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Research Article

Measurement of Protein C and protein S Level among Sudanese Hypertensive Patients

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Abstract

Background

Hypertension is a prevalent situation in which the long term force of the blood against artery walls is high enough that it may be eventually cause health problems, like heart disease.

Materials and Methods

This was Analytical case control study conducted at wad madani teaching hospital, Gazera , Sudan during the period from April 2022 to August 2022, to assess Protein C and protein S level among Sudanese hypertensive patients. 30 patients were selected as a case group, and apparently healthy donors with no history of any coagulation problems or any chronic disease were selected as control group. 2.8 ml of venous blood samples were collected in Tri Sodium Citrate anticoagulant. Protein C and protein S level was measured by (BIOBASE_EL_10 Microplate reader).

Results:

The mean of protein C in case was(101.3±33.5) and decreased in 23.3% of cases, protein S mean was (94.2±29.5) and decreased in only 10% of cases , while in the control group the mean of protein C was(125.8±20.2) and protein S mean was (116.3±18.3). when compared protein C and S means between case and control groups there was a highly significant decreased with (p value 0.00) , in the other hand when compared protein C and S means with the age ,gender, and other chronic diseases in the case group there was in significant differences , Also the result showed appositive correlation between protein C and S .

Conclusion:

In case group there was significant decrease of protein C and S when compared to control group, insignificant difference of protein C and S level with Socio- demographic data.

Keywords: Hypertension, Anticoagulant, Protein C , protein S, chronic diseases

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material,which is available to autho-rized users.

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Introduction

Blood pressure is a gauge of the force against the walls of arteries as the heart pumps blood through the body, also hypertension (HTN) or high blood pressure is a cardiac chronic medical situation in which the systemic arterial blood pressure is elevated.

Hypertension categorized as primary (essential) hypertension or secondary hypertension. Primary hypertension which means high blood pressure with no clear medical cause, Secondary hypertension is caused by other situations that affect the kidneys, arteries, heart or endocrine system. [1,2]

Protein C is a 62-kD vitamin K dependent glycoprotein produced by the liver as a zymogen and is activated by binding to the thrombin-thrombomodulin complex, with protein S (PS) acting as a cofactor. PC acts as a natural anticoagulant and its deficiency either homozygous or heterozygous, predisposes the individual to a state of thrombosis, essentially venous thromboembolism, and mainfests as myocardial infarction (MI) deep venous thrombosis, pulmonary embolism, or stroke [3]

Protein S synthesized in the endothelium, vitamin K-dependent plasma glycoprotein, subsist in two forms: complex form bound to complement protein C4b-binding protein (C4BP) and Free Protein S plays a part in the anti-coagulation pathway as a cofactor to Protein C in the inactivation of Factors Va and VIIIa.[4]

The evidence suggests that hypertension manifest to confer a prothrombotic or hypercoagulable state, which can be related to conventional risk factors, target organ damage, complications and long-term prognosis, as well as different antihypertensive treatments.

In Sudan there is many problems facing hypertensive patients in the awareness of the disease complications, diagnosis, suitable treatment, and the follow up. Also, there is clear gape in the important of anticoagulant therapy with the antihypertensive drugs, according to that this study designed to measure the natural anticoagulant (protein C and protein S) among Sudanese hypertensive patient.

Material and methods

This was analytical case control study, conducted at the laboratory of Madani Teaching Hospital at Gazera state during the period of April 2022 to august 2022. All hypertensive patients attending medicine clinic at the hospital for the follow up, and haven't history of bleeding, thrombi or under anticoagulant therapy were included as cases were included. Apparently healthy participants with no history of thrombi or bleeding were selected as control group. The data was collected using pre-designed structural questionnaire. In addition, the study was approved by the ethical committee of Madani teaching hospital, and the participants will be fully informed about the advantages and disadvantages before participation in the research (verbal informed consent).

From each participant 2.8 ml of blood samples were collected in trisodium citrate anticoagulant container for measurement of protein C and protein S by using (URIT 660 AESKULISA Protein C and S Microplate reader).

