Protein C Level Among Sudanese Patients with Ischemic Stroke at Khartoum State, 2023

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Abstract

Background: ischemic stroke is one of three types of strokes. It is caused by a blockage in an artery that supplies blood to the brain. If circulation isn't restored quickly, brain damage can be permanent. This study was aimed to measure the protein c level among sudanese patients with the ischemic stroke.

Material And Method: This was a case control hospital based study conducted at ribat university hospital at khartoum state during the period of December 2022 to April 2023, it included all patients attending ribat university hospital who were diagnosed with ischemic stroke during the aforementioned period compared to apparently healthy individuals with no history of thrombi or stroke who were included as control group. Eliza was used for protein c measurement.

Results: the mean of protein c levels in the study group was (95.5± 19.5), in the control group was (82.2±14.2). Comparison of protein c level mean between cases and controls group revealed highly significant decrease among cases (P. V= 0.005). However, there were insignificant differences in protein c level between cases and controls in gender, past medical history and risk factors (p. V > 0.05) except for the heart conditions and family history of thrombi. Furthermore, a negative correlation of protein c level was detected with age (p. V >0.05).

Conclusion: The study concluded that there was highly significant decrease in the mean of protein c level in case group when compared to control group. There was insignificant correlation of protein c level with gender, past medical history and risk factors.

Keywords: Ischemic Stroke, Protein C, ELIZA, Activated Protein, Vitamin K.

Introduction

Ischemic stroke is one of three types of stroke. It is caused by a blockage in an artery that supplies blood to the brain. If circulation isn't restored quickly, brain damage can be permanent. Ischemic stroke is also called brain ischemia and cerebral ischemia. The blockage caused by this stroke reduces the blood flow and oxygen to the brain, leading to damage or death of brain cells. Ischemic stroke occurs when an artery that supplies blood to the brain is blocked by a blood clot or fatty buildup, called plaque. This blockage can appear at the neck or in the skull. [1]

Protein C is an endogenously occurring plasma protein anticoagulant that plays a key role within the coagulation cascade. Protein C is a zymogen, or enzyme precursor, of a vitamin K-dependent anticoagulant glycoprotein (serine protease) that is synthesized in the liver. It is converted by the thrombin/thrombomodulin-complex on the endothelial cell surface to Activated Protein C (APC). Once in its activated, APC functions as a serine protease with potent anticoagulant effects, especially in the presence of its cofactor protein S. APC exerts its effect by inactivating essential components of the coagulation cascade (specifically factors V and VIII), which leads to a decrease in thrombin formation, and therefore a reduction in clot formation. The Protein C pathway provides a natural mechanism for control of the coagulation system and prevention of excessive procoagulant responses to activating stimuli. A lack of protein C in the body would lead to unchecked coagulation activation, resulting in thrombin generation and intravascular clot formation. [2]

Material And Methods

This was a Case-Control Hospital Based Study Conducted at Ribat University Hospital at Khartoum State During the Period of December 2022 to April 2023, And Aimed to Measure Protein C Level in The Sudanese Patients with Ischemic Stroke. All Patients Attended to Ribat University Hospital Aged ≥18 Years, Presented Within 48 Hours of Onset of Symptoms of Acute Ischemic Stroke, Diagnosed on The Basis of Clinical Examination and Neuro-Imaging (Compute Tomography/Magnetic Resonance Imaging brain) were included in the study. In addition to that apparently healthy people with no history of thrombi or stroke were selected as control group.

Patients presented after 48 hours of onset of symptoms of acute ischemic stroke, patients with recent infection, malignancy, anemia, or liver failure, patients received blood/blood component transfusion in the previous 7 days; and patients under anticoagulant therapy were excluded from the study. The data was collected using pre-designed structural questionnaire. The study was approved by the ethical committee of National University, faculty of medical laboratory, and the participants Were Fully Informed About the Advantages and Disadvantages Before Participation in The Research (Verbal Informed Consent). From Each Participant 2.8 Ml of Blood Samples Was Collected in Trisodium Citrate Anticoagulant. ELISA Was Used to Measure Serum Protein C Level (AESKULISA Protein C Kits (3901) From AESKU Diagnostics Company And Urit-660 Microplate Reader).

Results

A total of sixty participants were included, thirty as a case group and thirty as control group. The mean of age of the control group was (48.9±5.5). In the case group

53% were male and 47% were female, their mean of ages was (64.9±11. 9) (Figure 1 , 2). The past medical history of the patients showed; 20% had history of thrombi, 20% had high lipid level, 13.3% had one of the heart conditions, 63.3% were hypertensive (HT) and 36.7% were diabetic (D.M). Regarding the risk factors; 40% were overweight, 13.3 % Practicing exercise and only 3.3% were smoker(Table1).

