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Research Article

Measurement of Plasma Fibrinogen and D-dimer Levels in Sudanese Hypertensive Patients at Khartoum state

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Abstract

Background: Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end organ damage and results in increased morbidity and mortality. Thrombosis often appears to complicate the course of patients with hypertension; thrombosis in some patients with hypertension could be developed to organ damage. The aim of this study was to measure fibrinogen and D-dimer level among sudanese patients with hypertension.

Materials and method: This was a case control study conducted at Khartoum state, Sudan during the period from May 2022 to August 2022 to measure fibrinogen and D-dimer levels in sudanese patients with hypertension. Blood samples were collected, 50 from the patients as case group, and 50 from normal healthy subjects as control group. A total of three ml of whole blood were collected from each participant in sodium citrated tube. The fibrinogen and D-dimer level measurement was done by using coagulometer (M1 coatron) and ichroma II device respectively.

Results: The results of this study revealed that when compared Fibrinogen level and D-dimer between cases and control group; the results revealed that fibrinogen level was significant increase in hypertensive patients with P-value of 0.000. Also, D-dimer was significant increase in hypertensive patients when compared with the results of control group, and showed significant association with P-value of 0.000. There was a negative correlation between hypertension and the gender, but the age showed positive correlation with hypertension and with D-dimer, where both fibrinogen and D-dimer showed positive correlation with the duration of hypertension.

Conclusion: This study concluded; when compared the fibrinogen level and D- dimer between cases and control group, there was significant increase in fibrinogen and D- dimer.

Keywords: Hypertension, fibrinogen level, D-dimer, coronary artery disease, ischemic heart disease, Cardiovascular disease, DIC, fibrin degradation products

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] Thrombosis often appears to complicate the course of patients with hypertension; thrombosis in some patients with hypertension could be developed to organ damage. [2]

the prevalence of hypertension has increased, especially in low- and middle-income countries (LMICs). Estimates suggest that 31.1% of adults (1.39 billion) worldwide had hypertension in 2010. The prevalence of hypertension among adults was higher in LMICs (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people). [3] In Sudan, the prevalence of hypertension in an urban increased from 7.5% in 1985 to 18.2% in 2013. [4]

Variations in the levels of risk factors for hypertension, such as high sodium intake, low potassium intake, obesity, alcohol consumption, physical inactivity and unhealthy diet, may explain some of the regional heterogeneity in hypertension prevalence. [5]

Fibrinogen is a major determinant of blood viscosity, and it is involved in haemostasis and thrombosis pathway. [6] It has been identified as a major independent risk factor for cardiovascular disease. [7-8] 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. [9]

D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. [10] D-dimer is a good biochemical marker of thrombosis. [11] Elevation of D-dimer is associated with

increased risk of future myocardial infarction, stroke, and peripheral vascular disease. [12]

Some researchers identified elevated level of plasma fibrinogen and D-dimer in hypertensive patients. because there was no enough published data in Sudanese hypertensive patients regarding to the elevation of fibrinogen and D-dimer, the aim of our study was to measure the plasma fibrinogen and D-dimer in Sudanese hypertensive patients.

MATERIALS AND METHODS

This study was case – control study conducted at Sudan Heart Canter, Khartoum, Sudan during the period from May 2022 to August 2022. Patients attending at Sudan Heart Canter and diagnosed with hypertension during the aforementioned period were included. In addition to healthy participants with no history of thrombi or bleeding were selected as control group. Patients under anticoagulant treatment, also patients refuse to give consent, and those with previous history of thrombi were not recruited as controls and were excluded. From each participant 3 ml of venous blood samples were dispensed into sterile containers with tri-sodium citrate anticoagulant. Fibrinogen level was estimated by using the coagulometer (Semi-automated M1 coatron) by BioMed-Fibrinogen, while D-dimer was estimated by using Ichroma™ II. The data was gathered using pre-designed structural questionnaire and the SPSS 23.0 statistical software (SPSS Inc., USA) was used for statistical analysis. Finally, the study was licensed by the ethical committee ethical committee of national university.

