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Research Article

Levels of Protein S in Saudi Patients with Myocardial Infarction

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ABSTRACT

A heart attack - also known as a myocardial infarction (MI) or acute myocardial infarction (AMI)—happens when blood supply to a part of the heart stops, resulting in heart muscle damage. Coronary artery disease is the leading cause of MI. Risk factors include smoking, diabetes, lack of exercise, obesity, high blood pressure, poor diet, and excessive alcohol consumption. Protein S, a vitamin K-dependent protein, functions as a cofactor for activated protein C (APC), allowing it to inactivate factors Va and VIIIa more effectively. This study examines levels of protein S in Saudi patients with myocardial infarction. A case-control study was performed to estimate the level of protein S in Saudi patients with MI. A total of 150 samples (2.5/mL of venous blood) from patients with MI and healthy controls (n = 50) were obtained and analyzed using an enzyme-linked immunosorbent assay (ELISA) sandwich. Patients' mean protein S levels were within normal ranges (86.19.63 and 76.2030.64, respectively). Patients and controls had no significant difference in mean antithrombin (ATIII) and protein C levels (*p-value* = 0.26, 0.2, and 0.19, respectively). The findings also revealed that certain samples had low ATIII (8.7%) and protein C levels (11.3%). From this study, we conclude that protein S deficiency was not found to be a major risk factor for MI.

Keywords: Protein S, Myocardial infarction, Saudi patients.

INTRODUCTION

Cardiovascular disease (CVD) is still the major cause of death and morbidity worldwide, and its prevalence is rising. Myocardial infarction (MI) is the most frequent kind of CVD is caused by an atherosclerotic plaque and mainly affects adults [1]. When blood flow to a section of the heart is cut off, damage to the heart muscle occurs. This is known as MI or acute MI (AMI) [2]. Chest pain or irritation is the most prevalent symptom, which might spread to the shoulder, arm, back, neck, or jaw. [3]

Coronary artery disease is the most prevalent cause of MI, and risk factors include high blood pressure, smoking, diabetes, lack of exercise, obesity, poor nutrition, poor diet, and excessive alcohol consumption [4]. MI is one of the top five most expensive conditions during inpatient hospitalizations in the United States, with 612,000 hospital stays costing around $11.5 billion [6]. A highly personalized approach that tackles both acute risk factors and patient vulnerability could provide more widespread protection against MI and other coronary events.

The underlying mechanism of an MI is usually the complete occlusion of a coronary artery caused by a rupture of atherosclerotic plaque. Lifestyle changes, regular physical activity, and appropriate pharmacological regimens can all help to delay the beginning of coronary thrombosis, allowing time for collateral vessel formation, plaque stabilization, or invasive/surgical treatment [7]. Protein S, a vitamin K-dependent protein, is a cofactor for activated protein C (APC), helping it inactivate factors Va and VIIIa more effectively. It circulates in the bloodstream alongside C4b-binding protein, which controls the availability of protein S to serve as a cofactor for APC function [8]. Furthermore, a peptide is disrupted by thrombin between the Gla domain and the EGF-like domain of protein S. Following cleavage, a disulfide bond holds the Gla and EGF-like domains together.

Protein S loses its role as an APC cofactor after either its cleavage or binding C4BP. The most well-known role of protein S in the anticoagulation pathway is as a cofactor for protein C in the inactivation of factors Va and VIIIa. Only the free form of the cofactor has activity.[9] Protein S binds to the nascent complement complex C5,6,7, preventing it from entering a membrane. This function prevents the complement system from being activated in an unregulated manner, resulting in systemic inflammation. Protein sis is named after the membrane region in the complex where it is present and was discovered to perform this function in 1977 [10].

MATERIALS AND METHODS

Patients

In this case-control study, protein S levels were detected in Saudi patients with MI. The case group consisted of 150 Saudi patients with MI, and the control group consisted of 50 healthy volunteers. Patients were excluded if they had diabetes, hypertension, or atherosclerosis or if they used warfarin or heparin. Each participant obtained 2.5 mL of venous blood in a plastic vacutainer tube with sodium citrate anticoagulant for immunological testing.

Principle of Measurement of Antithrombin (ATIII) and Protein C Levels

The Saudi Arabian Ministry of Health's ethical council approved all study methodologies (Abha section). The AESKULISA protein S immunoassay is a sandwich ELISA in which patient plasma is incubated in wells covered with a capture antibody specific for protein S at 1:51 dilution, allowing the protein S present in the plasma to bind to the antibody. Washing removes the unbound portion. An anti-human protein S detection antibody conjugated to horseradish peroxidase (conjugate) is then incubated with the antigen-antibody complex on a micro-well surface to react with it. The unbound conjugate is rinsed away after incubation.

When TMB-substrate is added, an enzymatic colorimetric (blue) reaction occurs. Diluted acid is used to stop this (indicated by color change to yellow). A spectrophotometer set to 450 nm measures the rate of color production from the chromogen in optical density units. The relative concentration percentage of protein S antigen in patient plasma can be calculated using a curve built from the reference plasma provided with the kit [11].

