



DETERMINATION OF PROTEIN C LEVEL IN CORONARY HEART DISEASE IN SUDAN

Alaa Mohamed A. Alnoor*¹ and Mahdi H. A. Abdalla²

¹Department of Hematology, Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.

²Associate Professor of Hematology, Department of Hematology, Faculty of Medical Laboratory Sciences, Omdurman Ahlia University, Khartoum, Sudan.

*Corresponding Author: Alaa Mohamed A. Alnoor

Department of Hematology, Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.

Article Received on 07/09/2020

Article Revised on 28/09/2020

Article Accepted on 18/10/2020

ABSTRACT

Introduction: Coronary Artery disease is a leading cause of morbidity and mortality in the developed and developing countries. Several underlying genetic and environmental factors have been implicated in its etiology. Some of the coagulation risk factors implicated in the development of coronary heart disease include protein C. **Material and method:** in the present study we determined the plasma level of Protein C level by ELIZA methods. A total of 90 samples were collected (45 with Coronary Artery Disease Patients and 45 healthy controls), the mean of Protein C level among case group (62.1±9.1) was significantly lower than control group (121.2±20.0), (p. Value 0.000). **Results:** Data were analyzed using statistical package for the social science (SPSS) version 22. There was significantly lower in PC in Coronary artery patients when compared to control group. **Conclusion:** The Protein C level results where is significantly Lower in case than control correlate (p.value:0.000).

KEYWORDS: Coronary Artery Disease, Protein C, Sudan, 2020.

INTRODUCTION

Cardiovascular Disease (CVD) are generally stated to as conditions that involve narrowed or blocked (thrombosis) blood vessels that can lead to ischemic heart disease (IHD) (myocardial infarction, angina) or stroke.^[1] Worldwide, cardiovascular disease (CVD) is responsible for 30% of all deaths and 10% of DALYs (disability-adjusted life years).^[2] According to W.H.O CVD are number one cause of death globally: more die annually from CVDs than from any cause. An estimated 17.9 million people died from CVD in 2016, representing 31% of all global death.^[3]

Coronary heart disease is a frequently encountered multifactorial disorder and is recognized as a major cause of morbidity and mortality both in developed and developing countries.^[4] It is a leading cause of morbidity and mortality in the developed and developing countries. Clinical manifestations of heterozygous protein C deficiency include VTE and warfarin-induced skin necrosis (WISN). Heterozygous protein C deficiency does not appear to be associated with an elevated risk of arterial thrombosis.^[4]

Some of the hematological risk factors implicated in the development of coronary heart disease include antithrombin III deficiency, protein C and protein S deficiency, factor V Leiden mutation, prothrombin

gene (20210A) mutation hyper homocystinaemia, elevated factor VIII levels, plasminogen activator inhibitor type 1 and dysfibrinogenemia.^[5] Under normal conditions, antithrombin III (AT III), protein C, and protein S as an active protein C cofactor, are natural anticoagulants (hemostatics control) that balances procoagulant activity (thrombin antithrombin complex balance) to Prevent thrombosis.^[5]

The cause of CHD depends on the type the condition may also have more than one cause, including plaque buildup or problems that affect how the heart's blood vessels work.^[6]

Protein C is a vitamin K-dependent glycoprotein structurally similar to other vitamin K-dependent proteins affecting blood clotting, such as prothrombin, factor VII, factor IX and factor X. Protein C, also known as auto prothrombin IIA and blood coagulation factor XIV, is a zymogenic.^[7] Protein C interacts with thrombomodulin to become activated protein C (APC). APC has anticoagulant, anti-inflammatory, and cytoprotective properties and has been proposed for the treatment of sepsis. The signal cascade leading to APC can become distorted through many acquired or inherited mechanisms leading to APC resistance. Activated protein C inactivates coagulation factors V and VIII. The factor V Leiden mutation is a common cause for APC

resistance and the most frequent genetic thrombophilia.^[8] low protein C or low activated protein C is associated with venous thromboembolism.^[9] and with stroke.^[10,11] but not clearly with heart disease, although observational studies are not always a reliable guide to the effects of interventions. Protein C deficiency is associated with arterial thrombosis.^[12] in this study we tested the hypothesis that plasma protein C and different coagulation factors might be able to be used as a biomarker for coronary heart disease (CHD) Plasma protein C inhibitor is higher in myocardial infarction.^[13] The aim of this study was to determine Protein C level among Coronary Artery Disease Patients in Sudan.

