*Available online at* https://www.sjomr.org

SCIENTIFIC JOURNAL
OF MEDICAL RESEARCH

Vol. 6, Issue 21, pp 1-4 , 2022

ISSN: 2520-5234

ORIGINAL ARTICLE

# Role of ADAMTS13 in Pathogenesis of ST-Elevation Myocardial Infarction in Iraqi Patients

**Haneen A. A. Oudha[1]*, Shatha M. J. Al-Khateeb[2], Ahmed Q. J. Al-Haideri[3]**

[1]Biochemistry Department College of Medicine, University of Kerbala, Iraq.
[2]Department of Biochemistry, College of Medicine, Mustansiriyah University, Iraq.
[3]International Cardiologist - Kerbala Heart Center, Iraq

## ARTICLE INFORMATIONS

**Article history:**
Received: 24 September 2021
Revised: 27 October 2021
Accepted: 31 October 2021
Published: 24 March 2022

**Keywords:**
ADAMTS13,
CK-MB,
Extracellular matrix (ECM),
ST-elevation.

**Corresponding author:**
Haneen Abd Ali Oudha
Email: h.alsalammi@gmail.com
Msc Student, Biochemistry Department College of Medicine, University of Kerbala, Iraq

## ABSTRACT

**Background:** ST-elevation myocardial infarction (STEMI) is a medical condition characterized by myocardial ischemia symptoms in the presence of prolonged electrocardiogram-ST (ECG-ST) elevation (STE) and the consequent release of myocardial necrosis biomarkers. The ADAMT disintegrin-like metalloproteinases with thrombospondin type 1 motifs are a family of proteinase enzymes detected within the extracellular matrix (ECM) and plasma. The a disintegrin and metalloprotease with thrombo-spondin motif (ADAMT) family consists of nineteen enzymes with different functions.

**Aims:** To examine the sequence of changes in the levels o ADAMTS13 throughout ST-elevation myocardial infarction and to see how they relate to other cardiovascular risk factors in Iraqi patients

**Materials and Methods**: The study design is a case-control study. The present study is a case-control study comprised of 42 subjects of the patients with st-elevation myocardial infraction cases and 48 apparently healthy as control groups. The sample was collected from Karbala heart center in the AL-Imam AL_Hussein medical city in the period from20-1-2021 to 1-3-2021, the parameters is done worked in the laboratory of AL-Imam AL_Hussein medical city.

**Results:** The current study observed a weak positive relationship between ADAMT with von willebrand factor (VWF), HS Troponin T, and creatine kinase-MB (CK-MB) with $p \leq 0.05$.

There is a strong positive relationship between total count (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) with $p > 0.001$ and ADAMT, and a weak negative relationship between very-low-density lipoprotein (VLDL), TG, and B.sugar with ADAMT. The median levels of the VWF level were higher in ST-elevation MI patients compared to the control group with $p \leq 0.001$ and reduced level ADAM with $p = 0.01$

**Conclusion:** The current study is a case-control study comprised of 42 subjects of the patients who have st-elevation myocardial infractions as cases and 48 apparently healthy as control groups. There was observed a weak positive relationship between ADAMT



CITATION: Oudha HAA, Al-Khateeb SMJ, Al-Haideri AQJ. "Role of ADAMTS13 in Pathogenesis of ST-Elevation Myocardial Infarction in Iraqi Patients". Sci. J. Med. Res. 2022;6(21):1-4. DOI: 10.37623/sjomr.v06i21.1

with VWF, HS Troponin T, and CK-MB with $p \leq 0.05$, and a strong positive relationship between TC, LDL, and HDL with $p > 0.001$ and ADAMT, and a weak negative relationship between VLDL, TG, and B.sugar with ADAMT. The median levels of the VWF level were higher in ST-Elevation MI patients compared to the control group with $p \leq 0.001$ and reduced level ADAM with $p = 0.01$

# INTRODUCTION

## Heart Disease

The term "heart disease" refers to a wide variety of heart problems. The most common type is coronary artery disease., which could lead to a heart attack. Of other kinds, cardiac sickness can impair the heart's valves or cause cardiac failure by preventing the heart from pumping adequately. Heart disease is a congenital ailment that affects some people.[1]