Table 1: Distribution of Past Medical History

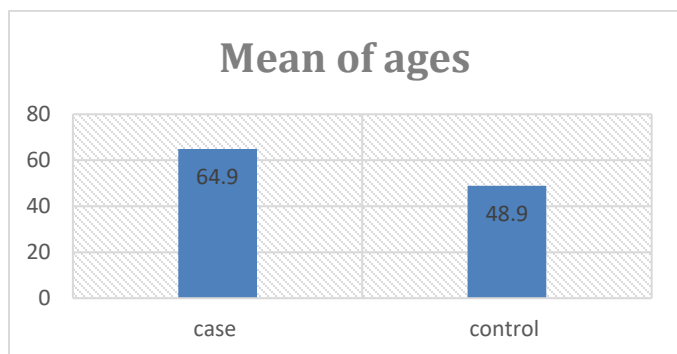| Variable	Yes		No	
	Frequency	Percent %	Frequency	Percent %
HT	19	63.3	11	36.7
D.M	11	36.7	19	63.3
History of previous thrombi	6	20.0	24	80.0
High lipid level	6	20.0	24	80.0
Heart conditions	4	13.3	26	86.7
Alcohol taker	0	0.0	30	100.0
Smoker	1	3.3	29	96.7
Practice exercise	4	13.3	26	86.7
Overweight	12	40.0	18	60.0
Family history of thrombi	12	40.0	18	60.0

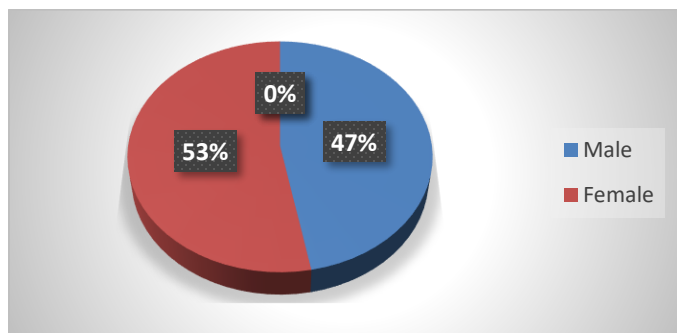Figure 1: Mean of ages in the case and control group

Figure 2: Distribution of gender among cases

Hematological Result

In the present study the results revealed that; the mean of protein C levels in the case group was (95.5± 19.5), in the control group was (82.2±14.2) (Figure3).

Comparison between case and control in protein C level showed highly significant decrease in the case group (p. v= 0.005) (Table 2). However, there were insignificant differences in protein C level between cases and controls in gender, past medical history and risk factors (p. v > 0.05) except for the heart conditions and family history of thrombi. Furthermore, a negative correlation of protein C level was detected with age (p. v >0.05). (Table 3, 4, 5).

Table 2: Comparison of protein C between case and control

Parameters	Study population		P. value
	Case	Control	
Protein C	82.2 ± 14.2	95.5 ± 19.5	0.005*

Table 3: Distribution of protein C level among gender

Parameter	Gender		P. value
	Male (n=14)	Female (n=16)	
Protein C	92.6 ± 22.4	98.1 ± 16.8	0.446

Table 4: Comparison of Protein C Level Between Patients According to Past Medical History

Past medical history		N	Protein C		P. value
			Mean	Std. Deviation	
B. P	Yes	19	95.7	17.4	0.942
	No	11	95.2	23.7	
D.M	Yes	11	97.1	17.1	0.746
	No	19	94.6	21.2	
History of previous thrombi	Yes	6	104.5	25.6	0.214
	No	24	93.3	17.6	
High lipid level	Yes	6	108.8	23.0	0.060

| Past medical history | | N | Protein C | | P. value |
			Mean	Std. Deviation	
B. P	Yes	19	95.7	17.4	0.942
	No	24	92.2	17.5	
Heart conditions	Yes	4	87.8	2.9	0.047*
	No	26	96.7	20.7	
Practice exercise	Yes	4	106.8	35.1	0.223
	No	26	93.8	16.4	
Overweight	Yes	12	97.8	15.4	0.607
	No	18	94.0	22.1	
Family history of thrombi	Yes	12	108.3	22.5	0.009*
	No	18	87.1	11.5	