MATERIALS AND METHODS

This was a case-control study, conducted in Khartoum, Sudan during the period from October 2019 to March 2020, samples were included (45) samples as coronary artery patients as Case and (45) sample of healthy individual as Control). 2.5 ml of venous blood was collected from coronary artery heart disease patients and then transferred in to disodium citrate and separated by centrifuged methods, Protein C was measured using ELISA commercial assay kit from Aesku, Diagnostics, Germany (normal range: 70-140%), this measure only the amount of Protein C present and not its functional activity. Data was collected using a structured questionnaire answered by coronary artery patients, sample size calculated by using following equation:

$$n = \frac{z^2 pq}{d^2}$$

N: sample size, **z:** stander deviation when significant level is 95%, **p:** previous prevalence, **q:** 1-p, **d:** desired margin of error and Data were analyzed by using statistical package for the social science (SPSS) Version 22. Ethical approval was obtained from AL Neelain university intuitional review.

ETHICAL CLEARNCE

Ethical approval was obtained from AL Neelain university intuitional review.

RESULTS

This study was conducted in Khartoum Sudan Among 90 individuals. There were divided into two groups 45 were patients with Coronary artery disease who considered as cases and 45 apparently healthy individuals, who considered as control. the mean of age 56 years in case and 39 years in control. Our study revealed statistically significant difference between cases and controls. Mean Protein C level among case group (45.2± 16.1) was significantly lower than control group (85.2±12.0) (P-value 0.000).

Table (1): Frequency of gender among study population.

Gender	Case	Control
Female	20 (44.4%)	21(46.6%)
Male	25(55.6%)	24(53.4%)
Total	45 (100%)	45(100%)

Table (2): mean and STD of Protein C among study population

Parameters	Case (mean ±Std)	Control (mean ±Std)	P. value
Protein C	45.2±16.1	85.2±12.0	0.000

The table shows the mean ± SD (mini - max) and probability (P)

Independent T-test was used for comparison. P value ≤ 0.05 was considered significant.