The pump and veins that distribute blood to every area of the body make up the cardiovascular system. This system enables the transport of necessary nutrients to body cells as well as the elimination of wastes organs (Figure 1).[2]

## ST-Elevation Myocardial Infarction

ST-Elevation myocardial infarction (STEMI) is a clinical illness characterized by signs of ischemia of the heart and the subsequent production of biomarkers of myocardial necrosis in the presence of persistent electrocardiographic ST-elevation (STE). The single most effective surrogate measure for identifying acute total coronary artery blockage without secondary circulation, indicating a large area of damaged myocardium at imminent danger of permanent infarction and needing urgent reperfusion treatment, is STE.[3] When an atherosclerotic plaque ruptures or erodes, it results in transmural ischemia and thrombotic blockage of an epicardial coronary artery, culminating in myocardial infarction with ST-segment elevation. The area of the ischemic area at risk, (ii) duration and recurrence of coronary occlusion, and (iii) the quantity of remaining collateral blood flow and the severity of coronary microvascular dysfunction dictate the amount of infarction that occurs.[4] Clinical signs and symptoms, ECG alterations, and a distinct pattern of changes in blood enzymes such as creatine kinase (CK), creatine kinase isoenzyme MB (CK-MB), and lactate dehydrogenase isoenzyme (LDH) , as well as cardiac-specific proteins such as troponin, are all used to identify MI. ECG is the most frequently a common way of diagnosing myocardial infarction since clinical signs are not always trustworthy. However, the relevance of myocardial damage serum biochemical indicators to make a cardiac injury diagnosis emerges when the ECG reveals an ambiguous pattern.[5]

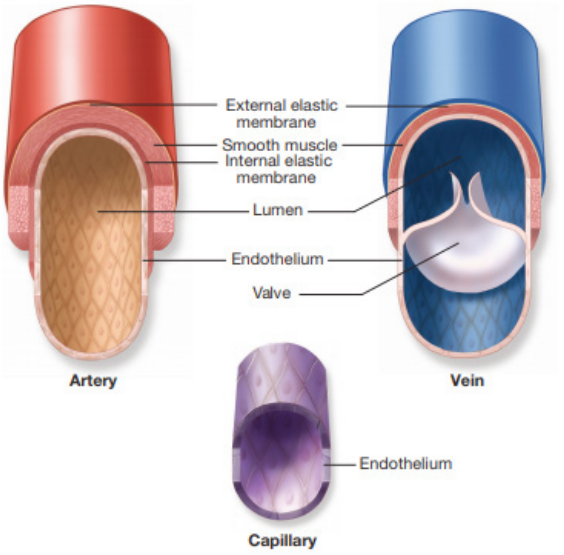


**Figure 1:** Comparative structure of arteries, capillaries, and veins

## ADAMS 13

Disintegrin-like metalloproteinases with thrombospondin type 1 motifs (ADAMTS) are a class of proteinase enzymes found in the extracellular matrix (ECM) and plasma. There are 19 enzymes in the ADAMTS family with various functions. vWF encompassing a wide range of physiological activities. ADAMTS13, The von Willebrand factor cleaving protease is one of the best-known members of the family. It breaks up the large von Willebrand factor (UL-VWFM) into smaller multimers VWF pieces. Which lowers VWF coagulation activity. Endothelial cells (ECs) and hepatic cells are the main locations for the synthesis and secretion of ADAMTS13.[6] Clinical research have linked low ADAMTS13 (and high VWF) levels to a severe risk of MI. Patients with coronary artery disease (CAD) are at a higher risk of developing coronary artery disease; SNPs in the ADAMTS13 gene that diminish ADAMTS13 activity have also been associated with a higher risk of death.[7]

