. In this study, an attempt was made to correlate the laboratory results and to detect any subtle change in standard coagulation test results of the CKD patients before and after dialysis compared to those for a control group.

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MATERIALS AND METHODS:

A total 30 patients suffering from renal failure of both sexes were included in this study. All of the CKD patients were admitted to the medicine department at the Nil Ratan Sircar Medical College for the Management of Renal Failure. CKD was diagnosed in accordance with available clinical, biochemical, and radiological guidelines [3,].

Patients were excluded if they were predisposed to bleeding diathesis such as those with Ischemic Heart Disease (IHD) and those on medications or with a known hematological and connective tissue disorder.

Patients were categorized into two groups:

Group A—10 CKD patients on the verge of hemodialysis (HD); Group B—10 CKD patients who were clinically and biochemically stable and on renal replacement therapy in the form of HD; and Group C—10 CKD patients who were in the early stages of standard medical treatment

Written informed consent was obtained from each patient before participation and the study was approved by Institutional Ethics Committee. The mean time period of these patients suffering from renal failure was 45.25 ±18.25 months. Patients undergoing dialysis was three times in a week for about 3 to 4 hours per session at blood flow rates of 180 to 375 ml/min using poly-sulphone hollow-fiber filter.

Blood collection and Analysis:

Blood samples were collected by a qualified phlebotomist. A 2-mL blood sample from each patient was taken into a Lavender cap containing tube with 2.0 mg/mL EDTA salt and preserved at 37˚C for platelet analysis. The blood sample was measured using the automatic quantitative hematology analyzer (XP-100, Transasia). The blood sample for coagulation function tests were taken into a blue capped tube containing sodium citrate (32.06 mg/mL, final concentration 3.8%) in a 9:1 volume ratio. The samples were analyzed using the ACL-TOP700 automatic blood coagulation analyzer (BECKMAN COULTER, U.S.A.).

Platelet aggregation seems to correlate with bleeding time, but a platelet function study was not included in our study due to financial constraints.

RESULTS AND ANALYSIS

The collected data were treated using SPSS software (version 11.5). The following statistics were calculated: Mean ± standard deviation,p value of each parameter, Correlation coefficient (r) comparing the degree of coagulopathy
present and the degree of uremia (GFR-creatinine clearance), All tests were two-tailed, and the level of significance was P<0.05

Table 1: Age and sex distribution of the 30 selected patients

	25-30 years	31-40 years	41-45 years	Total
Total patients	8	11	11	30
Male	7	6	4	18
Female	1	5	7	12

From Table 1, it can be seen that the greatest number of patients are in their fourth or fifth decade, with just 26% of the patients in their third decade. The youngest was 25-years-old and oldest was 45-years_old; the mean age was 37 ±6.4 years.

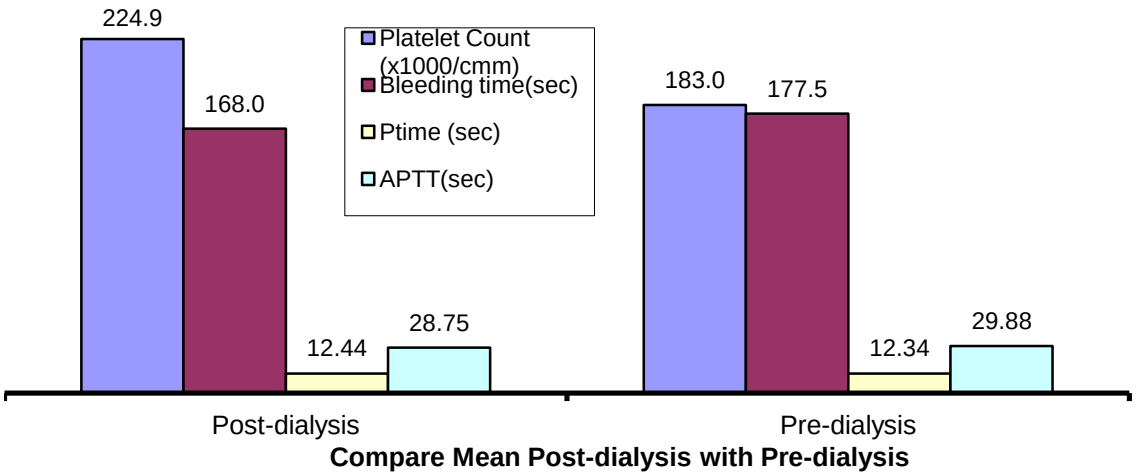
Table 2: Showing presenting features of 30 cases of chronic renal parenchymal disease