RESULTS

Socio- demographic data

Total of 100 samples were collected from the study population, 50 of them were hypertensive patients and selected as case group, and 50 of them apparently healthy subjects were selected as control group.; the mean age of the control group was (58.4 ± 13.3), where the means age of the case group was (64.6 ± 8.5). The age showed positive correlation with the disease (hypertension), the P-value was 0.007. The distribution of the gender in the control group, was 44.4% and 56.5% for female and male respectively, were in the case group; 55.6% and 43.5% for female and male respectively. the gender showed negative correlation with the disease (hypertension), the P-value was 0.229. The distribution of the duration among case group was 10-15 years (12.7±2.1), followed by 5-10 years (8.8±1.2), and the least frequent duration was more than 15 years (23.9±6.1). Regarding to the distribution of anti-hypertensive drugs in this study was as follow; the most frequent drug was Thiazide, followed by Beta blocker, then Lisinopril, then calcium channel blocker, then Nifibidin, and the least frequent drug used by cases in this study was Thiazide +calcium channel blocker. On the follow up for a month only three patients were died. (Tables 1.2.3.4)

Table 1: Comparison of study population according to the age

		N	Mean	Std. Deviation	Std. Error Mean	P-value
AGE	**Case**	50	64.680	8.5056	1.2029	0.007
	Control	50	58.440	13.3953	1.8944	

Table 2: Distribution of gender in the study population

					P-value
			Case	**Control**	
Gender	**male**	**Count**	20	26	
		% Within Gender	43.5%	56.5%	0.229
	female	**Count**	30	24	
		% Within Gender	55.6%	44.4%	
Total		**Count**	50	50	
		% Within Gender	50.0%	50.0%	

Table 3: Distribution of duration in the cases

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**5-10**	11	11.0	22.0	22.0
	10-15	31	31.0	62.0	84.0
	more than 15 years	8	8.0	16.0	100.0
	Total	50	50.0	100.0	
Missing	**System**	50	50.0		
Total		100	100.0		

Table 4: Distribution of antihypertension drugs in the cases

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**calcium channel blocker**	7	7.0	14.0	14.0
	Thiazide	15	15.0	30.0	44.0
	lisinopril	10	10.0	20.0	64.0
	Beta blocker	13	13.0	26.0	90.0
	Thiazide + calcium channel blocker	2	2.0	4.0	94.0
	nifibidin	3	3.0	6.0	100.0
	Total	50	50.0	100.0	
Missing	**System**	50	50.0		
Total		100	100.0		

Haematological data finding

When compared Fibrinogen level and D-dimer between cases and control group; the results revealed that fibrinogen level was highly increased in hypertensive patients (10.4 ± 3.9), where the control group was normal (2.8 ± 0.5). which showed significance with P-value of 0.000. Also, D-dimer was highly elevated in hypertensive patients (313 ± 38.2) when compared with the results of control group (119 ± 55.8), and showed significant association with P-value of 0.000. when compared fibrinogen and D-dimer with duration of hypertension (5 years, 5-10 years, 10-15 years); in the fibrinogen level the mean was 13.5 ± 3.5, 15.3 ± 11.1, 9.7 ± 1.4 respectively. Which showed positive correlation (P-value=0.003). In D-dimer, the mean level was 311.5 ± 21.5, 294.5 ± 18.5, 325.5 ± 50.5 respectively, which showed positive correlation (P-value=0.004). in Age, there was positive correlation with D-dimer only with P-value of 0.044. Regarding to the antihypertensive drugs distribution in the cases, there was negative correlation with fibrinogen and Dimer levels with P-value of 0,243 and 0,078 respectively. (Tables 5,6,7,8,9)

Table 5: Comparison of study population according to the Fibrinogen level and D-dimer

		N	Mean	Std. Deviation	Std. Error Mean	P-value
Fibrinogen	Cases	50	10.4	3.9	0.5	0.000
	Control	50	2.8	0.5	0.07	
D-dimer	Cases	50	313.3	38.2	5.4	0.000
	Control	50	119.6	55.8	7.9	

NB: The unit we used for fibrinogen was g/l and the normal range is 2-4 g/l where the unit we used for D-dimer was ng/ml, and the normal range was less than 250 ng/ml.

