EUROPEAN ACADEMIC RESEARCH
Vol. IV, Issue 2/ May 2016

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

Assessment of Fibrin \ Fibrinogen Degradation Products (FDBs) in Sudanese Chronic Renal Failure

MAYADA MUZAMIL ABDELLA
LEENA BABKIKER MIRGHANI
Department of Hematology
Faculty of Medical Laboratory Sciences
Alneelain University, Sudan

Abstract:

Background *End Stage Renal Disease (ESDR) occurs for renal failure patients and treatment is initiated when the patient is clinically "uremic" and /or cannot adequately maintain physiologic balance. Disturbances in hemostasis are common complications of kidney diseases. Their occurrence and severity correlate quite well with the progressive loss of renal function to end-stage renal disease. The aim of this study was to determine the level of Fibrinogen Degradation Products (FDBs) in Sudanese Chronic Renal Failure (CRF) patients.* ***Method*** *A total of 60 Sudanese chronic renal failure patients attending Academic Hospital Center of renal diseases in Khartoum were enrolled in the study, 30 as cases and 30 healthy individuals as control group. FDBs were measured by semi quantitative method.* ***Results*** *Most of the patient showed significant increase in Fibrinogen Degradation Products level in compare with normal control with (p-value < 0.00). The results showed that cases group has an increased level of FDBs (10% less than 200* ***µg/ml****), (10% 200 to 400****µg/ml****), (40%less than 500 to 800* ***µg/ml****),(10%less than 900 to 1600* ***µg/ml****) and(30% less than1700 to3200* ***µg/ml****), comparing to the control group.* ***Conclusion*** *FDBs might indicate an increased risk for thrombosis in CRF patients.*

Key words: Fibrinogen Degradation Products, Chronic Renal Failure, Sudanese, Thrombosis, Semi quantitative.

INTRODUCTION

Renal failure becomes symptomatic only when metabolites abnormalities become severe, End Stage Renal Disease (ESDR) occurs and treatment is initiated when the patient is clinically "uremic" and /or cannot adequately maintain physiologic balance, despite medical intervention. Systems of uremia are nonspecific and include gastrointestinal symptoms, sleep disturbances, mental changes, and an overall failure to thrive, when uremia develops, the patient's Glomerular Filtration Rate (GFR) were as low as 5-12cc/min. (1)

CRF is a growing global health problem, and although ESRD is a prominent and much feared complication of the disease, the high mortality rate associated with CRF (42.4 per 100,000) According to world health rankings. Treatment options for ESDR include hemodialysis, peritoneal dialysis, chronic ambulatory peritoneal dialysis and renal allograft transplantation. If one of those options is not initiated when renal failure become severe, the patient will die within a fairly short period, usually weeks. (2)

Disturbances in hemostasis are common complications of kidney diseases. Their occurrence and severity correlate quite well with the progressive loss of renal function to end-stage renal disease. **(6)** The principal cause of these abnormalities is the uremic state, the pathogenesis of uremic bleeding is increased levels of clotting factors and decreased levels of clotting inhibitors, hyper fibrinogenemia, diminished fibrinolytic activity, and platelet hyper aggregability, at present the incidence of bleeding is apparently declining; whereas thrombotic complications have become the predominant causes of mortality. (4)

Main hemostatic abnormalities in patients with chronic Kidney Disease includes increased tissue factor, increased Von Willebrand factor, increased factor XIIa increased factor VIIa, increased activated protein C, increased fibrinogen, ieduced tissue plasminogen activator and increased plasminogen activator inhibitor 1[5]

In patients with such abnormalities, knowing more about fibrinolysis could give a great help in prevention, treatment and prognosis of bleeding or thrombotic events. [5] Nakamura Y, et al in (*1991)* was studied Thirty-three patients with chronic uremia on regular hemodialysis treatment to determine whether coagulation and fibrinolysis are enhanced or not. They examined pre dialysis values of coagulation and fibrinolysis parameters including alpha fibrin degradation products, FDPs were significantly higher (PV less than 0.001) in patients than in normal controls. [6]

Mohammed Jomaa Ali Al-haj Faraj in Sudan (2006) studied 60 chronic renal failure patients studied for FDPs, pre dialysis (Hemodialysis 66.7% and Peritoneal 33.3%), 63.3% of overall shows significant increase in FDPs level in compare with normal controls. [7].

Hemostatic abnormalities have been described in patients with even mild CRF in addition to platelet hyperactivity. Impaired release of tissue plasminogen activator (tPA). **[8]** Because acute release of tPA by the endothelium is important in modulating the thrombotic process, the impairment of its release likely affects timely thrombolysis in patients with CRF and may contribute to the hypofibrinolytic state and the increased risk of atherothrombotic events in this patient population. **[9]**As CRF advances, the procoagulant abnormalities such as impaired release of tPA, increased Plasminogen activator inhibitor-1, elevated fibrinogen and D-dimer,22 and increased TF/FVIIa persist. **[10.11]** In patients with such abnormalities, knowing more about fibrinolysis could give

a great help in prevention, treatment and prognosis of bleeding or thrombotic events. (12)

In this context, we conducted descriptive study to determine the FDP among Sudanese renal failure patients.