Clinical features	Male	Female	Total
Bleeding	3	1	4 (13.3%)
Pallor	13	5	18 (60.0%)
Edema	7	6	13 (43.3%)
Oliguria	3	5	8 (26.6%)
Nausea and Vomiting	6	8	14 (46.0%)
Weakness/Lethargy	11	8	19 (63.3%)

Table 3: showing coagulation profile in pre & post dialysis group

Analyte	Predialysis group (Group A)	Postdialysis group (Group B)	Significance (P Value)
Platelet count (x1000/cmm)	183±98.77	224.90±107.31	NS (0.21)
Bleeding Time (seconds)	177.50±46.14	168±31.55	NS(0.68)
P Time (seconds)	13.09±1.36	12.44±1.17	NS(0.13)
APTT (seconds)	29.88±3.95	28.75±3.53	NS(0.19)

Value represented as mean ±SD, p value significant at the level of < 0.05



Bar Graph 1: Comparison of coagulation parameters between the predialysis group (Group A) and patients who were clinically stable postdialysis (Group B).

Changes in coagulation parameters in Group A patients (n = 10) (predialysis group)

- Level of platelet count was (mean ±SD) = (183 ±98.77) × 1000/cmm.
- Number of patients having thrombocytopenia (<150×1000/cmm) 6 cases (60%), which is significant in this group (p 0.04).
- Bleeding time (BT) was (mean ±SD) = (177.50 ±46.14) seconds.Prolonged bleeding time (>180 seconds) was found in 4 cases (40%), which is not significant in this group (p>0.10).
- Prothrombin time (P Time) (mean SD) was = (13.09 ±1.36) seconds.Prolonged P Time (>13.5 seconds) was found in 5 cases (50%), which is significant in this group (P 0.005).
- Activated partial thromboplastin time (APTT) was (mean ±SD) = 29.88 ±3.95 seconds.Prolonged APTT (>33 seconds) found in 4 cases (40%), which is not statistically significant (p>0.10).
- No statistical correlation was found between the uremia (creatinin clearance) and platelet count (r = -0.3133), Bleeding time (r = 0.1950),Prothrombin time (r = 0.3884) and Activated partial thromboplastin time (r = 0.4518).
- GFR was (mean ±SD) = (8.15 ±1.75) ml/min.

Changes in coagulation parameters in Group B patients (n=10) (Post-dialysis group)

- Level of platelet count was (mean ±SD) = (224.09±107.31) × 1000/cmm.
- Number of patient having thrombocytopenia = 3 cases (30%), which is not significant in this group (P > 0.10).
- Bleeding time was (mean ±SD) = (168 ±31.55) seconds.Number of patients having BT prolongation = 3 cases (30%), which is not significant in this study group.
- Prothrombin time (mean ±SD) = (12.44 ±1.17) seconds.Number of patients having prolonged P time found in one case (10%), which is statistically not significant (P>0.10).
- Activated partial thromboplastin time (APTT) was (mean ±SD) = (28.75 ± 3.53) seconds.Number of patient having prolonged APTT is found in one case (10%), which is not significant in this study group.
- Significant correlation was found between uremia and platelet count (r = 0.03112),P Time (r = - 0.5938) and APTT (r= -0.03359).where as uremia and bleeding time correlation yields nonsignificant (r = 0.3444).
- GFR was (mean ±SD) = (8.15 ±1.75) ml/min in this group.

Changes in coagulation parameters in Group C patients (n = 10) (patients stable with conservative management)

- In this group, platelet count was (mean ±SD) = (211 ± 85.38) × 1000/cmm.only two patients (20%) were suffering from thrombocytopenia which is not significant(P = 0.0733).
- Bleeding time was (mean ± SD) i.e (174± 25.03) seconds.Number of patient having prolonged bleeding time found in 3 cases (30%), which is statistically insignificant (P > 0.10).
- Prothrombin Time (P Time) was (mean ± SD) = (12.34 ±1.24) seconds.Number of patient having prolonged P Time was 2 cases (20%), which is again not significant in this group (P>0.10)
- Activated partial thromboplastin time was (28 ± 3.86) seconds and prolongation was noted insignificantly in two cases (P>0.10).
- Here significant correlation found between uremia and Platelet count (r = 0.2952), P time (r = -0.1181), and APTT (r = -0.7972).But correlation between

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uremia and bleeding time was not significant in this study group (r = -0.6620).