## ADAMTS-13 Regulation

Function The modulation of coagulation enzymes by cofactors is well known, and it enhances the pace at which an enzyme works process by many orders of magnitude. ADAMTS-13 is released as a protease that is always active. Unlike other clotting factors, which are produced as inactive zymogens. To date, no inhibitor has been discovered. Many other matrix metalloproteases, such as ADAMTS-4, -5, -7, and -12, are inhibited by plasma a 2- macroglobulin. However, it does not appear to bind and impair ADAMTS-13 action toward VW. As a result, At the substrate level, the function of ADAMTS-13 must be regulated (Figure 2).[9]


**Figures 2:** The domain structure is represented schematically by ADAMTS. Signal peptide (S), propeptide (P), metalloprotease (M), disintegrin-like (D), TSP1 (T), cysteine-rich (Cys), CUB (C) domains

**Table 1:** Correlation of ADAMTS13 level with other biomarkers among St-elevation MI patients group

| | *ADAMTS13 level* | |
|---|---|---|
| *Biomarkers* | $r_s$ | *p-value* |
| VWF level | 0.3 | 0.05 |
| HS troponin T | 0.4 | 0.02 |
| CK-MB | 0.4 | 0.02 |
| TC | 0.5 | 0.0005 |
| LDL | 0.5 | 0.003 |
| HDL | 0.6 | 0.0024 |
| VLDL | -0.3 | 0.03 |
| TG | -0.3 | 0.07 |
| B.sugar | -0.3 | 0.1 |

The nonparametric (Spearman rank test) (Coefficient rs ) was used to analyze the difference in quantitative data between markers.

## MATERIALS AND METHODS

The study design is a case-control study. The current study is a case-control study comprised of 42 subjects of the patients who have st-elevation myocardial infractions as cases and 48 healthy as control groups. The sample was collected from Karbala heart center in the AL-Imam AL_Hussein medical city in the period from20-1-2021 to 1-3-2021. The parameters are done in the laboratory of AL-Imam AL_Hussein medical city and determine ADAMTS 13 level by enzyme-linked immunosorbent assay (ELISA) in serum.

### Assay Principle

This kit uses an enzyme-linked immunosorbent test (ELISA). Human ADAMTS13/vWF-cp contained in the sample is added to the plate and binds to antibodies coated in the wells, followed by biotinylated human ADAMTS-13/vWF-cp antibody, which binds to ADAMTS-13 in the sample, and finally streptavidin-HRP, which binds to the biotinylated ADAMTS13/vWF-cp antibody. During the washing step following incubation, any unbound streptavidin-HRP is rinsed away. Color starts in response to the amount of human ADAMTS13/vWF-cp added to the substrate solution. The absorptance is measured at 450 nm when The process has been stopped. with an acidic stop solution.

## RESULT AND DISCUSSION

The current study observed a weak positive relationship between ADAMT with VWF, HS Troponin T, and CK-MB with a $p \leq 0.05$ (Table 1).

Reduced levels of ADAMTS activity may play a factor in the etiology of acute myocardial infarction. According to the findings of this study, they may act as significant mediators in the course of the disease.[10] Coronary heart disease and myocardial infarction were the real cause effects of reduced ADAMTS activity on the increased likelihood of developing cardiovascular disorders.[11] The findings corroborate the occurrence of VWF anomalies in STEMI patients and could be exploited to design novel treatment strategies.[12] Increased

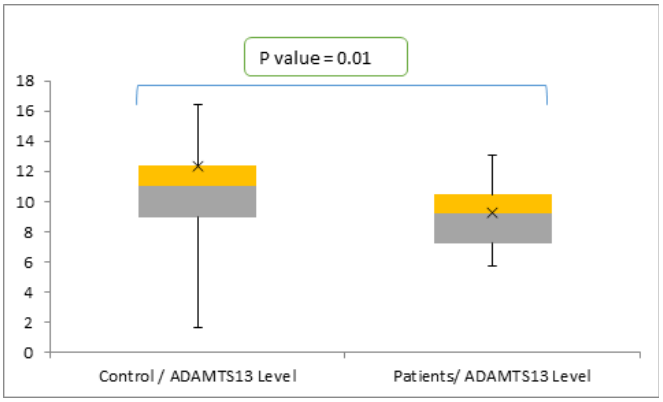


**Figure 3:** Distribution of serum ADAMTS13 level in ST-elevation MI patients compared to control group.

ADAMTS13 activity could be linked to the development of acute myocardial infarction (Figure 3).[9]

