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Evaluation of Vimentin and Some Biochemical Parameters in the Blood of Acute Myocardial Infarction Patients

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Abstract

Aim of the work: The aim of this study was to evaluate Vimentin, Fetuin-A, and Lipoprotein(a) (Lp(a) levels in the sera of Acute Myocardial Infarction (AMI) patients and to determine its relation with disease activity and severity. Patients and methods: Fifty three adult AMI patients (26 females and 27 males) and 41 healthy subjects (23 males and 18 females) matching age serving as the control group, were included in this study. Five milliliters of blood were collected from patients and control, then centrifuged and the serum was separated and frozen as aliquots at -20 ºC until use. Measurement of the serum Vimentin, Fetuin-A, and Lp(a) levels in AMI patients and control was done using the ELISA Kit. Results: Serum levels of Vimentin, and Lp(a)were significantly increased in AMI patient as compared to control group. Serum Fetuin-A, albumin, and Total proteins level in patients with Acute myocardial Infarction was significantly lower than control group. Hence present study concluded that Vimentin, Fetuin-A, and Lp(a) could be a useful marker for disease activity in AMI.

Keywords: Myocardial infarction; Vimentin; Fetuin-A; Lipoprotein (a)

Introduction

Acute myocardial infarction (AMI) commonly known as heart attack, is a life-threatening coronary artery disease, evokes a systemic inflammatory response and locally the degradation of the necrotic tissue, followed by scar formation, with the classic symptoms of sudden, severe, and persistent pain in the back of the chest (accompanied by pain radiating to the shoulder and sometimes the arm) [1-3]. Myocardial ischemia may occur either from increased demand of oxygen by the myocardium, or decreased oxygen supply to the myocardium, or both[4].Vimentin, a cytoskeleton protein of 57 kilo Dalton (kDa), which belongs to the type 3 intermediate filament. Vimentin is expressed in a wide range of cell types. It plays important role in positioning of organelles within the cytoplasm and regulates numerous cellular processes including cell migration, autophagy, and plasticity of mesenchymal cells, as well as considered a markers of epithelial-mesenchymal transition (EMT) [5-7]. Fetuin-A (Human fetuin-A or alpha-2 Heremans Schmid glycoprotein) is 55–59 kDa an endogenous a 55–59 kDa phosphorylated glycoprotein which produced predominantly in the hepatocytes and secreted into serum[8], play a key role in the safety from vascular calcification by solubilizing calcium and phosphorus in serum[9], is an anti-inflammatory glycoprotein declined during systemic inflammatory process that is to say it is a negative acute phase reactant. Lp(a) is a Lipoprotein that contains similar to low density lipoprotein (LDL) apolipoprotein B and in addition apolipoprotein(a) which is attached by a disulfide bridge[10]. Apo(a) , which is similar to plasminogen in structure and may interfere with plasminogen activation that potentiates atherothrombosis through its content of the pro-inflammatory oxidized phospholipids[11]. Lp(a) interact with other molecules in a plethora of pathways related to thrombosis including inhibition of activation of transforming growth factor-β (TGF-β) and platelet activation[12].

Lipoprotein (a) is also an acute-phase reactant, within the macrophages that present in atherosclerotic lesions the very low density

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lipoprotein (VLDL) receptors can bind to and mediate the catabolism of Lp (a) by endocytosis, leading to its degradation within lysosomes, leading to a cellular accumulation of lipids within macrophages[13,14].

Thus, the aims of the present study were to delineate the serum levels Vimentin , Fetuin-A , and Lipoprotein(a) in patients with Acute Myocardial Infarction.

Materials and Methods

Samples

A total of 53 patients with age group of 41-66 year (56.3 ± 10.5), including both 26 females and 27 males who had recent AMI and admitted conducted at Cardiology and Medicine Department from Kirkuk teaching hospital of the department of internal medical, in Kirkuk governorates, from August 2019 to June 2020.

Forty one healthy controls, including 23 males and 18 females with an average age of 57 ± 4.3 year, were recruited from among subjects who were referred to for an annual checkup or pre-employment examination as they were assumed not to have AMI and gave no history of cardiovascular symptoms.

Patients with surgery, trauma within the prior month, malignant diseases, vascular heart disease, diabetes, cardiomyopathy, liver disease, renal failure, , other inflammatory disease (such as septicemia and pneumonia) and oral anticoagulant therapy were excluded. All of the patients were assessed by trained cardiologists by using the 2014 ESC Guidelines for the Management of Acute Myocardial Infarction [15].