- GFR was estimated (23±5.98) ml/min in this group.

Comparison of coagulation parameters between predialysis and post dialysis groups

Total number of patient was in each group was 10 and included both sexes. The platelet count, bleeding time, prothrombin time, and activated partial thromboplastin time were measured in each group.

In the predialysis group, the platelet count was (183 ±98.77) x 1000/cmm. (mean ±SD). In the post dialysis patients, the platelet count was (224.90 ±107.31) x 1000/cmm. (mean ±SD) (Table 3).

Showed mild improvement of platelet count after dialysis, but this value was not statistically significant (P>0.1).

Bleeding time estimation was (177.50 ±46.14) seconds (mean ±SD) in the predialysis group; in the post dialysis group, it was (168 ±31.55) seconds (mean ±SD), which shows a small reduction in bleeding time after dialysis, but this value is not statistically significant (P>0.1).

Prothrombin time was (13.09 ±1.36) seconds (mean ±SD) and (12.44 ±1.17) seconds in predialysis patients and post dialysis patients, respectively. There was a small reduction of value in the post dialysis group.

Alteration of P Time between these groups (P>0.10) was not statistically significant.

Activated partial thromboplastin time was (29 ±3.95) seconds (mean ±SD) and (28.75 ±3.53) seconds (mean ±SD) in predialysis patients and post dialysis patients, respectively. Reduction of APTT was observed in the post dialysis group, but it was not statistically significant (P>0.1).

DISCUSSION:

Increasing understanding of mechanism of progression of renal failure during the last decade may not yet have brought about any great changes in our current method of slowing the progression of renal failure, but our current methods of slowing the progression of various complications surely has added a scientific basis to some of the currently employed strategies.

The precise cause of bleeding in uremia remains poorly understood and probably varies from person to person.

Although the frequency of thrombocytopenia in patients with chronic renal failure is controversial, thrombocytopenia has been mostly implicated as an important cause of hemorrhagic diathesis in these patients[3].

In our study, we found that six patients (60%) of those waiting for haemodialysis had significant thrombocytopenia. In other patients, Group C (patients stable on conservative management) and Group B (patients from the post dialysis group) had few cases of thrombocytopenia— 2 (20%) and 3 (30%) cases, respectively. These results are similar to the results obtained by Grafter U *et al.* (1987), and Ezimol *et al.* (2004) showing thrombocytopenia[4, 5].

Steiner R.W *et al.* (1979) and Mezzano D *et al.* in their studies showed that bleeding time in uremia provides a useful test to assess clinical bleeding due to platelet dysfunction [6,7].

In our study, bleeding time was prolonged in 4 (40%) cases from the predialysis group (Group A), 3 (30%) cases from the post dialysis group (Group B), and 3 (30%) cases from the patients stable with conservative management (Group C). This result indicates bleeding time is prolonged in chronic renal parenchymal disease but is not statically significant (similar to findings by Shetty HG *et al.*) (1982)[8].

In our study, significant prolonged prothrombin time was found in the predialysis group (Group A) in 5 cases (50%), but only 1 (10%) case in the post dialysis group (GroupB) and 2 (20%) cases of the patients on conservative treatment (Group C) had prolonged P time. The results reported above are consistent with studies done by Rath *et al.* (1957)[9] and Chenoy K *et al.* (1962)[10].

Activated partial thromboplastin time was found prolonged in some patients in our study— 4(40%) cases from the predialysis group, 1 (10%) case from the post dialysis group, and 2 (20%) cases from the patients on conservative management group. These findings were not statistically significant.

The above results from this study differ from those in the study done by Hutton RA *et al.* (1968)[11], but contrast with the studies done by Shetty H.G. *et al.*[8], which show prolonged APTT in uremia patients before dialysis, and Mohamed *et al.* (2008),which show a significant increase in APTT after haemodialysis [12].

