

Full Length Research Paper

Evaluation of D-dimer concentration in Pre-haemodialysis in Sudanese patients

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Abstract

Background: Advanced chronic renal failure (CRF) is referred to as end stage renal disease (ESRD). Patients undergoing chronic haemodialysis treatment represent a high risk group for thromboembolic complications. The aim of this study is to measure concentration of D-dimer of end stage renal failure in pre-haemodialysis and to determine the effect of duration of dialysis on D-dimer concentration. **Methods:** Forty blood samples from patients with end stage renal failure were collected and compared to 30 samples from healthy persons as control group. D-dimer was measured in both groups using AGAPPE (MISPA-i2). This reagent is used for in vitro quantitative of fibrin degradation product, D-dimer, in human plasma by nephelometric immunoassay. **Results:** The mean value of the D-Dimer concentration was significantly elevated in the patients group (1.25mg/L) compared to the control group (0.178mg/L). Furthermore, according to the duration of dialysis, D-dimer was 1.04 mg/L in less than 4 yrs and 1.41mg/L in more and 4 yrs hemodialysis duration. **Conclusion:** The concentration of the D-Dimer was elevated in the patients pre-hemodialysis. Moreover the duration of hemodialysis was also elevated the D-dimer concentration with increased duration of dialysis.

Key words: D-Dimer, pre-hemodialysis, Thromboembolic, Renal failure.

INTRODUCTION

Renal failure is a condition in which the kidneys are less functioning than normal in removing excess water, failure to control blood pressure and red blood cells manufacturing. The condition can be characterized as acute renal failure (ARF) or chronic renal failure (CRF). However when the case is advanced CRF is called end stage renal disease (ESRD) (Moorthy *et al.*, 2009). The D-dimer is considered as a fibrin degradation product (FDP). Biochemically, the D-dimer is considered as a small protein fragment present in the blood when blood clotting undergoes degradation by fibrinolysis process and it contains two cross linked D fragments of the fibrin

protein (Adams *et al.*, 2009). The significance of the D-dimer in patients with hemodialysis investigation comes from its negative predictive value for the development of thrombosis and the test routinely used to exclude deep venous thrombosis and pulmonary embolism (Wada *et al.*, 2006; Kelly *et al.*, 2002)

The level of the D-dimer can be increased in different non-thrombotic disorders. For instance, the level is elevated in some inflammatory diseases, liver diseases, postoperatively, in eclampsia and sickle cell disease crises (Wada *et al.*, 2006); Kelly *et al.*, 2002). Most importantly patients with malignancy demonstrated high levels of D-dimer (Kelly *et al.*, 2002). It is noteworthy that, the D-dimer levels are even increased during pregnancy and in old aged peoples as physiological condition (Vurušić *et al.*, 2013). Dialysis procedures commonly

performed to remove nitrogenous end products of catabolism and maintain the correction of the salt concentration process, water and acid base detergents that are associated with renal failure.

However, dialysis mainly is not associated with the correction of the endocrine functions of the kidney (Hamilton, 2011). The possibly serious complications such as ischemic heart disease and stroke in addition to the thrombosis of the vascular access are associated with thrombotic tendency and the complications in chronic hemodialysis patients (Hamilton, 2011). Complex coagulation abnormalities occur, ranging from bleeding to thrombosis and the likelihood increasing bleeding tendency in these patients is mainly dependent on the functional platelet abnormalities and the failure to attach to the vessel wall (Sana and Emad, 2014). Furthermore multiple coagulation abnormalities contribute to an increased thrombotic tendency (Sana and Emad, 2014). For instance hypercoagulability in patients with chronic haemodialysis is caused by multiple factors, mainly consisting of platelet abnormalities and plasma factor abnormalities (Sana and Emad, 2014).

On the other hand the reduced activity of von Willebrand factor results in reduced interaction of platelets with the endothelium of blood vessels accompanied by reduced adhesive and aggregation capability. Fibrinogen synthesis accompanied by antithrombin III deficiency rises in kidney diseases with the development of nephrotic syndrome (Brunet *et al.* 2011; Kaw *et al.*, 2006).

In Sudan, according to ministry of health records, the prevalence of renal failure is increasing through the few past years; approximately 70 to 140 new patients undergo dialysis each year. This high frequency is thought to be due to epidemic malarial infection, which is well known to cause glomerulonephritis (Banaga *et al.* 2015). It is reported that the concentration of the D-dimer was elevated in patients post hemodialysis as well as the duration time (Sana and Emad, 2014). But there is no study measures the D-dimer concentration in patients pre-hemodialysis. Moreover there are no enough data of chronic kidney disease patients under hemodialysis that screened for coagulation defects to avoid bleeding tendency or any other thromboembolic phenomenon. Moreover whether chronic renal failure (CRF) impacts the value of the D-dimer test to predict the occurrence of thromboembolic event in hemodialysis patients and/ or whether the duration of dialysis impacts the D-dimer levels are not well clarified.