The diagnosis was based on to the presence of two of the these criteria: i-prolonged chest pain compatible with AMI, ii- raising of cardiac enzymes, iii- typical ECG changes[16].After an eight-to-twelve hour overnight fast, morning blood was sampled from the antecubital vein within 24 hours after the onset of AMI or most recent unstable angina pectoris (UAP) attack. The samples were centrifuged at 3000 rpm for 15 minutes at 4°C and stored at -20°C until the assay was performed.

Statistical Analysis

All calculations were made using SPSS software v.10.0 for Windows. Student's *t*-test was used to compare two-group data. The data are expressed as means ± SD (standard deviation). A P value <0.05 was considered to be statistically significant.

Results:

Patient mean age was 56.3 ± 10.5 years and they were 26 females and 27 males. Acute myocardial infarction patients revealed a significant increase of serum Vimentin, (ranges from 243.2 to 201 ng/mL, mean value 220.5 ± 67.7ng/mL versus normal controls' ranges from 192.7 to 175 ng/ mL, mean value 181.3 ± 31.8ng/mL; p<0.0001), and Lp(a) levels (ranges from 48.06 to 47.03 µg/dl, mean value 46±8.48 µg/dl versus normal controls' ranges from 20 to 16.2 µg/dl, mean value 18.1±5.7 µg/dl; p<0.0001) , respectively.

On the other hand, in patients with AMI, the decrease of serum Fetuin-A level were significant (ranges from131.62 to 305.1 ng/ mL, mean value 125.7 ±6.67ng/mL versus normal controls' ranges from 14.77 to 41.33 ng/mL, mean value 282±19.7ng/mL; p(<0.0001). Albumin (ranges from 4.171 to 4.3 mg/dl, mean value 4. 16±1.84 mg/dl versus normal controls' ranges from 2 to 2.3 mg/dl, mean value 2.03±0.92 mg/dl; p(<0.0001),and total proteins(ranges from 89 to100.3 g/dl, mean value 92±0.31g/dl versus normal controls' ranges from 47.1 to 52.02 g/dl, mean value 50.8±0.11g/dl; (p<0.01) ,respectively.

Correlation

Our study shows that serum Vimentin correlates positively with Fetuin-A (.048) but correlates negatively with Lp(a) (-.021-) AMI group

Table 1. Biochemical parameters of patients with AMI and the control group.

Study group	No.	Vimentin (ng/mL)	Fetuin-A (ng/ mL)	Albumin (mg/dl)	Lp(a) ((µg/dl)	Total proteins (g/dI)
AMI	53	220.5 ± 67.7	125.7±6.67	4. 16±1.84	46±8.48	92±0.31
Control	41	181.3 ± 31.8 *	282±19.7 ***	2.03±0.92 ***	18.1±5.7 ***	50.8±0.11 **

*p <0.05,** p<0.01,*** 0.0001

Table 2: Comparison of ROC curves for Fetuin-A , Vimentin, and Lp(a)in AMI group

	Difference between areas	SE	95% CI	P-value
Fetuin-A ~ Vimentin	0.0245	0.017	-0.008 to 0.05	P = 0.149
Fetuin-A ~ Lp (a)	0.000	0.000	0.000 to 0.000	P = 1.0000

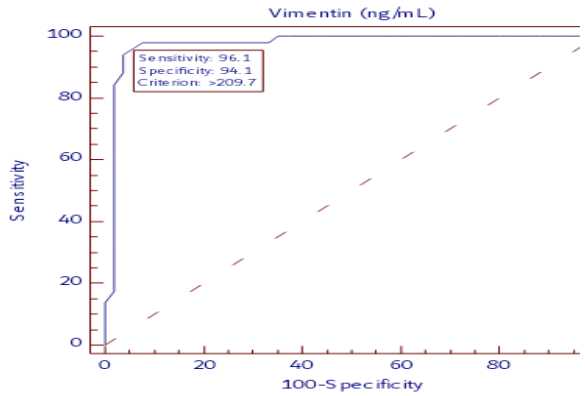

Figure (1):ROC curve for vimentin

The ability of Fetuin-A, Vimentin and Lp(a)as a predictor for acute myocardial infarction was explored using a receiver operator characteristic curve. The area under the ROC curve of fetuin-A were 1.000 (95% CI: 0.964 to 1.000) (sensitivity 100.0 and specificity 100.00) and cut of point ≤153 respectively with P value <0.01, Figure (2).

