

Assessment of some coagulation parameters in chronic kidney disease patients attending Specialist Hospital in Sokoto, Nigeria

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BACKGROUND: Chronic kidney disease (CKD) has become a major health concern in developing countries while the risk of bleeding episodes has been reported to be in 2- fold in patients with renal failure. The aim of this study was to assess coagulation parameters in CKD patients.

MATERIAL AND METHODS: Fifty patients with CKD and 50, apparently healthy subjects were recruited and studied for prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen level using standard techniques.

RESULTS: The study showed significantly higher mean values for PT and APTT in CKD patients compared to the control groups ($P < 0.05$). Age and stages of CKD showed no significant effects on PT, APTT and fibrinogen level ($P > 0.05$). Gender showed no significant influence on PT and APTT values ($P > 0.05$) but revealed significant impact on fibrinogen level ($P < 0.05$).

CONCLUSION: Changes in coagulation parameters in CKD patients are associated with prolonged PT and APTT while gender, age and stages of CKD had little or no influences on PT, APTT and fibrinogen level. These findings will serve as guide to the physicians in the management and monitoring of CKD patients.

Key Words: Chronic kidney disease; Haemodialysis

Chronic kidney disease (CKD) has become a major health concern globally, especially in developing countries with a marked burden in sub-Saharan Africa (1). In Nigeria, (2) reported that renal failure constituted 8% of the hospital admissions while (3) reported a prevalence of 19.9% of undetected disease in a rural populace in Nigeria. However, (4) reported an incidence of 45.5% of impaired kidney function among hospitalized hypertensive patients in Maiduguri. Bleeding has been reported in 40-50% of patients with chronic renal failure or on haemodialysis (5,6) while another study reported bleeding events in 24% of patients on haemodialysis (7). However, a hospital based study showed that risk of bleeding episodes is increased in approximately 2- fold in patients with renal failure (8). Apart from the patients with renal failure being prone to episodes of prolonged bleeding, they may also develop excessive formation of thrombi (9). Bleeding disorders have been attributed to insufficient function of platelets, the coagulation cascade and/or activation of the fibrinolytic system while hypercoagulability could be due to disorders of the coagulation regulatory factors as well as platelet hyperactivity (9,10). Several haemostatic abnormalities have been described in patients with even mild CKD in addition to platelet activity (11). In CKD, increased concentrations of fibrinogen, coagulation factors XIIa and VIIa as well as activated protein C complex and thrombin-antithrombin complexes have been reported by earlier authors (12-16) while reduced activity of antithrombin has been documented by another researcher (12). The aim of this study was to assess the levels of prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen of patients with chronic kidney disease in Sokoto.

MATERIALS AND METHODS

The study recruited 50 CKD patients (34 males and 16 females), aged 18-64 years and 50, age- and sex-matched, apparently healthy subjects resident in Sokoto as control groups. Informed consent was sought from each of the participants and the ethical clearance obtained from hospital ethics and research committee of Specialist Hospital Sokoto while the study was carried out between June and December 2017. Consenting CKD patients diagnosed with clinical criteria by the nephrologists were included in this study while CKD patients on anti-platelet therapy, anticoagulant therapy and patients with septicemia and bleeding disorders were excluded from the study.

A total of 4.5 ml of venous blood collected from each participant was added to 0.5 ml of 3.2% tri-sodium citrate solution in a tube and this was mixed and centrifuged at 3000 revolutions per minute for 15 minutes. The plasma

was separated and used for the determination of prothrombin time (PT) and activated partial thromboplastin time (APTT) using Diagen reagents kits while plasma fibrinogen level was determined using Diatest fibrinogen assay kit. All the tests were performed according to the manufacturers' instructions.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 20 software and the results were expressed as mean \pm standard deviation. Comparisons of results for significance were made using student's t-test and analysis of variance. P-values of less than 0.05 were considered to be statistically significant.