Table 5: Correlations of age with protein C level

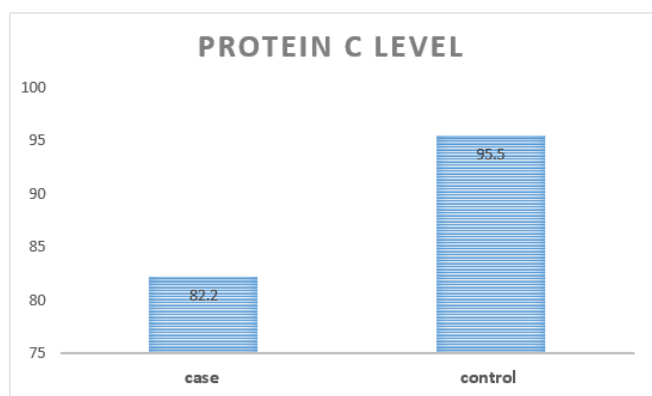| | Age | |
	Pearson Correlation	P. value
Protein C	0.227	0.227

Figure 3: Mean of protein C in cases and controls

Discussion

Protein C Is a Vitamin K Dependent Coagulation Inhibitor Produced in The Liver, Acting Together with Its Cofactor Protein S, Activated Protein C Inhibit Activated Factor V And VII Thus Down Regulating Thrombin Generation Which May Predispose to Inappropriate Clot Formation. Several researches Have Examined the Relationship Between Protein C Level and Ischemic Stroke, On the Field of Weather Low Levels of Protein C Are Related to The Prevalence and Mortality of Ischemic Stroke. [3]

This was case-control hospital-based study conducted at ribat university hospital at khartoum state and aimed to measure protein c level among sudanese patients with ischemic stroke. The results showed; in the case group 53% were female and 47% were male, their mean of ages was (64.9±11. 9), 20% had history of thrombi, 20% had high lipid level, 13.3% with heart conditions, 63.3% were hypertensive and 36.7% with d.m. regarding the risk factors; 40% were overweight, 13.3 % practicing exercise and only 3.3% were smoker.

This finding agreed with meaghan et al which reported; stroke is a disease of aging most strokes Occur In People >65 Years,Aged Patients Have Higher Mortality And poorer quality of life after stroke compared with younger patient. Sex also affects stroke incidence and outcome; although men have a higher incidence of stroke throughout theirlifespan, but women have higher stroke prevalence overall due to a longer average lifespan in females and hence increase in risk of stroke with aging. [4] also fahimfar et al said; the risk factors for ischemic stroke include aging, hypertension, diabetes, smoking, history of cardiovascular diseases (cvd), atrial fibrillation, and left ventricular hypertrophy. [5]

In the current research, the protein c level comparison between the case and control groups revealed an extremely significant decline in the case group. With the exception of cardiac conditions and a family history of thrombi, there were no appreciable variations in protein c levels between patients and controls in terms of

gender, prior medical history, or risk factors. Additionally, a negative association between the protein c amount and age was found.

these results consist with the study of folsom et al which mentioned; a low protein c level is associated with increased thrombosis in the large arteries of the neck or heart leading to ischemic stroke. In addition, in some cases low protein c may contribute to paradoxical embolism through a patent foramen oval. [6]

Boekholdt et al noted; protein c deficiency increases risk of venous thrombosis and children stroke. Also, some evidence confirmed that it increases risk of adult atherothrombotic events, including ischemic stroke [7]. However, folsom et al observed; protein c was inversely associated with ischemic stroke incidence, though not statistically significant so after adjustment for other stroke risk factors [8]

Similar results were observed in a study conducted by camerlingoet al,who evaluated the cause of non-hemorrhagic stroke in 50 individuals younger than 45 years of age and found pc deficiency to be the trigger in 6% of the cases. [9]

In loweet al study, the researchers found that despite low protein c being associated with increased stroke risk, also those with low protein c levels had significant changes in serum level of fibrinogen and von wille brand factor (possibly as acute phase reactants), hence modulation of anticoagulant functions might be of more important in ischemic stroke etiology.[10]

However, zakaiet al found no significant association of isolated protein c deficiency with stroke, but there was a relevant association in cardiovascular events with borderline low levels of protein c. [11] these findings were supported by hankeyet al study that assessed the role of protein c, protein s, antithrombin iii, factor v leiden, and prothrombin deficiencies as risk factors for ischemic stroke and reported low prevalence (0.9-5.2%) of isolated thrombophilias in patients with first ischemic stroke.[12]

Conclusion

The study concluded that there was highly significant decrease in the mean of protein c level in case group when compared to control group. Insignificant correlation of protein c level with gender, past medical history and risk factors was detected.

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