Test principle

The AESKULISA Protein C and S is a sandwich ELISA using micro plates coated with a capture antibody specific for human Protein C and S. diluted patient plasma is incubated in the wells allowing Protein C and S present in the plasma to bind to the antibody. The unbound fraction is removed by washing. Afterwards anti-human Protein S detection antibody conjugated to horseradish peroxidase (conjugate) is incubated and reacts with the antigen-antibody complex on the microwell surface. Following incubation, unbound conjugate is washed off. Addition of TMB-substrate generates an enzymatic colorimetric (blue) reaction, which is stopped by diluted acid (color changes to yellow). The rate of color formation from the chromogen is measured in optical density units with a spectrophotometer at 450 nm. Using a curve prepared from the Reference Plasma provided with the kit, the Protein S antigen relative percent concentration in patient plasma can be determined.

Results

The epidemiological study

In the present study 30 hypertensive patients were included, there mean of age (61.1±10.6) among them 60% were female and 40% were male. In addition to that 30 apparently healthy participant were selected as

control group there mean of age was (42.5±10.8), 53.3% were male and 46.7% were female. In the case group about 23.3% had diabetes, 10.0% had Asthma, 10% had renal failure, while about 56.7% hadn't any types of chronic disease. (table1,2) (figure1,2,3)

Table (1): Distribution of age and gender in case and control

	N	Minimum	Maximum	Mean	Std. Deviation
Case					
Age (years)	30	42	83	61.1	10.6
Control					
Age (years)	30	24	64	42.5	10.8
	Gender	**Frequency**	**Percent**		
Case	Male	12	40.0		
	Female	18	60.0		
	Total	30	100.0		
Control	Male	16	53.3		
	Female	14	46.7		
	Total	30	100.0		

Table (2): Distribution of other chronic disease

Other chronic disease	Frequency	Percent
No	17	56.7
Diabetes	7	23.3
Asthma	3	10.0
Renal failure	3	10.0
Total	30	100.0