Table 6: Comparison of fibrinogen and D-dimer according to the duration of hypertension

		N	Mean ± SD			P-value
			5-10 yrs	**10-15 yrs**	**>15yrs**	
Fibrinogen	**Cases**	50	13.5 ± 3.5	15.3 ± 11.1	9.7 ± 1.4	0.003
D-dimer	**Cases**	50	311.5 ± 21.5	294.5 ± 18.5	325.5 ± 50.5	0.004

Table 7: Correlations of age with study fibrinogen

		Age
Fibrinogen	Pearson Correlation	0.482*
	P. value	0.129

Table 8: Correlations of age with study D- dimer

		Age
D-dimer	Pearson Correlation	0.291*
	P. value	0.044

Table 9: Comparison of fibrinogen and D-dimer according to the antihypertensive drugs

	Antihypertensive drugs	**Fibrinogen Mean ± SD**	**D-dimer Mean ± SD**
Valid	**Calcium channel blocker**	11 ± 3	346.5 ± 28.5
	Thiazide	13.3 ± 8.7	317 ± 50
	Lisinopril	11.7 ± 4.3	316 ± 14
	Beta blocker	10.9 ± 6.9	345.5 ± 65.5
	Thiazide + calcium channel blocker	10.8 ± 2.2	318 ± 6
	Nifibidin	4.9 ± 1.1	342.5 ± 65.5
P-value		0.243	0.078

DISCUSSION

Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end organ damage and results in increased morbidity and mortality. Thrombosis often appears to complicate the course of patients with hypertension; thrombosis in some patients with hypertension could be developed to organ damage. The present study is a Case control hospital-based study conducted at Sudan heart canter-Khartoum state, for the assessment of Fibrinogen and D-dimer in Sudanese patients with hypertension. [1]

The results revealed that; the mean age of cases was (64.6 ± 8.5), while the mean age of the control group was (58.4 ± 13.3), which show that there is positive correlation between Age and hypertension development (P-value= 0.007). these findings agree with a study done by Leonardo A, et al. which stated that Age, blood pressure levels, duration of hypertension, smoking, HDL-cholesterol, triglycerides, and plasma fibrinogen, fibrin D-dimer, levels were significantly related to the presence and severity of target organ damage in essential hypertensive patients. [23]

Regarding to the duration of the disease, the most frequent duration was 10-15 years, followed by 5-10 years, and the least frequent duration was more than 15 years. Also, Leonardo A, et al stated that duration of hypertension has significant relation with hypertension development and organ damage. [23]

For the fibrinogen level and D-dimer measurement, when compared Fibrinogen level and D-dimer between cases and control group; the results revealed that fibrinogen level was highly increased in hypertensive patients and the mean difference between all cases and control group showed significance with P-value of 0.000. Also, D-dimer was highly elevated in hypertensive patients when compared with the results of control group, and showed significant association with P-value of 0.000. these findings agree with a study done by Samah Saif Alden Osman, that stated, 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, and the D-dimer level was insignificantly increased in hypertensive patients when compared with control group (p value= 0.301). But this study disagrees with her regarding D-dimer results. [25]

Also, many other studies agree with the present study regarding to the fibrinogen and D-dimer levels, and includes A study done by Leonardo A. Sechi in Relationship of Fibrinogen Levels and Haemostatic Abnormalities with Organ Damage in Hypertension, showed that Plasma fibrinogen and D-dimer levels were related to organ damage independent of age, blood pressure, duration of hypertension, and smoking status. Separate analysis indicated significant association of fibrinogen and D-dimer levels with cardiac, cerebrovascular, peripheral vascular, and renal damage. In conclusion, elevated plasma levels of fibrinogen and a prothrombotic state are associated with the presence and severity of target organ damage in patients with essential hypertension and may contribute to the development of atherosclerotic disease in these patients. [23] and another study done by Roberto Foggara Fibrinogen levels in normotensive and hypertensive men, that confirms the strong association between fibrinogen levels and smoking and the weaker association with age and total-cholesterol levels. Mean fibrinogen level was not significantly related to blood pressure, although the distribution of fibrinogen levels appeared to be J-shaped in hypertensive men. [24]

CONCLUSION

This study concluded; when compared the fibrinogen level and D- dimer between cases and control group, there was significant increase in fibrinogen and D- dimer**.** There was a negative correlation between the hypertension development and gender, and positive correlation between age and hypertension development.

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