The corresponding values of Vimentin was 1.000 (95% CI: 0.964 to 1.000) (sensitivity 96.1and specificity 94.1) ,and the cut of point >209.7with P value <0.01Figure (1).

This article indicating that serum levels of Fetuin-A, Vimentin and Lp(a) are the best biomarkers differentiating study group.

When it comes to that of Lp(a), the area under the curve was 1.000((95% CI: 0.964 to 1.000) and the cut of point >22 (sensitivity: 100.0; specificity: 100.0).

Correlation

Our study shows that serum vimentin correlates positively with fetuin-A (.048) but correlates negatively with Lp(a) (-.021-)in AMI group.

Discussion

Acute Myocardial Infarction is defined as a part of acute coronary syndrome associated with an inflammatory process raised [17].Vimentin facilitates the inflammatory response by regulating activation of the pyrin domain-containing protein 3 (NLRP3) inflame some and anchors and organizes adhesion molecules as well as actomyosin complexes to regulate cell adhesion and migration. The present study reveals that the serum Vimentin activity were significantly higher at P value of 0.05, in AMI as compared with control group. This could be due to vimentin is probably related to immune function .Vimentin induced macrophages to release pro-inflammatory cytokine and augmented (oxidized low-density lipoproteins (oxLDL)) - induced release of Tumor necrosis factor and IL-6 [18]. Whereas the anti-inflammatory cytokine. IL-10 blocks the secretion of vimentin, suggesting the involvement of secretory vimentin in inflammation raised[18,19].

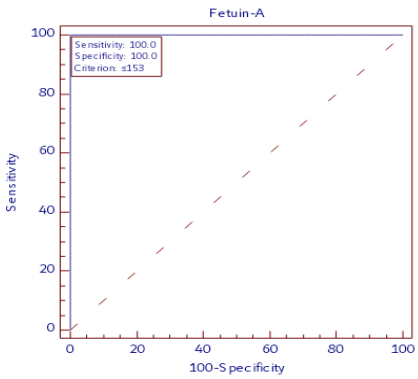

Figure (2):ROC curve for Fetuin-A

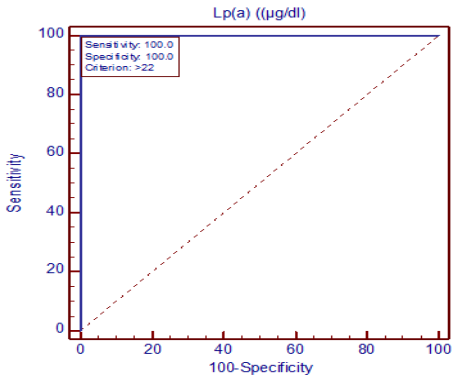

Figure (3):ROC curve for Apo-A

Fetuin-A is an anti-inflammatory glycoprotein, its level decreased accompanied by the promote the continuous inflammatory process, aggravated

synthesis of pro inflammatory cytokines over-production of cardiotoxic cytokines as TNF-alpha , and may impair directly functions of heart and producing cardiac calcification and fibrosis which depress ventricular function and promote remodeling and hence lead to evolvement of congestive heart failure[20,21].Hence present study concluded that reduced level of Fetuin-A in AMI might play a role in the formation of atherosclerotic plaque[20].

This study revealed that there was a significantly higher level of Lp (a) among the AMI patients when compared to normal people. Due to increased levels of oxidized phospholipids during inflammation and oxidative stress may cause the overexpression of Lp(a) raised [22]. As well as Lp(a) may compete with it for binding to endothelial and mononuclear cells as well as platelets, thereby reducing the conversion of plasminogen to plasmin and inhibiting fibrinolysis. The finding that Lp(a) also binds to glycoprotein further supports the important role of Lp(a) in fibrinolysis raised [23].

Albumin is a hepatic protein, and has a half-life of approximately 3 weeks [24], and its serum concentration is mainly influenced by several factors, including the maintaining oncotic pressure and microvascular integrity, regulating metabolic and vascular functions, providing binding ligands for substances, antioxidant activities, and anticoagulant effects raised [25,26]. Hypoalbuminemia in patients are probably due to multiple causes including the decrease of albumin synthesis, plasma volume expansion, overload excretion by the kidneys or direct loss of protein from the body. The rate of albumin synthesis is affected by nutritional intake and systemic inflammation raised [26,27].