Therefore the main objectives of this study were to measure the concentrations of the D-dimer in patients pre-hemodialysis and to determine the effect of duration of dialysis on D-dimer concentration.

Materials and Method

Samples

This was a prospective case control study conducted in Khartoum State at Dr. Salma dialysis centre. Forty samples from patients with end stage renal failure under hemodialysis their ages between 16 to 60 years from both genders, exposed to different periods of haemodialysis were conducted as patients group. Thirty healthy persons were considered as the controls. 1.8 ml of blood samples were collected in blood containers containing tri-sodium citrate as an anticoagulant for measuring the D-dimer concentration. For measuring the concentration of urea and creatinine, lithium heparin was used as anticoagulant.

D-Dimer measurements

Patients with end stage renal failure, who were pre-hemodialysis, included. D-dimer was measured by AGAPPE (MISPA-i2). The reagent was used for in vitro quantitative of fibrin degradation product D-dimer in human plasma by nephelometric immunoassay. The principle of this D-dimer assay is a nephelometric assay that utilizes antibodies coated latex particles. In the presence of D-dimer, the particles aggregate and the light scattering increase. The increase of scattering light is proportional to the amount of D-dimer in the sample.

Urea and creatinine measurements

Urea and creatinine were measured using the commercial kits (Biosystem). The samples were analyzed using the chemical analyzer (Mindray BA-88A).

Statistical analysis

The collected data were analyzed using statistical package for social sciences (SPSS) computer programme to determine the mean of D-dimer level in patients and control use t- test for the significance of $p \leq 0.05$ between patients and control groups, and correlation was measured using Pearson test.

Ethical consideration

Every individual involved in this study was informed by its importance. This study approved by ethical committee of Medical laboratory Science College.

Result

The present study included 40 patients on chronic hemodialysis at the age from 18 to 60 years. In 87.5% of patients the D-dimer concentrations were above the upper limit. While the results of 12.5% of the patients were within normal reference limits in this study. The mean value of concentration D-dimer was 1.25 mg/l in the pre-hemodialysis patients compared to 0.178 mg/L in control with statistical significant differences (P value=

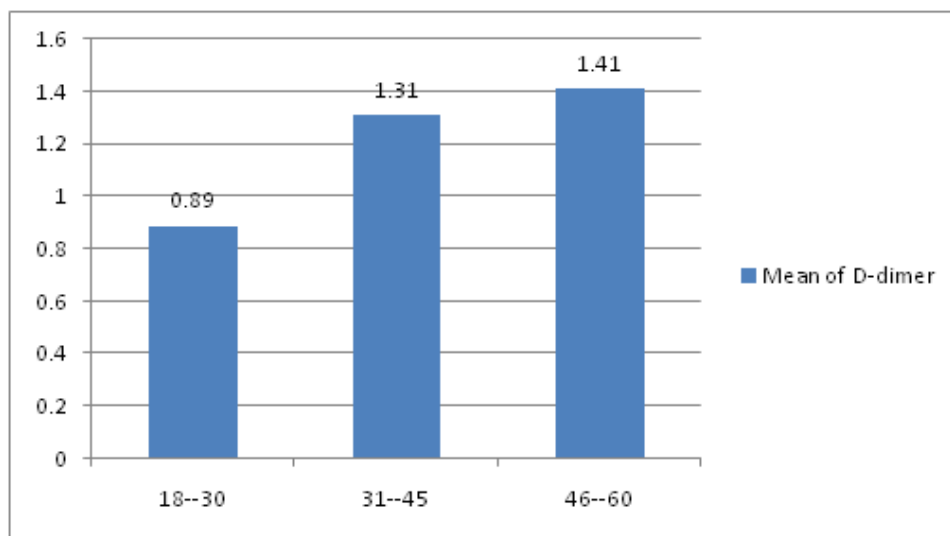
Table 1. The concentration of D- dimer level in hemodialysis patients versus control group

Measured unit	Means ± SD		p- value
	Patients No. =(40)	Control No. =(30)	
D Dimer	1.25±.49	0.178±.016	0.000

Table 2. Comparison the levels of D dimer, Urea and Creatinine in hemodialysis patients according to gender