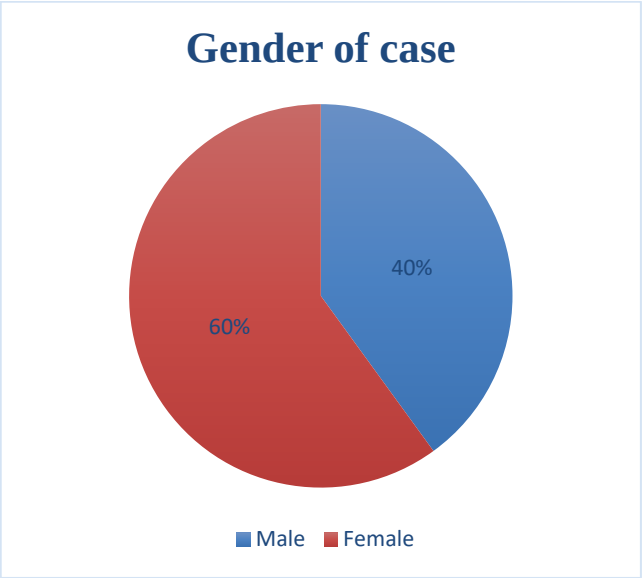

Figure (1): Distribution of gender in case

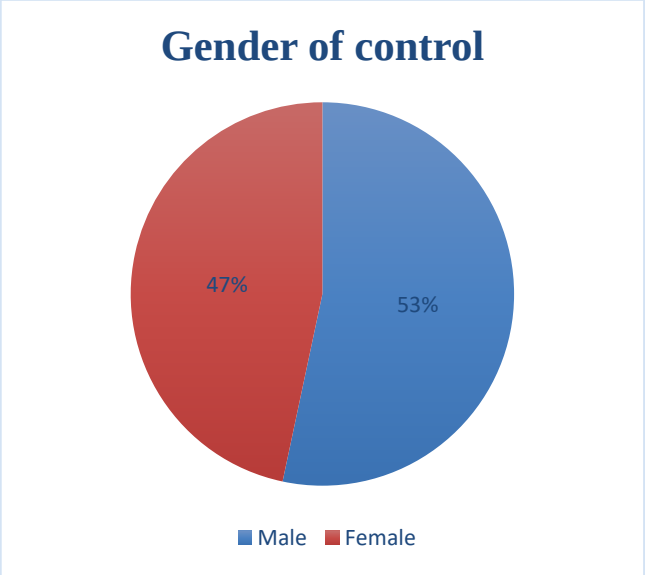

Figure (2): Distribution of gender in control

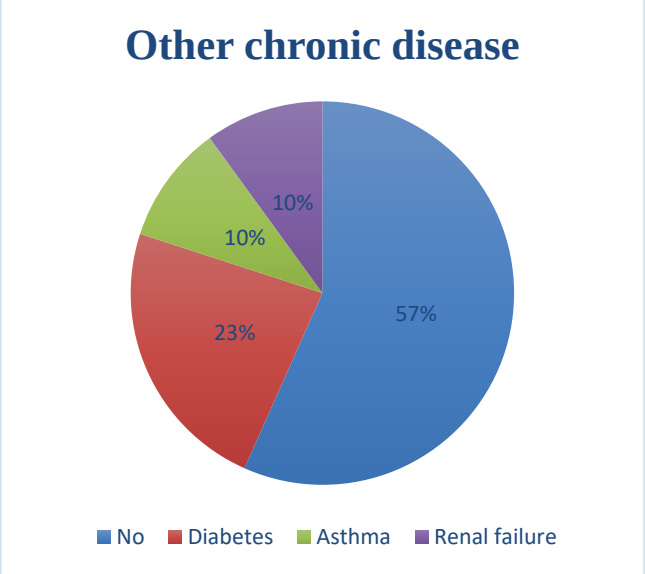

Figure (3): Distribution of other chronic disease

3.2 protein C and S results

protein C and S results revealed; the mean of protein C in case was (101.3±33.5) and decreased in 23.3% of cases, protein S mean was (94.2±29.5) and decreased in only 10% of cases, while in the control group the mean of protein C was (125.8±20.2) and protein S mean was (116.3±18.3). (table3, 4, 5) (figur4, 5, 6).

when compared protein C and S means between case and control groups there was a highly significant decreased with (p value 0.00) , in the other hand when compared protein C and S means with the age ,gender, and other chronic diseases in the case group there was in significant differences with (p value >0.05). Also, the result showed appositive correlation between protein C and S (p value 0.00). (Table 6,7,8,9,10) (figure 7).

Table (3): Descriptive Statistics of study parameters

	N	Minimum	Maximum	Mean	Std. Deviation
Case					
Protein C (%)	30	62	155	101.3	33.5
Protein S (%)	30	57	149	94.2	29.5
Control					
Protein C (%)	30	82	156	125.8	20.2
Protein S (%)	30	79	145	116.3	18.3

Table (4): Distribution of Protein C in case and control groups

Study population	Protein C (%)	Frequency	Percent
Case	Decreased	7	23.3
	Normal	23	76.7
Control	Normal	30	100.0

Table (5): Distribution of Protein S in case and control groups

	Protein S (%)	Frequency	Percent
Case	Decreased	3	10.0
	Normal	27	90.0
Control	Normal	30	100.0

Table (6): Comparison of Protein C and S between case and control

Parameters	Study population		P. value
	Case (n=30)	Control (n=30)	
Protein C (%)	101.3 ± 33.5	125.8 ± 20.2	0.001*
Protein S (%)	94.23 ± 29.5	116.3 ± 18.3	0.001*

Table (7): Comparison of Protein C and S according to gender of case

Parameters	Gender		P. value
	Male (n=12)	Female (n=18)	
Protein C (%)	102.7 ± 38.5	100.4 ± 30.8	0.862
Protein S (%)	96.4 ± 33.3	92.8 ± 27.6	0.747

Table (8) Comparison of Protein C and S according to age of gender

Parameters	Age		P. value
	≤ 60 years (n=15)	> 60 years(n=15)	
Protein C (%)	105.7 ± 34.9	97.0 ± 32.7	0.488
Protein S (%)	98.5 ± 32.6	90.0 ± 26.5	0.422

Table (9): Comparison of Protein C and S according to other chronic disease

Parameters	Other chronic disease	Mean ± SD	P. value
Protein C (%)	No (n=17)	102.0 ± 31.6	0.143
	Diabetes (n=7)	81.7 ± 32.6	
	Asthma (n=3)	111.7 ± 44.4	
	Renal failure (n=3)	133.0 ± 10.5	
Protein S (%)	No (n=17)	92.5 ± 27.7	0.232
	Diabetes (n=7)	82.7 ± 30.4	
	Asthma (n=3)	101.0 ± 41.6	
	Renal failure (n=3)	124.0 ± 10.1	