The Lipoprotein(a) is a low-density lipoprotein (LDL)-like particle that may accelerate atherogenesis and promote thrombosis. Lipoprotein (a) might take a role in the initiation and development of AMI through inducing the chemotactic activity to peripheral monocytes, attenuating fibrinolysis and promoting coagulation raised [28], because the main component of the fibrinolytic system is plasmin, which dissolves fibrin or thrombus and which is converted from plasminogen by tissue-plasminogen-activator(t-PA). Fibrinolysis is initiated by the release of t-PA from the endothelium[29].

Conclusion

Hence present study concluded that Vimentin, Fetuin-A, and Lp(a) could be a useful marker for disease activity in AMI. Reduced level of Fetuin-A in AMI might play a role in the formation of atherosclerotic plaque.

Conflicts of interest:

No potential conflicts of interest are disclosed.

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References

1. Entedhar Rifaat Sarhat. Acute Myocardial Infarction: Melatonin, Apelin, and Visfatin as Predictors of Disease . Diyala Journal of Medicine.2017; 13(2):11-17.
2. Sattler K, El-Battrawy I, Zhao Z, et al. Serum of patients with acute myocardial infarction prevents inflammation in iPSC-cardiomyocytes. Sci Rep. 2019;9(1):1-13. Published 2019 Apr 4. doi:10.1038/s41598-019-42079-z
3. Mahde S.Hamad, Entedhar R. Sarhat , Thuraia R. Sarhat , Kasim Sakran A. Impact of Serum Adropin and Irisin in Iraqi patients with Congestive Heart Failure .P J M H S.2021; 15(2):497- 499.
4. Entedhar R. Sarhat, Intesar J. Mohammed, Noor Y. Mohammed, Bdoor S. Khairy, Fhosoon F. Hassan. Evaluation of Salivary Oxidative Stress Marker (Lipid Peroxidation), and Non-Enzymatic Antioxidants (Vitamin C and Vitamin E) in Patients with Acute Myocardial Infarction. Tikrit Journal for Dental Sciences.2019; 7(1):20-26.
5. Patteson AE, Vahabikashi A, Pogoda K, Adam SA, Goldman A, Goldman R, Janmey P. Vimentin protects the structural integrity of the nucleus and suppresses nuclear damage caused by large deformations. bioRxiv. Cell Biology.2019 1:566174.
6. SeoYeon Kim , Inyeong Kim , Wonkyoung Cho , Goo Taeg Oh , Young Mi Park. Vimentin Deficiency Prevents High-Fat Diet-Induced Obesity and Insulin Resistance in Mice .DMJ.2020;15:1-12