RESULTS AND DISCUSSION

This study examined 150 patients with MI and 50 healthy volunteers as controls. Among the participants, 101 (67.3%) of the patients and 39 (78%) of the controls were male, while 49 (32.7%) of the patients and 11 (22%) of the controls were female (Table 1). The most prevalent age bracket was 51 to 60 years, followed by 61 to 70 years, 41 to 50 years, >70 years, 31 to 40 years, 21 to 30 years, 10-, and 10 to 20 years (Table 2). Most patients (80.7%) had normal protein S levels, with the remaining (19.3%) having low levels. Among the controls, 49 (98%) participants had normal levels, and one (2%) had low levels.

DISCUSSION

Hereditary thrombophilia (also known as hypercoagulability) is an inherited increased proclivity for intravascular thrombi (either venous or arterial), which primarily affects young people (under 45 years old) and is recurrent. A considerable percentage of those affected have a noticeable anomaly, but the majority develop thrombosis only when other risk factors are present [12, 13]. MI is a common occurrence in adults but not in younger populations. Many biochemical factors have an impact on coagulation and the production of clots, and protein S is one example.

In a considerable majority of instances, the cause of MI is unknown. The discovery of naturally occurring components like protein S and the fibrinolytic system has contributed to a better understanding of hemostatic diseases that can result in thrombosis and, as a result, MI [14]. The levels of naturally occurring coagulation inhibitor (protein S) in the blood of patients with MI were examined to see whether inhibitor deficiency was a risk factor for MI.

Males made up 101 (67.3%) of the patients and 39 (78%) of the controls in the current study, while females made up 49 (32.7%) of the patients and 11 (78%) of the controls (22%). Males were found to have a greater occurrence of MI than females (Table 3). The highest risk of MI was found in the age range of 51 to 60 years, followed by 61 to 70 years, 41 to 50 years, >70 years, and 31 to 40 years. Protein S deficiency was discovered in everyone over the age of 30 years. Protein S levels were greater only in patients above the age of 70 years. Protein S deficiency was more common in men than in women (Table 4).

Patients and controls exhibited similar PS levels, whereas 19.3% of patients had protein S insufficiency. This discovery contradicts the findings of Callas *et al.*, who found that the mean protein S level in patients with MI was low [15]. Acquired protein S deficit may play a role in the development of MI in some patients because genetic protein S deficiency is uncommon [16].

Table 1: Age distribution in the study population

Age group (years)	*Patients*		*Control*	
	Frequency	*%*	*Frequency*	*%*
<10	4	2.7	3	6
10–20	3	2.0	3	6
21–30	10	6.7	12	24
31–40	14	9.3	5	10
41–50	27	18.3	9	18
51–60	36	24.0	8	16
61–70	30	20.0	3	6
>70	26	17.3	7	14
Total	150	100%	50	100%
Mean ± SD	53.90 ± 11.13		44.49 ± 24.93	

Table 2: Protein S levels in the study participants

Protein S Level %	Patients		Control	
	Frequency	%	Frequency	%
Low <60	29	19.3	1	2
Normal 60–150	121	80.7	49	98
High > 120	0	0	0	0
Total	150	100	50	100

Table 3: Association between gender and protein S levels among the study population

Inhibitor	Gender				*p-value*
	Male	Female	Male	Total	
Protein S	Low	8(5.3%)	21(14%)	29(100%)	0.666
	Normal	41(33.9%)	80(66.1%)	121(100%)	

Table 4: Association between age groups and protein S levels among the study population

Age group	*Protein S level*			*p-value*
	Low	*Normal*	*High*	
<10	1 (0.7%)	4 (2.7%)	0	0.303
10–20	1 (0.7%)	3 (2%)	0	
21–30	2 (1.3%)	10 (6.7%)	0	
31–40	3 (2%)	11 (7.3%)	0	
41–50	3 (2%)	24 (16%)	0	
51–60	6 (4%)	30 (20%)	0	
61–70	3 (2%)	27 (18%)	0	
>70	10 (6.7%)	16 (10.7%)	1 (0.7%)	

CONCLUSION

This study revealed that the mean protein S level was not substantially different between patients and controls. Some patients had low levels of protein S. There was no effect of age or sex on protein S levels. There may be other causes of MI and AMI.

Ethics Approval and Consent to Participate

This cross-sectional study was approved by the Ministry of Health, Abha area, Abha, Saudi Arabia. A waiver of consent was given because no direct contact with participants was made, and data were collected anonymously and discreetly in accordance with the Declaration of Helsinki.

Statement for Data Sharing

Data will be provided upon request after acceptance and signing an agreement with Taif University.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

The experiments were carried out by Tariq E. Elmissbah and Mohammed Essam Idierous, and the manuscript was written with the help of Kahal Alsharif. Fawaz Mushabab Al-Qathami, Haya Elhuthali, and Amal Shuwaiman Alosaimi directed the study and assisted with the experiments.

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