Myocardial infarction and coronary artery disease were the causal effects of reduced ADAMTS activity on the increased likelihood of developing cardiovascular disorders.[11]

Other research has revealed no link between VWF, ADAMT, and the size of infarcts in patients. Patients with IMH, on the other hand, exhibited considerably increased VWF activity and significantly reduced ADAMTS13 activity.[12] Acute ischemic stroke patients had the lowestADAMTS13 levels.[13]

## REFERENCE


1. Abdul-Ghani M, DeFronzo RA, Del Prato S, Chilton R, Singh R, Ryder RE. Cardiovascular disease and type 2 diabetes: has the dawn of a new era arrived?. Diabetes Care. 2017 Jul 1;40(7):813-20.
2. Acharya UR, Fujita H, Oh SL, Hagiwara Y, Tan JH, Adam M. Application of deep convolutional neural network for automated detection of myocardial infarction using ECG signals. Information Sciences. 2017 Nov 1;415:190-8.
3. Smith KR, Frumkin H, Balakrishnan K, Butler CD, Chafe ZA, Fairlie I, Kinney P, Kjellstrom T, Mauzerall DL, McKone TE, McMichael AJ. Energy and human health. Annual Review of public health. 2013 Mar 18;34:159-88.
4. Hwang C, Levis JT. ECG diagnosis: ST-elevation myocardial infarction. The Permanente Journal. 2014;18(2):e133.
5. Nigam PK. Biochemical markers of myocardial injury. Indian Journal of Clinical Biochemistry. 2007 Mar;22(1):10-7.
6. Heusch G, Gersh BJ. The pathophysiology of acute myocardial infarction and strategies of protection beyond reperfusion: a continual challenge. European heart journal. 2017 Mar 14;38(11):774-84.
7. De Meyer SF, Savchenko AS, Haas MS, Schatzberg D, Carroll MC, Schiviz A, Dietrich B, Rottensteiner H, Scheiflinger F, Wagner DD. Protective anti-inflammatory effect of ADAMTS13 on myocardial ischemia/reperfusion injury in mice. Blood, The Journal of the American Society of Hematology. 2012 Dec 20;120(26):5217-23.
8. Zheng XL. Structure-function and regulation of ADAMTS-13 protease. Journal of Thrombosis and Haemostasis. 2013 Jun;11:11-23.
9. Al-Masri AA, Habib SS, Hersi A, Al Zamil H. Effect of Acute Myocardial Infarction on a Disintegrin and Metalloprotease with Thrombospondin Motif 13 and Von Willebrand Factor and Their Relationship with Markers of Inflammation. International journal of vascular medicine. 2020 Feb 11;2020.
10. Rutten B, Maseri A, Cianflone D, Laricchia A, Cristell NA, Durante A, Sparta M, Ancona F, Limite L, Hu D, Li H. Plasma levels of active Von Willebrand factor are increased in patients with first ST-segment elevation myocardial infarction: a multicenter and multiethnic study. European Heart Journal: Acute Cardiovascular Care. 2015 Feb 1;4(1):64-74.

11. Ye Z, Zheng J. Verification of the Role of ADAMTS13 in the Cardiovascular Disease Using Two-Sample Mendelian Randomization. Frontiers in genetics. 2021 Jul 1;12:1055.
12. Eerenberg ES, Teunissen PF, van den Born BJ, Meijers JC, Hollander MR, Jansen M, Tijssen R, Belien JA, van de Ven PM, Aly MF, Kamp O. The role of ADAMTS13 in acute myocardial infarction: cause or consequence?. Cardiovascular research. 2016 May 12;111(3):194-203.
13. Denorme F, Kraft P, Pareyn I, Drechsler C, Deckmyn H, Vanhoorelbeke K, Kleinschnitz C, De Meyer SF. Reduced ADAMTS13 levels in patients with acute and chronic cerebrovascular disease. PLoS One. 2017 Jun 7;12(6):e0179258.