Measurement of Plasma Fibrinogen and D-dimer levels in Sudanese Hypertensive Patients

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Abstract

Background Hypertension has become a public health problem in both developed and developing countries with serious morbidity and mortality. Fibrinogen has been identified as a major independent risk factor for cardiovascular diseases. D-dimer is a good biochemical marker of thrombosis. We aimed to measure the plasma fibrinogen and D-dimer levels in primary hypertensive patients.

Materials and methods This is a descriptive cross sectional study, conducted in Al-Enqaz medical center in Khartoum state (Sudan) during the period of May to October 2012. One hundred hypertensive patients and fifty normal controls were enrolled in this study. Fibrinogen level is assayed by the Clauss method, while D-dimer is assayed by the Nycocard D-dimer single test.

Results In spite of Plasma fibrinogen level was significantly increased with the D-dimer level in the studied group. The mean of plasma fibrinogen level was significantly higher in hypertensive patients (395.59 mg/dl) than in control group (354.69 mg/dl) (p=0.000), while D-dimer level was insignificantly increased in hypertensive patients when compared with control group (p = 0.301).

Conclusion This study concluded that plasma fibrinogen level was significantly increased in hypertensive patients, so measurement of fibrinogen level may be of some benefit in detecting thrombosis which appears to complicate the hypertension.

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Introduction

Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end organ damage and results in increased morbidity and mortality [(1)]. In Sudan, the prevalence of hypertension in an urban increased from 7.5% in 1985 to 18.2% in 2002 [(2)]. In about 90% of cases of hypertension has no known cause (primary or essential hypertension); the remainder are mostly secondary to renal disease or (less often) to renal artery stenosis (renovascular hypertension), endocrine abnormalities, vascular malformations, or neurogenic disorders [(3)]. Thrombosis often appears to complicate the course of patients with hypertension; thormbosis in some patients with hypertension could be developed to organ damage [(4)]**.** Fibrinogen is a major determinant of blood viscosity, and it is involved in haemostasis and thrombosis pathway [(5)]. It has been identified as a major independent risk factor for cardiovascular disease [(6),(7)]. Moreover, the results of the Leigh study, in which hypertensive patients with plasma fibrinogen above 3.5 g/L had a 12-fold greater coronary risk than those with fibrinogen below 2.9 g/L, suggest that fibrinogen levels may affect prognosis in hypertension [(8)]. D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis [(9)]. D-dimer is a good biochemical marker of thrombosis [(10)]. Elevation of D-dimer is associated with increased risk of future myocardial infarction, stroke, and peripheral vascular disease [(11)].

Materials and methods

Study population

This is a descriptive cross sectional study, conducted in Al-Enqaz medical center in Khartoum state (Sudan) during the period of May to October 2012 to measure the plasma fibrinogen and D-

dimer levels among 100 (40%male and 60% female) diagnosed hypertensive Sudanese patients treated with anti hypertensive drugs, their age ranged (35 -65) years and 50 non-hypertensive individuals as control group. Patients with diabetes mellitus, cardiovascular diseases, liver disease, kidney disease, under anticoagulant therapy, smoking, pregnancy, disorders associated with inflammation and other diseases such as DVT or treatments that may affect coagulation system were excluded, also secondary causes of hypertension and hypertensive patients with target organ damage have been excluded. Ethical clearance approved from institutional ethical committee and data was obtained from each participant by direct interview using structured questionnaire and signed informed consent was obtained from each participants.

Specimen collection and preparation

A total of 3.5 ml of citrated anti coagulated venous blood samples were collected (9 part blood to 1 part anticoagulant). The blood is thoroughly mixed with the anticoagulant. The samples were centrifuged at 2000g for 15 minutes to obtain platelet-poor plasma (PPP).Plasma was separated from cells into plane container. PPP will be stored and refrigerated on (2-8 ^{O} c) and tested within 4 hours.

Methods

Plasma fibrinogen level was assayed by the Clauss technique using automated blood coagulation analyzer (Sysmex CA-500 series). D-dimer was measured by NycoCard D-dimer single test, it is vitro test based on an immune technique, for the rapid determination of the fibrin degradation product D-dimer in plasma.

Data analysis

The SPSS-version 16 software was used for statistical analysis. T-Test, Chi-Square Test and ANOVA were used to calculate P value. Differences were considered statistically significant when P value ≤ 0.05.