Four patients presented with bleeding symptoms (Case No. 3, 8, 10 and 13). Only Case No. 3, 8, 10 (from the predialysis group) have thrombocytopenia; their other coagulation parameters are within normal range. Case No. 13 has no abnormality in platelet count or other coagulation parameters.

In various studies, haemostatic disturbance has been correlated with patient, severity of renal failure, and hematocrit—hemoglobin concentration overcomes the problem to some extent.

In our study, a correlation was done between the degree of uremia (GFR) and the coagulation parameters of patients in each group.

Our study shows:In Group A patients (predialysis group), no significant correlation was found between the degree of uremia and platelet count, bleeding time, prothrombin time, or activated partial thromboplastin time.

In Group B patients (the post dialysis group), a significant correlation was found between uremia and the studied coagulation parameters, except bleeding time.

In Group C patients (those stable on conservative management), a significant correlation also was observed between uremia and the studied coagulation parameters. And a significant correlation was found between uremia and bleeding time in this study group (Group C).

A moderately significant correlation was discernible between creatinine clearance (GFR) and partial thromboplastin time in chronic renal parenchymal disease, Shetty H G *et al* [8].

In this study, the coagulation parameters of post dialysis group were compared with patients of the predialysis group to document whether the coagulation parameters changed.

Our study shows mild improvement of platelet count, bleeding time, prothrombin time, and activated partial thromboplastin time in the post dialysis group, but this result is not statistically significant.

A previous study by M L Butt (1998) showed mild improvement in platelet count after haemodialysis, but the value was not statistically significant [13].

Mohamed *et al.* (2008) studied 90 patients finding no statistically significant increase in the number after haemodialysis. Knawczyk *et al.* (1994) observed an unchanged platelet count after haemodialysis[14]. In our study, the change of platelet count after haemodialysis is similar to that of the previous study.

Previous studies show there is improvement of platelet function after haemodialysis and significant improvement of bleeding time. M L Butt *et al.* (1998) studied 33 patients with chronic renal failure[13]. Bleeding time corrected for 27 patients (81.8%) after haemodialysis, which was significant. Our result is in contrast to the result of this study.

In our study there was no significant alteration of P time or APTT in post dialysis patients who were stable after haemodialysis when compared to the predialysis group.

SUMMARY AND CONCLUSIONS

Haemostasis disturbance is a common complication in chronic kidney disease.

Both bleeding and thrombosis are present in chronic kidney patients. The main cause of this is the patient's uremic state and their accumulation of other unidentified toxic materials. As a rule, the condition is at least partly reversible with adequate renal replacement therapy.

In the present study, coagulation parameter investigation performed at varying intervals from diagnosis showed a disturbed coagulation pattern. A subtle change of platelet count, P time, APTT, and bleeding time was found in various study group patients. These variables also correlated with uremia in some study group patients.After haemodialysis, their coagulation pattern improved to some extent.The possible causes of defective haemostatic in this situation are numerous; multiple mechanisms may be simultaneously involved. Additionally patients on haemodialysis receive various doses of heparin, which may cause changes in platelet count and coagulation factor abnormality.However, in the present study our effort was given to explaining subtle coagulation abnormalities and determining whether there were any changes with renal replacement therapy (haemodialysis) to prevent serious bleeding complications for those patients who may be planning surgical intervention or invasive diagnostic procedures in the future.

Conclusions we have drawn from the present study are:

(1) In the predialysis group, all of the studied parameters were affected more than in the group of patients who were stable with conservative management. So the coagulation parameters are progressively affected as the renal disease progresses.

(2) In the group that was studied after dialysis, all the coagulation factors improved to a certain extent. So dialysis has an important impact on coagulopathy in CKD.

(3) In all of the groups studied, the coagulation parameters have no statistically significant correlation with the degree of uremia, *i.e.* GFR. This may be because each of the three patient groups was different and each case was not studied as the disease progressed.

The study is a cross-sectional study comprising a small population of patients, so no firm conclusion can be drawn whether coagulopathy is related to the degree of chronic renal damage.

More study is necessary with a large number of cases to arrive at a definite conclusion regarding coagulation abnormality in chronic renal parenchymal disease. However, the present study gives an overall idea about coagulopathy in CKD in our population, as depicted in previous literatures.

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