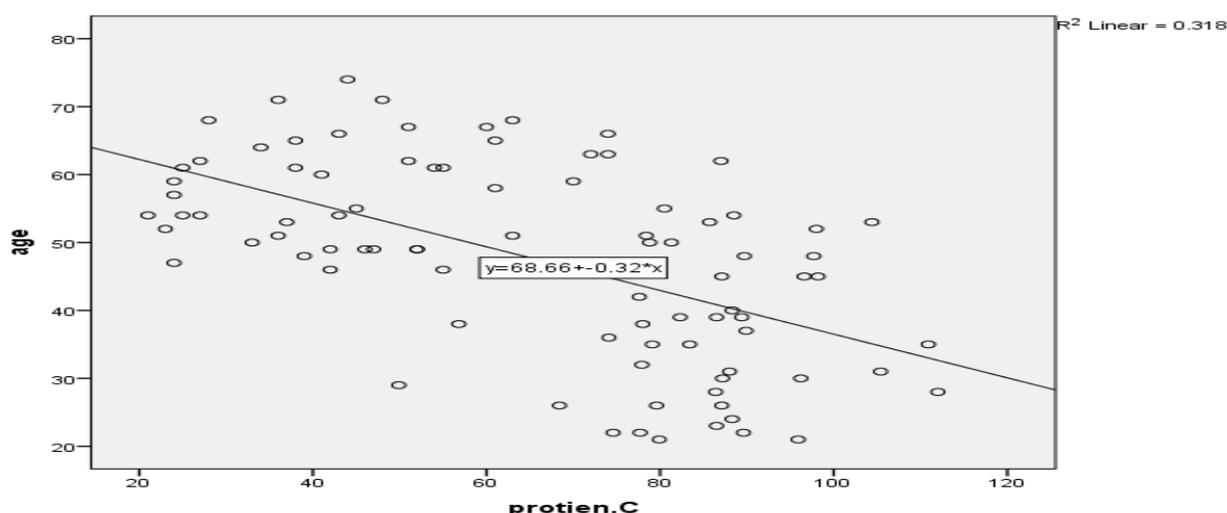


Figure (1): Correlation of Protein C and age of patients among study group (R=-0.3, P.value 0.06).

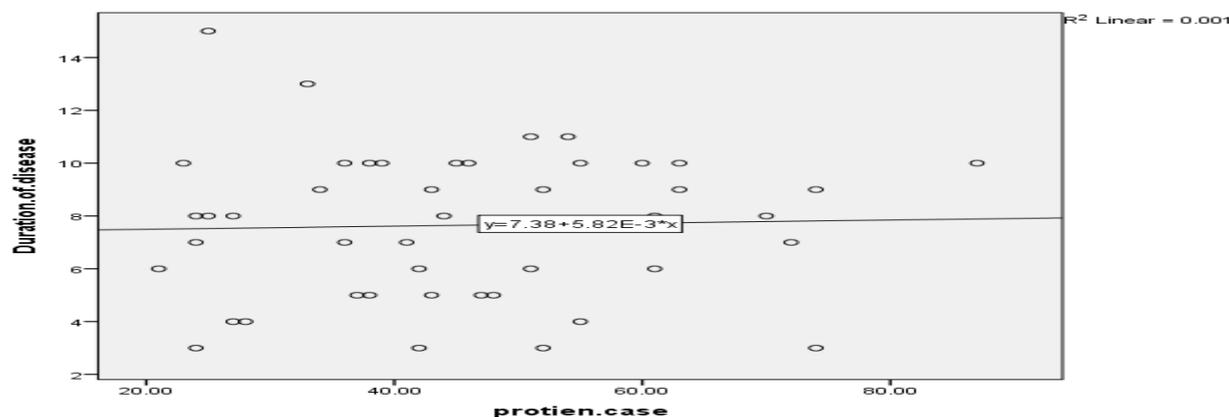


Figure (2): Correlation of Protein C and duration of patients among study group ($R=-0.013$, P .value 0.69).

DISCUSSION

Protein C (PC) is a vitamin K-dependent glycoprotein activated by thrombin thrombomodulin complex on the surface of endothelial cells. Protein C is a precursor of the serine protease, activated protein C (APC).^[14,15]

In the present study Ninety patients were enrolled in this study (45 were coronary artery patients and the others were healthy controls). Our study revealed statistically significant difference between cases and controls concerning Protein C level (Mean=45.2 ±16.1 and 85.2±12.0, P value=0.000 respectively).

In our study the mean of Protein C level was significantly lower than that of the healthy control group ($P < 0.00$) Our observation was matched with Khalil et al.^[16] that found Protein C in case was 85 it lower than in control 109 in coronary artery patients. Lauribe et al.^[17] found The raised fibrinogen and decreased protein C appeared to be risk factor for sudden cardiac death. Gibbs et al.^[18] reported increase in the procoagulants fibrinogen, factor VIII, and decrease in protein C and antithrombin III in cases of myocardial infarction.

CONCLUSION

The Protein C level results where is significantly Lower in case than control correlate (p .value:0.000).

RECOMMENDATION

We recommend designing cohort study for Coronary Artery disease to evaluate the Protein C, also we recommend increasing sample size.

Recommended protein C routinely in clinics, and should be funded because the price is too expensive

ACKNOWLEDGMENT

We are indebted to the staff of Haematology Department (Alneelain University). And, special thanks to the patients for being cooperative. And special thanks to Dr. Mahdi Hussein.