Result

The mean of plasma fibrinogen level was significantly higher in hypertensive patients (395.59 mg/dl) than in control group (354.69 mg/dl), with p value= 0.000, (Table 1). The D-dimer level was insignificantly increased in hypertensive patients when compared with control group (p value= 0.301) (Table 2). D-dimer concentrations have been categorized into 4 groups : < 0.1 mg/l, 0.1mg/l, 0.2 mg/l and 0.3 mg/l. ANOVA test showed significant difference in plasma fibrinogen level between these groups (p value = 0.037) (Table 3). LSD test (Least Significant Difference) showed that the plasma fibrinogen level was significantly higher in hypertensive patients with D-dimer concentration of 0.3 mg/l than in those with D-dimer concentration of less than 0.1 mg/l (p value =0.012) and 0.1 mg/l (p value=0.008), while there was insignificant difference in plasma fibrinogen level between hypertensive patients with D-dimer concentration of 0.3 mg/l and 0.2 mg/l (p value =0.64) (Table 4).

Table 1: T test for plasma fibrinogen level between hypertensive patients and control group

Variables	Study group	N	Mean	Std. Deviation	P value
Fibrinogen mg/dl	Test group	100	395.5910	50.15413	0.000
	Control group	50	354.6940	53.87585	

Table 2: Chi-Square Test for the D-dimer level between hypertensive patients and control group

D dimer mg/l	Study group		P value
	Test group	Control group	
<0.1	55	25	0.301
0.1	33	23	
0.2	10	2	
0.3	2	0	
Total	100	50	

Table 3: ANOVA test for the plasma fibrinogen level between D-dimer (mg/l) groups

D-dimer (mg/l) groups	N	Fibrinogen (mg/dl) mean value	Std. Deviation	P value
< 0.1	55	393.9836	41.91109	0.037
0.1	33	387.5576	56.36925	
0.2	10	413.2700	53.81565	
0.3	2	483.500	73.60982	
Total	100	395.5910	50.15413	

Table 4: The LSD test for multiple comparisons in plasma fibrinogen level between D-dimer groups

D-dimer mg/l (I)	D-dimer mgl (J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
< 0.1	0.1	6.42606	10.73125	0.551	-14.8753	27.7274
	0.2	-19.28636	16.75416	0.253	-52.5431	13.9704
	0.3	-89.96636	35.08234	0.012 *	-159.6043	-20.3285
0.1	< 0.1	-6.42606	10.73125	0.551	-27.7274	14.8753
	0.2	-25.71242	17.59238	0.147	-60.6330	9.2082
	0.3	-96.39242	35.49028	0.008 *	-166.8401	-25.9448
0.2	< 0.1	19.28636	16.75416	0.253	-13.9704	52.5431
	0.1	25.71242	17.59238	0.147	-9.2082	60.6330
	0.3	-70.68000	37.75053	0.064	-145.6142	4.2542
0.3	< 0.1	89.96636	35.08234	0.012 *	20.3285	159.6043
	0.1	96.39242	35.49028	0.008 *	25.9448	166.8401
	0.2	70.68000	37.75053	0.064	-4.2542	145.6142

* significant difference.

Discussion

The present study demonstrated that, the plasma fibrinogen level was significantly higher in the hypertensive patients than in control group. This result was in agreement with Letcher et al, Tabak et al and Mehrotra TN et al, their studies demonstrated that the plasma fibrinogen level was significantly increased in hypertensive patients[12] [13] [14]. Also the present study showed that, the D-dimer level was insignificantly increased in hypertensive patients when compared with control group. This result was in agreement with Sechi et al in D-dimer level, but in contrast to it in plasma fibrinogen level [15].

The data analysis showed that the plasma fibrinogen level was significantly increased with the increased D-dimer level and this was in agreement with Lip et al [5], while disagreed with Vaziri ND et al who their study demonstrated that D-dimer level was significantly increased and plasma fibrinogen level was insignificantly increased in hypertensive patients [16]. These differences from our findings could be explained by interference of anti hypertensive treatments and difference in blood pressure values of hypertensive patients.

Conclusion

In conclusion, the plasma fibrinogen level was significantly increased in hypertensive patients and it is level was significantly increased with the increased D-dimer level,so measurement of fibrinogen level may be of some benefit in detecting thrombosis which appears to complicate the hypertension.

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