MATERIALS AND METHODS

Study population

A total of 60 Sudanese chronic renal failure patients attending Academic Hospital in the center of renal diseases during the period from October 2015 May 2016 were enrolled in this study, 30 of them were patients with Chronic renal failure, excluding Chronic renal failure patient whom has other diseases directly affect hemostatic status (Inflammations, Trauma, Liver, disease, pregnant Infections, malignant, and Congenital hemostatic disorders etc), also those whom using drugs affect the hemostatic status (Aspirin, Warfarin and heparin), and 30 healthy individuals were used as control group.

Sample Collection and preparation:

Blood samples were collected from all patients and control group tri sodium citrate anticoagulant solution; the blood samples centrifuged at 2,500 g for 15 minutes and PPP was collected.

FDBs:

Analysis of the FDBs was performed by ActiScreen XL-FDP machine which depend on principle of immunoagglutination assay that utilize the latex beads coupled with a highly specific monoclonal antibody. XLFDP present in a plasma sample binds to the coated latex beads, which results in visible agglutination occurring when the concentration is above the upper limit of detection for the assay.

The test performed in disposable test card with positions on the test card for specimens, positive and negative controls.

The Immunoagglutination Reagent dropper bottle held vertically and 1 drop placed of the reagent within a well on a test card. Accurately 20 µL of undiluted plasma were added, or one drop of control solution, inside the same well next to the drop of Immunoagglutination Reagent.

Immunoagglutination Reagent and test samples were mixed with a stirrer until the latex is uniformly distributed, the test card gently rocked by hand for exactly 3 minutes, checked for agglutination under a strong light source.

(NOTE: If test reading is delayed beyond 3 minutes, the latex suspension may dry out giving a false agglutination pattern. If this is suspected, the specimen must be retested). The test Card and stirrer were discarded into a biohazard container.

Prepared doubling dilutions of the test plasma with Buffer Solution as follows:

1:2 dilutions: Add 100µL of plasma to 100µL of Buffer.

1:4 dilutions: Add 100µL of 1:2 dilution to 100µL Buffer.

1:8 dilutions: Add 100µL of 1:4 dilution to 100µL Buffer.

The patient's plasma dilution tested along with a positive and negative control so as to have agglutination patterns for comparison.

Table (1) Approximate levels of XL-FDP for specimen dilutions

XL-FDP Levels ng/mL (mg/L)	SAMPLE DILUTION			
	Undiluted	1:2	1:4	1:8
< 200 (<0.20)	-	-	-	-
200-400 (0.20-0.40)	+	-	-	-
400-800 (0.40-0.80)	+	+	-	-
800-1600 (0.80-1.60)	+	+	+	-
1600-3200 (1.60-3.20)	+	+	+	+

Normal result: Normal expected values in plasma are less than 0.20µg/l.

Statistical analysis

Data of this study was collected by structured questionnaire from patients and patients file and analyzed using Statistical Package for Social Sciences (SPSS)

Ethical Consideration

The study was approved by the ethical committee of the faculty of medical laboratory sciences, Alneelain University, Also approval for implication of this study was be obtained from Academic Hospital in Sudan with an informed consent from each patients.

RESULTS

The Total of 60 Sudanese patients were enrolled in this study, 30(50 %) were end stage renal failure patients on hemodialysis were as 30(50%) the control group.

The age ranged from 20- 80 year in case and control (Mean ±SD= 52.43 ±15.088, 49.23 SD 17.807) respectively. FDPs test was performed for all the samples.

All participants in the control group showed normal FDPs results (less than 200), while the case group was (10% less than 200 **µg/ml**), (10% 200 to 400**µg/ml**), (40%less than 500 to 800 **µg/ml**),(10%less than 900 to 1600 **µg/ml**) and(30% less than1700 to3200 **µg/ml**) shown in Figure **(1).**

There was a statistical significant difference in FDPs test between the case groups in compare to the control groups with p-value (0.000) shows in table (2).

There was no correlation between the FDPs level and duration of disease p-value (0.788) shows in table (3), there is significant correlation between the FDPs level and age with p-value(.0521) that show in table (3). The result of FDPs in relation to the tripe showed insignificant correlation with p-value (0.537) show in table (4).

The result of FDPs in relation to the gender showed strong significant with p-value (0.000).show in table (5).