Measured units	Means SD		p- value
	Male 57.5%	Female 42.5%	
D.dimer	1.24±0.48	1.26±0.51	0.801
Urea	127.12±23.4	116.17±25.4	0.831
Creatinine	7.0±2.4	6.94±2.22	0.988

Figure 1. Comparison of level of D Dimer in hemodialysis patients according to age groups



0.000) (table1). Also the D-dimer concentration was measured according to the gender. The mean of D-dimer of male was 1.24mg/l and female 1.26mg/dl but without statistical significant differences (table 2). Also the concentration of D-dimer was compared according to age of the patients. The mean concentration of D-dimer in the age between 18-30 yrs was 0.89 mg/l and mean of the age between 31-45 yrs was 1.31 mg/l and in the age between 46-60 yrs was 1.41 mg/l (P value=0.011) (figure 1). In addition to that the study measured the concentration of the D-dimer according to the duration time of hemodialysis. The result showed that the mean concentration of D-dimer in patient with less than 4 years hemodialysis was 1.04mg/l and patients more than 4 years

hemodialysis was 1.41mg/dl (Pvalue =0.016).

Discussion

The study demonstrated a significant increase in the D-Dimer concentration in patients pre-hemodialysis compared to the control group with a high statistical significant (P value=0.000). In another study the D-dimer was measured post hemodialysis (Sana and Emad, 2014). That study demonstrated mean concentration of D-dimer of 2.26mg/L which was elevated in patients post hemodialysis (Sana and Emad, 2014). This indicated that the D-dimer concentration pre or post hemodialysis is

characterized by increase concentration of the D-dimer. From those results one might anticipated that hemodialysis may affect the concentration of the D-dimer whether before or after hemodialysis. Moreover Gubensek et al, 2016 reported the association of hemodialysis with the elevation of the D-dimer levels in hemodialytic patients (Gubensek et al, 2016). Our result was also in agreement with the result of Silverberg et al, 2004 who showed that there was association between renal dysfunction and cardiovascular risk in the inflammatory and coagulation cascades. The activation of hemostasis is a common feature of uremia and its link with inflammation. Moreover the concentration of the D-dimer, urea and creatinine were measured in this study depending on the gender of the hemodialysis patients. The results demonstrated no statistical significance differences between the two categories. One previous study demonstrated that D-dimer concentration was elevated depending on the gender (Christopher *et al.*, 2013). That report showed that women were more likely to have a positive D-dimer than were men with statistical significant differences between male and female. Our result also showed elevated level of the D-dimer in the female category but without statistical significant differences. These two reports clearly showed the association of the gender with D-dimer concentration but the mechanism of this association needs to be clarified in further studies.

Also the D-dimer concentration was measured according to age of the patients. For instance the D-dimer was measured for 40 patients whose their ages ranged between 18 years to 60 years and result showed statistical significant as the concentration of the D-dimer is elevated with increasing age of the patients. This agreed with the report of Christopher *et al* (2013), that reported the association with age became statistically significant in the fourth to fifth decades of life. In addition to that in this study there was statistical significance in the D-dimer concentration according to duration of hemodialysis. The result showed that the patients with less than 4 years hemodialysis the D-dimer concentration was low compared the patients with more than 4 years hemodialysis. This agreed with the previously published report of Sana and Emad (2014). They reported that the duration of hemodialysis elevated the coagulation parameters. Moreover they also reported that the mean of D-dimer concentration in hemodialysis patient's the duration in less than 4 years was 1.6mg/l and more than 4years (4-8) years was 2.5 mg/l. Furthermore another report showed that the dysfunction of the activated coagulation may be due to the elevated D-dimer levels that not cleared by the kidneys.

Also Shlipak M *et al.*, (2003) has reported that there was a clear association between the renal insufficiency and increased levels of inflammation and procoagulant biomarkers. Therefore the increased level of the D-dimer in this report may be associated with this scenario. Also,

Oda *et al.*, (2000) in Japan, reported abnormalities of coagulation and fibrinolysis in patients with end stage renal disease as their results of D-dimer levels were significantly higher in the dialysis groups than in the control group.

Conclusion

The concentration of the D-Dimer was elevated in the patients pre-hemodialysis. Moreover the duration of hemodialysis elevates the D-dimer concentration with increased duration of dialysis. Taken together the results of this report clearly demonstrated the importance of the D-dimer concentration in the pre-hemodialytic patients and association of the D-Dimer as a screening for risk of thromboembolic complication. According to these results it is recommended to measure the D-Dimer concentration in hemodialytic patients' through different intervals of time particularly with increasing age of the patients.

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