RESULTS

Table 1 shows coagulation parameters in CKD patients and control group. The differences between the mean values for PT, APTT and fibrinogen concentration of 19.4 ± 8.2 seconds, 46.2 ± 9.0 seconds and 1.96 ± 0.6 g/L, respectively compared to control values of 14.8 ± 2.1 seconds, 32.8 ± 3.5 seconds and 1.86 ± 0.6 g/L, respectively, showed P-values of 0.0002, 0.0001 and 0.5066, respectively.

Table 2 reveals coagulation parameters in CKD patients according to gender. The mean values for PT, APTT and fibrinogen concentration of 20.5 ± 9.1 seconds, 47.6 ± 8.3 seconds and 1.79 ± 0.6 g/L, respectively in

TABLE 1

Coagulation parameters in CKD patients

| Parameters | Control (n=50) | CKD patients (n=50) | P- value |
|------------------------|----------------|---------------------|----------|
| PT (seconds) | 14.8 ± 2.1 | 19.4 ± 8.2 | 0.0002 |
| APTT (seconds) | 32.8 ± 3.5 | 46.2 ± 9.0 | 0.0001 |
| Fibrinogen level (g/L) | 1.86 ± 0.6 | 1.94 ± 0.6 | 0.5066 |

TABLE 2

Coagulation parameters in CKD patients according to gender

| Parameters | Males (n=34) | Females (n=16) | P-value |
|------------------------|----------------|----------------|---------|
| PT (seconds) | 20.5 ± 9.1 | 17.9 ± 6.6 | 0.3123 |
| APTT (seconds) | 47.6 ± 8.3 | 44.1 ± 9.9 | 0.1974 |
| Fibrinogen level (g/L) | 1.79 ± 0.6 | 2.16 ± 0.6 | 0.0475 |

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TABLE 3**Blood coagulation parameters for stages of CKD**

| Parameters | I | II | III | IV | V | P-value |
|------------------------|------------|------------|------------|------------|------------|---------|
| PT (s) | 17.4 ± 6.9 | 18.8 ± 5.0 | 15.3 ± 3.1 | 15.6 ± 5.9 | 23.5 ± 9.9 | 0.074 |
| APTT (s) | 46.1 ± 9.1 | 50.6 ± 8.0 | 42.7 ± 9.8 | 42.0 ± 9.2 | 47.3 ± 9.0 | 0.496 |
| Fibrinogen level (g/L) | 1.98 ± 0.6 | 2.16 ± 0.7 | 1.95 ± 0.6 | 1.99 ± 0.6 | 1.83 ± 0.6 | 0.857 |

TABLE 4**Coagulation parameters in CKD patients according to age**

| Parameters | 15-24yrs | 25-34yrs | 35-44yrs | 45-54yrs | 55-64yrs | P-value |
|------------------------|-------------|------------|------------|-------------|------------|---------|
| Number | 5 | 11 | 14 | 9 | 11 | |
| PT (s) | 17.2 ± 2.9 | 20.4 ± 7.4 | 20.1 ± 9.5 | 21.3 ± 11.2 | 17.2 ± 6.2 | 0.7668 |
| APTT (s) | 48.2 ± 11.9 | 48.3 ± 7.6 | 44.4 ± 8.7 | 44.4 ± 10.2 | 46.9 ± 9.3 | 0.7815 |
| Fibrinogen level (g/L) | 2.70 ± 0.8 | 1.75 ± 0.5 | 2.02 ± 0.7 | 2.08 ± 0.7 | 1.85 ± 0.5 | 0.7162 |

males compared to 17.9 ± 6.6 seconds, 44.1 ± 9.9 seconds and 2.16 ± 0.6 g/L, respectively in females, showed P- values of 0.3123, 0.1974 and 0.475, respectively.