Table (2) Comparison of FDPs level between case and control group

		Type				
		Case	**Control**	**Total**	**P value**	**Comment**
FDPs level	Less than 200	3	27	30	0.000	Significant
	200 to 400	3	3	6		
	500 to 800	12	0	12		
	900 to 1600	3	0	3		
	1700 to 3200	9	0	9		
	Total	30	30	60		

Figure (1) FDPs level in case and control

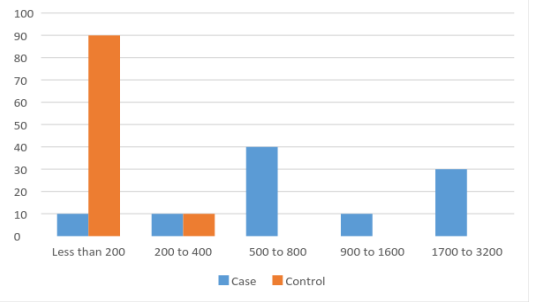

Table (3) Relationship between FDPs level and Age, duration of disease and duration of starting dialysis

	Correlation Coefficient	**P value**	**Comment**
Age	0.122	0.521	Insignificant
duration of disease	0.051	0.788	Insignificant

Table (4) Comparison of FDPs level between different tribes

		Tribe						
		North Sudan	**West Sudan**	**South Sudan**	**Middle Sudan**	**Total**	**P value**	**Comment**
FDPs level	Less than 200	2	1	0	0	3	0.537	Insignificant
	200 to 400	2	1	0	0	3		
	500 to 800	4	3	2	3	12		
	900 to 1600	2	1	0	0	3		
	1700 to 3200	2	2	0	5	9		
	Total	12	8	2	8	30		

Table (5) Correlation of FDPs level to the gender

		Gender				
		Male	**Female**	**Total**	**P value**	**Comment**
FDPs level	Less than 200	0	3	3	0.006	Significant
	200 to 400	3	0	3		
	500 to 800	5	7	12		
	900 to 1600	2	1	3		
	1700 to 3200	9	0	9		
	Total	19	11	30		

DISCSSION

The results show significant increase of FDPs level in patients when compared to normal control; that indicate excess activation of fibrinolysis that agree with Mohammed J. [11] This may be due to compensatory increase in tPA secondary to coagulation activation, although some patients show normal FDPs level (10%) most of patients shows increase may be as results of uremia level, this confirm the findings of Nakamura Y et al.[6]

Concerning the duration of starting dialysis the weak correlation, the duration of dialysis is not attributed to the FDPs level because the process of fibrinolysis is related to dialysis status rather than the duration of the starting dialysis Concerning the FDPs level with different age there was no correlation as well as with tripe, the gender with FDPs level showed significant correlation..

In conclusion; The FDPs level is increased in most of CRF patients indicating excessive fibrinolysis, the duration of starting dialysis has no association with the FDPs level in CRF patients. There was association between gender and the FDPs, while there were no correlations with age and tribe.

We recommended that Patients should do continuous screening for FDPs in our health facilities, large sample size should be performed with advanced method.

REFERENCES

1. Carl A.Burtis & Edwart R. Ashwood. Tietz fundamentals of clinical chemistry, 4th edition, W.B.SAUDERS company, 1999, chapter23, (P; 571,573)
2. Rose BD. Clinical assessment of renal function .in Rose BD, ed. Pathophysiology of Renal Disease, 2nd ed .New York: McGraw-Hill, 1987: 1-39.
3. Eberst E, Berkowitz LR. Hemostasis in renal disease: Pathophysiology and management. Am J Med, 1994; 96: 168-79
4. Locatelli F, Del Vecchio L, Manzoni C. Morbidity and mortality on maintenance hemodialysis. Nephron, 1998; 80: 380-400.
5. Sechi LA, Novello M, Colussi G, et al. Relationship of plasma renin with a prothrombotic state in hypertension: relevance for organ damage. Am J Hypertens 2008, P; 1347–1353
6. Nakamura Y, Chida Y, Tomura S Enhanced Coagulation-Fibrinolysis in Patients on Regular Hemodialysis Treatment, *Nephron, Japan, 1991;58:201–204.*
7. Mohammed Jomaa Ali Al-haj Faraj, Measurement of fibrin degradation products in chronic renal failure patients using d-dimer test, University of Jazera, Sudan 2005.
8. Hrafnkelsdo´ ttir T, Ottosson P, Gudnason T, Samuelsson O, Jern S. Impaired endothelial release of tissue-type plasminogen activator in patients with chronic kidney disease and hypertension. Hypertension 2004;44(3):300–304.
9. Cantin B, Despre´s JP, Lamarche B, et al. Association of fibrinogen and lipoprotein (a) as a coronary heart disease risk factor in men (The Quebec Cardiovascular Study). Am J Cardiol 2002;89(6):662–666.
10. Segarra A, Chaco´n P, Martinez-Eyarre C, et al. Circulating levels of plasminogen activator inhibitor type-1, tissue plasminogen activator, and thrombomodulin in hemodialysis patients: biochemical correlations and role as

independent predictors of coronary artery stenosis. J Am Soc Nephrol 2001;12(6):1255–1263.

11. Matsuo T, Koide M, Kario K, Suzuki S, Matsuo M. Extrinsic coagulation factors and tissue factor pathway inhibitor in end-stage chronic renal failure. Hemostasis 1997;27(4):163–167.

12. Sechi LA, Novello M, Colussi G, et al. Relationship of plasma renin with a prothrombotic state in hypertension: relevance for organ damage. Am J Hypertens 2008, P; 1347–1353.