7. Ankita Makol , Harpreet Kaur , Sakshi Sharma , Shruthi Kanthaje , Ramanpreet Kaur , and Anuradha Chakraborti. Vimentin as a potential therapeutic target in sorafenib resistant HepG2, a HCC model cell line . Clinical and Molecular Hepatology 2020;26:45-53.
8. Entedhar Rifaat Sarhat and Saba Khair alddin Ibrahim. Assessment of Serum Levels of Fetuin-A, Lipocalin-2 ,Interleukin-18, and C-Reactive Protein in Rheumatoid Arthritis Patients: A Biochemical Study. Cellular and Molecular Science.2020;22(55):1-9.
9. Al-Said NH, Taha FM, Abdel-Aziz GM, Abdel-Tawab MS. Fetuin-A level in type 2 diabetic patients: relation to microvascular complications. Egypt J Intern Med 2018;30:121-30.
10. Roth C, Krychtiuk KA, Gangl C, Schrutka L, Distelmaier K, Wojta J, et al. Lipoprotein(a) plasma levels are not associated with survival after acute coronary syndromes: An observational cohort study. PLoS ONE.2020; 15(1): e0227054.
11. Enas A. Enas, Basil Varkey , Dharmarajan, Guillaume Pare, Vinay K. Bahl. Lipoprotein(a): An independent, genetic, and causal factor for cardiovascular disease and acute myocardial infarction. Indian Heart Journal.2019; 71: 62-66.
12. Dewa Gde Dwi Sumarjaya, Ketut Badjra Nadha, Anak Agung Wiradewi Lestari. High Lipoprotein(a) Levels as a Predictor of Major Adverse Cardiovascular Events in Hospitalized-Acute Myocardial Infarction Patients. Vascular Health and Risk Management 2020:16:125-132.
13. Kamariya CP, Gorasia JH, Vachhani U, Gohel M. Evaluation of serum lipoprotein (a) in young patients with myocardial infarction. Int J Med Public Health 2014;4:107-9.
14. Khaled Abd El-Aziz Mowafy., et al. Prognostic Value of Serum Lipoprotein (a) and Apo lipoprotein-B in diabetics with Myocardial Infarction and Chronic limb Threatening ischemia. Archives of Endocrinology and Diabetes.2020; 2(1).
15. E. A. Amsterdam, N. K. Wenger, R. G. Brindis et al., AHA/acc guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines," Journal of the American College of Cardiology.2014;64(24): e139–e228.
16. Jafarinia M, Firuzsalari FG, Zaringol M, et al. Serum levels of interleukin (IL)-33 in patients with ischemic heart disease. MOJ Immunol. 2018;6(2):29–32.
17. Entedhar R. Sarhat , Ayhan R. Mahmood.Evaluation of serum concentration Interleukins in Patients with Myocardial Infarction by ELISA Technique. KUJSS.2018; 13(1): 2018:43-51.
18. Kim, S., Cho, W., Kim, I. et al. Oxidized LDL induces vimentin secretion by macrophages and contributes to atherosclerotic inflammation. J Mol Med.2020;98, 973–983.
19. Dong Huo Gong, Yang Dai, , Shuai Chen , Xiao Qun Wang , Xiao Xiang Yan , Ying Shen , Jing Liu , Zhen Kun Yang, Jian Hu , Lin Jun Yu , Li Li Liu , Rui Yan Zhang , Wei Feng Shen , Qiu Jing Chen , Feng Hua Ding, Lin Lu.Secretory vimentin is associated with coronary artery disease in patients and induces atherogenesis in ApoE−/− mice. International Journal of Cardiology 283 (2019) 9-16.
20. Feistritzer H-J, Klug G, Reinstadler SJ, et al. Fetuin-A is related to infarct size, left ventricular function and remodelling after acute STEMI. Open Heart 2015;2: e000244. doi:10.1136/ openhrt-2015-000244
21. Haydar H Al-Shalah, Oday Al-Salihi , Dina Ayed Mohammed . The Impact of Fetuin-A Level on Patients with Acute Myocardial Infarction. RJPBCS.2017; 8(1): 537- 541.
22. Anil Batta . Serum lipoprotein (a) levels in type 2 diabetes mellitus patients. International Journal of Medical and Health Research . 2018; 4(4): 01-04.
23. Keijiro Saku, Bo Zhang, Rui Liu, Kazuyuki Shirai, Kikuo Arakawa. Associations Among Serum Lipoprotein(a) Levels, Apolipoprotein(a) Phenotypes, and Myocardial Infarction in Patients With Extremely Low and High Levels of Serum Lipoprotein(a). Jpn Circ J 1999; 63: 659 –665.
24. Soo Hyun Kim, Chun Song Youn, Hyo Joon Kim, Seung Pill Choi, "Prognostic Value of Serum Albumin at Admission for Neurologic Outcome with Targeted Temperature

Management after Cardiac Arrest", Emergency Medicine International , 2019(1):1-7.

25. Chien, S., Chen, C., Lin, C. et al. Critical appraisal of the role of serum albumin in cardiovascular disease. Biomark Res 5, 31 (2017). https://doi.org/10.1186/s40364-017-0111-x
26. Suzuki S, Hashizume N, Kanzaki Y, Maruyama T, Kozuka A, Yahikozawa K (2019) Prognostic significance of serum albumin in patients with stable coronary artery disease treated by percutaneous coronary intervention. PLoS ONE.2019; 14(7):1-9.
27. Entedhar Rifaat Sarhat , Husamuldeen Salim Mohammed Saeed1 Siham A. Wadi. Altered Serum Markers of Omentin and Chemerinin Chronic Renal Failure Patients on Hemodialysis. Research J. Pharm. and Tech.2018; 11(4): 1667- 1670.
28. Gaojun Cai; Zhiying Huang; Bifeng Zhang; Lei Yu; Li Li. Elevated lipoprotein (a) levels are associated with the acute myocardial infarction in patients with normal low-density lipoprotein cholesterol levels. Biosci Rep (2019) 39 (4):1-10.
29. Kunihisa Miwa, KeikoNakagawa , Naohiro Yoshida ,Yoshiharu Taguchi, HiroshiInoue. Lipoprotein(a) is a risk factor for occurrence of acute myocardial infarction in patients with coronary vasospasm. Journal of the American College of Cardiology.2019; 35 (5) :1200-1205.