Table (10): Correlations of Protein C with Protein S

		Protein S (%)
Protein C (%)	Pearson Correlation	.979*
	Sig. (2-tailed)	.000

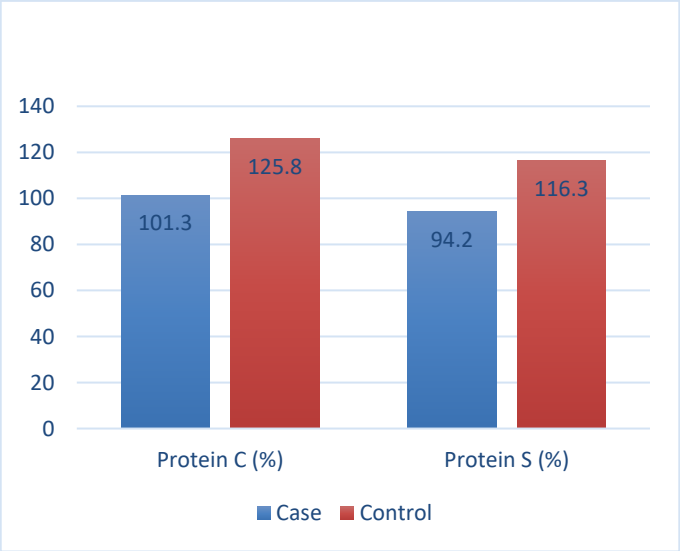

Figure (4): Mean of protein C and S in case and control

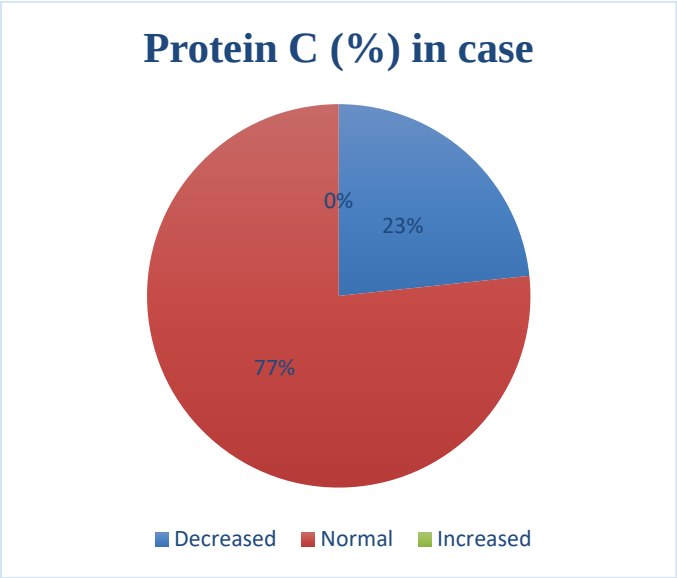

Figure (5): Distribution of Protein C

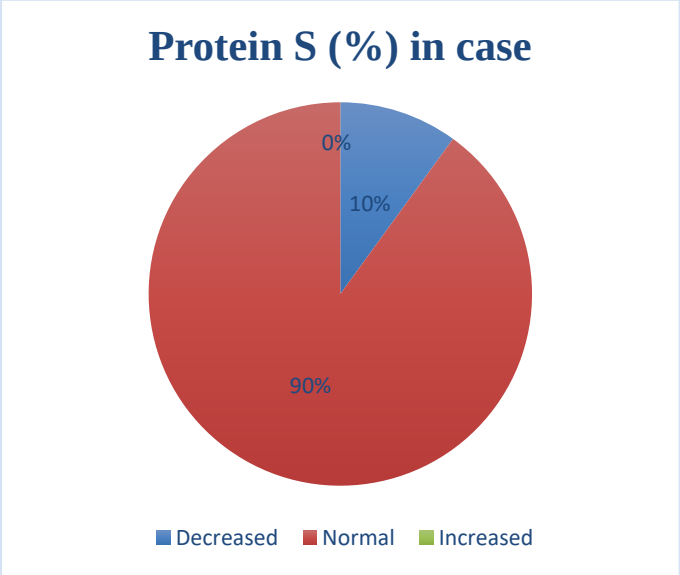

Figure (6): Distribution of Protein S

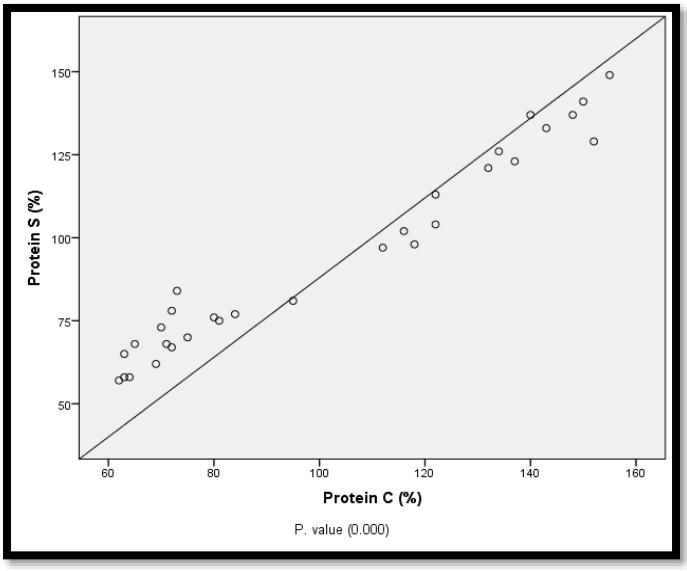

Figure (7): Correlations of Protein C with Protein S

Discussion

Hypertension is the prevalent diseases effecting human through the world, it is a risk factor for cardiovascular, cerebrovascular disease and mortality. [5] This study aimed to Assess protein C and protein S level among Sudanese hypertensive patients, the results of this study revealed that; mean of the patients age was (61.1±10.6), among them 60% were female and 40% were male. This agree with Nguyen et al which reported; hypertension prevalence is highest in older populations, almost 20 percent of young adults are hypertensive. [6]

And disagree with Sandberg etal which said; Men have higher blood pressure than women through much of life regardless of race and ethnicity, also Santosa et al; Men had a higher prevalence of hypertension (43% in Sweden, 39% in China) than their female counterparts (29 and 36%, respectively). [7,8]

In addition, Song et al mention; there were significant differences in epidemiology and clinical characteristic of hypertension between men and women. Moreover, gender differences are linked with several specific types of hypertensions, including postmenopausal hypertension, white coat hypertension, masked hypertension, and hypertensive disorders of pregnancy. [9]

In the present study about 23.3% had diabetes, 10.0% had Asthma, 10% had renal failure, while about 56.7% hadn't any types of chronic disease. These agree with one of the Ethiopian studies which found that; there is high prevalence of hypertension among diabetic patients. Age of ≥50 years, and having BMI of ≥25 kg/m^2 were associated with hypertension among participants.