Table 3 shows coagulation parameters on the basis of stages of CKD. Comparisons of the mean values for PT, APTT and fibrinogen level of 17.4 ± 6.9 g/L, 46.1 ± 9.1 seconds and 1.98 ± 0.6 g/L, respectively in stage I; 18.8 ± 5.0 seconds, 50.6 ± 8.0 seconds and 2.16 ± 0.7 g/L, respectively in stage II; 15.3 ± 3.1 seconds, 42.7 ± 9.8 seconds and 1.95 ± 0.7 g/L, respectively in stage III; 15.6 ± 5.9 seconds, 42.0 ± 9.2 seconds and 1.99 ± 0.6 g/L, respectively in stage IV; and 23.5 ± 9.9 seconds, 47.3 ± 9.0 seconds and 1.83 ± 0.6, respectively in stage V, showed no significant difference (P>0.05).

Table 4 reveals coagulation parameters in CKD patients according to age. The comparison of mean values for PT, APTT and fibrinogen level of 17.2 ± 2.9 seconds, 48.2 ± 11.9 seconds and 2.07 ± 0.8 g/L, respectively for age group of 15-24 years; 20.4 ± 7.4 seconds, 48.3 ± 7.6 seconds and 1.75 ± 0.5 g/L, respectively for 25-34 years; 20.1 ± 9.5 seconds, 44.4 ± 8.7 seconds and 2.02 ± 0.7 g/L, respectively for 35-44 years; 21.3 ± 11.2 seconds, 44.4 ± 10.2 seconds 20.08 ± 0.7 g/L, respectively for 45-54 years; and 17.2 ± 6.2 seconds, 46.9 ± 9.3 seconds and 1.85 ± 0.5 g/L, respectively, for 55-64 years, showed no statistically significant difference (P>0.05).

DISCUSSION

Chronic renal failure (CRF) is associated with multiple complex alterations in coagulation. Although, excessive bleeding following trauma and during surgical procedures in patients with CRF continues to be a problem. However, an increased incidence of thrombotic complications has also been reported (17-19). This study has shown significantly higher values of PT and APTT in CKD patients. This is in agreement with some of the previous reports (20-22) but in contrary with the findings of other researchers who showed no significant differences when PT and APTT were compared to healthy individuals (23,24). However, variation of sample sizes, methods of analysis and peculiarities of different stages of CKD could contribute to the divergent opinions expressed by the authors (20,22-24). Prolongation of PT and APTT in CKD patients could be associated with bleeding and this may probably be due to deficiencies of blood coagulation factors that are linked to extrinsic and intrinsic blood coagulation pathways. Our study has revealed that gender had no significant influence on PT and APTT values and this observation is similar to the previous study (21). Fibrinogen level in this study showed a significantly higher value in females with CKD compared to the males with CKD (25,26). However, elevated level of plasma fibrinogen has been linked to an increased prevalence of coronary heart disease (CHD) both in normal situation (27) as well as in dialysis patients (28), apart from contributing directly to a hypercoagulable state (29). This study has further revealed that PT and APTT levels were not significantly influenced by stages of CKD. Limited data are available on the effects of CKD on coagulation parameters. These findings are in agreement with the earlier reports (22-24,30). Fibrinogen levels have shown no significant differences with respect to stages of CKD in this study but these are in contrary to earlier reports (22,24). The mechanisms responsible for the inconsistency in fibrinogen levels with respect to stages of CKD are not understood. However, variation in sample numbers and laboratory techniques could be contributory factors.

CONCLUSION

It was also observed in this study that age had no effect on PT, APTT and fibrinogen level. However, this is in partial agreement with the study of Aral et al. (31) who showed that PT levels differ between ages but APTT

levels showed no difference with ages. In conclusion, changes in coagulation parameters in CKD patients could be associated with prolonged PT and APTT. However, gender, age and stages of CKD had little or no influence on the values PT, APTT and fibrinogen level in CKD patients. These findings will serve as guide in the management and monitoring of CKD patients. It is therefore recommended that PT and APTT be carried out as routine tests on every CKD patient since insufficient function of coagulation cascade has been associated with bleeding disorders (9,10).

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