REFERENCES

1. Sarwar, M.H., Mughal, A.R., Mughal, S. and Sarwar, M., Concerns of Heart Diseases and Mediations to Encourage Healthful Actions for Their Deterrence. *International Journal of Bioinformatics and Biomedical Engineering*, 2015; 1(2): 70-76.
2. World Health Organization. The global burden of disease: update, 2004.
3. Hoffmeister HM. Overview of the relevant aspects of the blood coagulation system-focus and cardiovascular hemostasis. *Kongressbd Dtsch Ges Chir Kongr*, 2001; 118: 572-575.
4. El-Hazmi, M. A. Hematological risk factors for coronary heart disease. *Medical Principles and Practice*, 2002; 11(Suppl. 2): 56-62.
5. Al-Nozha, M. M., Abdel-Gader, A. G., Arafah, M. R., Al-Maatouq, M. A., Al-Shahid, M. S., Al-Harthi, S. S., ... & Abdullah, M. A. Tissue factor pathway inhibitor, natural coagulation inhibitors and hemostatic activation markers in patients with acute coronary syndromes. *Saudi medical journal*, 2005; 26(6): 937-942.
6. Zaman, A. G., Helft, G., Worthley, S. G., & Badimon, J. J. The role of plaque rupture and thrombosis in coronary artery disease. *Atherosclerosis*, 2000; 149(2): 251-266.
7. Mosnier, L. O., & Griffin, J. H. Protein C anticoagulant activity in relation to anti-inflammatory and anti-apoptotic activities. *Front Biosci*, 2006; 11(2): 381-2.
8. Ranjan, S. Activated protein C protects from GvHD by inducing regulatory T-cell expansion and signaling via the PAR2/PAR3 heterodimer in T-cells, 2017.
9. Folsom AR, Aleksic N, Wang L, et al. Protein C, antithrombin, and venous thromboembolism incidence: a prospective population-based study. *Arterioscler Thromb Vasc Biol.*, 2002; 22: 1018-1022.
10. Folsom AR, Ohira T, Yamagishi K, et al. Low protein C and incidence of ischaemic stroke and coronary heart disease: the Atherosclerosis Risk in

- Communities (ARIC) Study. *J Thromb Haemost*, 2009; 7: 1774–1778.
11. Van der Bom JG, Bots ML, Haverkate F, et al. Reduced response to activated protein C is associated with increased risk for cerebrovascular disease. *Ann Intern Med*, 1996; 125: 265–269.
 12. Soare AM, Popa C. Deficiencies of proteins C, S and antithrombin and activated protein C resistance—their involvement in the occurrence of Arterial thromboses. *J Med Life*, 2010; 3: 412–415.
 13. Anderson, L. Candidate-based proteomics in the search for biomarkers of cardiovascular disease. *The Journal of physiology*, 2005; 563(1): 23-60.
 14. Christiaans SC, Wagener BM, Esmon CT, et al. Protein C and acute inflammation: a clinical and biological perspective. *Am J Physiol Lung Cell Mol Physiol*, 2013; 305: L455–466
 15. Munir MS, Weng LC, Tang W, et al. Genetic markers associated with plasma protein C level in African Americans: the atherosclerosis risk in communities (ARIC) study. *Genet Epidemiol*, 2014; 38: 709–713.
 16. Khalil, O.A., Ramadan, K.S., Hamza, A.H. and El-Toukhy, S.E., Association of plasma protein C levels and coronary artery disease in men. *African Journal of Biotechnology*, 2013; 12(50): 6986-6991.
 17. Lauribe P, Benchimol D, Dartigues J, Dada S, Benchinol H Biological risk factors for sudden death in patients with coronary artery disease and without heart failure. *Int. J. Cardiol*, 1992; 34(3): 307-318.
 18. Gibbs NM, Graw Ford GP, And Michalo P Postoperative changes in coagulant factors following abdominal aortic surgery. *J Cardio. Vasc*, 1992; 6(9): 680-685.