Also, Ridao etal revealed; There is a high prevalence of hypertension in renal patients, which depends on the type of nephropathy and the degree of renal failure. Disagree with The Salako et al finding which reported;

frequency of hypertension among asthmatics is quite high and concurrent family history of hypertension. [10,11,12]

Regarding the protein C and S results the study revealed; protein C was decreased in 23.3% of cases, and protein S was decreased in only 10% of cases. Furthermore, when compared protein C and S between case and control groups there was a highly significant decreased, and insignificant differences when protein C and S compared with the age, gender, and other chronic diseases in the case group. Also, the result showed appositive correlation between protein C and S. this is similar to Gülsüm et al results which said; protein C was significantly decreased in the hypertensive group, another study showed; Protein C and S activity was significantly lower in hypertensive group as compared with the control group, Protein C and S showed significant correlation with both systolic and diastolic blood pressure. [13,14]

Gidon Berger et al reported in hypertension; Deficiencies of the classical inhibitors of coagulation (e.g., antithrombin, protein C, protein S) and abnormal procoagulantfactors (e.g., factor V Leiden) are well-recognized risk factors for thrombosis. With the rare exception of PAH associated with antiphospholipid antibodies, there is no evidence to suggest an increased tendency to PAH in inherited thrombophilic states. Five studies suggesting that anticoagulation therapy may be an effective intervention, two retrospective cohort studies did not support these findings [15] . while Frank et al. revealed; improved 5 year and 10-year survival were reported in warfarin-treated versus warfarin-naive PAH patients associated with systemic diseases. However, warfarin-treated and warfarin-naive idiopathic PAH patients had similar outcome as manifested by the 5-year survival rate.[16]

Conclusion

The study concluded that; there was significant decreased of protein C and S in the hypertensive patient, and there was significant positive correlation between protein C and S.

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