

Blood Biomarkers Associated with Acute Coronary Syndrome in Normal or High BMI Patients

Sarah Abdul-Khaleq Mahdi¹, Ahmed Modher Nabat Al-ajrash², Dakhel Ghani Omran³

^{1,3}Biology Department/College of Science for Women/University of Babylon/Iraq

²Ph. D. (MD)/Ministry of Health, Imam Sadiq Teaching Hospital, Iraq

Abstract

Myocardial infarction (MI) which is called cardiac attack, it is a dangerous condition resulted from a deficiency of blood perfusion to heart muscle. The individuals that included in the present study were 80 subjects of both sexes (men and women). Of those, forty (40) women (20 women with MI and 20 healthy women). The remaining number (40 men) were 20 affected with MI and 20 healthy men). Furthermore, the individuals were classified into four groups according to their ages (40-49, 50-59, 60-69, and 70-79 years old). Data that were observed in this study showed that MI incidence was proportionate with body mass index (BMI), it was found that patients with BMI 25-33 kg/m² comprised 70% whereas patients with BMI 19-23 kg/m² constituted 30%. Concerning blood parameters, they had been recorded a significant increase ($p < 0.01$) in the levels of total white blood cells (WBCs), granulocyte percentage ratio, lymphocyte percentage ratio, and blood platelets count in all patients affected with MI in matching with their counterparts of healthy individuals. Results of biomarkers (fibrinogen, C-reactive protein, and troponin) were significantly higher ($p < 0.0001$) in patients with MI compared to those healthy one. In addition, the values of studied biomarkers had been showed a significant elevation ($p < 0.0001$) in patients who had high BMI (25-33 kg/m²) when compared with those patients with BMI ranged between (19-23 kgandm²). Statistical analyses of correlation coefficients pointed out the following data, there was a significant negative correlation between granulocytes and lymphocytes ($r = -0.99$, sig= 0.0001) in patients with MI. Also, it was found a significant negative correlation between blood platelets and troponin ($r = -0.66$, sig= 0.0001) in those patients with MI. The ROC analysis of biomarkers that were tested showed the following results, the ROC of troponin showed that AUC was 0.813 with cutoff equal to 1.650, fibrinogen ROC analyses indicated that AUC was 0.816 and cutoff results of CRP were 0.724 and 6.150 respectively. Finally, these results that illustrated above, may be return to systemic inflammation associated with MI and might implicated in progression and worsening of MI disease. As well as there was no gender differences in studied parameters among patients with MI.

Keywords: Myocardial infarction, Fibrinogen, BMI, CRP.

1. Introduction

Myocardial infarction, means death (necrosis) of the myocardium due to inadequate oxygen supply, In the clinical context however, defining myocardial infarction is far more complex due to the number of aspects by which myocardial necrosis can be assessed: histopathologic, biochemical markers, electrocardiographic changes and imaging [1].

White blood cells, also called leukocytes or leucocytes, are the cells of the immune system that are involved in protecting the body against both infectious disease and foreign invaders, all white blood cells are produced and derived from multipotent cells in the bone marrow known as hematopoietic stem cells, leukocytes are found throughout the body, including the blood and lymphatic system.

Platelets, or thrombocytes, are the smallest of the formed elements in the plasma, platelets are roughly disk-shaped and average about 3 μm in diameter, the normal platelet count ranges from 250,000 to 500,000/mm³ of blood, the platelets play an important role in preventing blood loss from a traumatized area by (1) forming platelet plugs that seal holes in small blood vessels and (2) forming blood clots, which work to seal off larger tears in the blood vessels, the platelets also contain serotonin, which, when

released, causes smooth-muscle constriction and reduced blood flow [2].

FI is produced by three closely related genes including FGA, FGB, and FGG, each of these genes can determine and specificity of the primary polypeptide structure of one of its own three polypeptide chains that are $\text{A}\alpha$, $\text{B}\alpha$, and Y chains respectively [3].

All genes encoding human fibrinogen are located on chromosome 4 [4]. Hepatocytes are the main synthesis of fibrinogen and then it exported into blood circulation, before its secretion from hepatocytes, it altered and modified to assembly of its own synthesized polypeptide chains and then translocated into the endoplasmic reticulum in order to interact of polypeptide chains with chaperons (proteins enhance polypeptide chains folding) to help assembly and folding of FI polypeptide chains, this process also help to distinguish between correctly folding and assembly of FI polypeptides, if there is in proper folding of polypeptide chains they are degraded [5].

Acute myocardial infarction (MI) results in an inflammatory response involved in myocardial repair [6]. C-reactive protein (CRP), an acute phase reactant as downstream marker of inflammation, has been shown to correlate with the extent of cardiac injury in the acute phase of MI [7, 8]. Although the resolution of post-MI inflammation is generally expected after

2 to 4 weeks, a prolonged inflammatory phase can occur [9]. The measurement of Cardiac troponin concentration in systemic venous blood has become a core component of the assessment of patients with acute and chronic cardiovascular disease, this is enshrined in the Universal Definition of Myocardial Infarction (UDMI). Now in its fourth iteration with the aim to (i) guide the clinician through the numerous differential diagnoses that result in cardiac troponin elevation, and (ii) provide classification and naming conventions to assist a structured approach, however, the 4th UDMI has stimulated considerable debate [10, 11].

2. Materials and Methods

The research subjects

The present investigation was carried out at a variety of establishments, such as Marjan teaching hospital (the ischemic heart disease unit), Imam Al-sadiq hospital, private laboratories, and Babylon university/college of science for women. These establishments were all included. The current investigation started during the months of November 2021 and April 2022.

A total of eighty (80) people, including both men and women, were chosen to participate in the study. Twenty men out of those eighty reported symptoms of myocardial infarction, while another twenty men out of those eighty appeared to be in good health and served as a control group. Twenty (20) of the remaining forty (40) women were diagnosed with myocardial infarction, and twenty (20) of the remaining forty (40) women were recruited to serve as a control group.

The ages of all of the participants in the current study ranged anywhere from 40 to 79 years old. The participants in this study, which included both patients and healthy controls, had their ages recorded and were placed into one of four categories, according to how old they were (40-49, 50-59, 60-69, and 70-79 years old). Patients with diabetes mellitus, malignant diseases, lung diseases, thyrotoxicosis, and hypertension, as well as auto immune diseases, do not meet the criteria for inclusion in this study. The women who participated in this research project did not take any form of hormonal replacement treatment or oral contraceptives.

All of the victims were sent to hospitals and other medical facilities to have their individual myocardial infarctions checked out and were given treatment medications. Concerning the control individuals, those who signed up for the study came from public health centers, workers in hospitals, and people who had previously had good health.

3. Methods

Measurements of fibrinogen and troponin were carried out according to instructions of Hemostat and Abbott companies. In addition to this, C- reactive protein was measured in accordance with the directives provided by the Biotech Company.

Statistical Analysis

The findings of this investigation were presented in the form of means together with standard deviations (SE). A statistical analysis was performed on the data with the SPSS 23 program, and an explanation of analysis of variance was provided. The least significant differences (LSD) between the groups that were analyzed were p values less than 0.05 [12].

4. Results

Relation of body mass index and MI

Results that explained in the Figure (1) explained an increased incidence of MI was 70% in patients who had BMI equal 25-33 kg/m² compared to those with BMI equal 19-23 kg/m² were lower 30%.

Results of hematological parameters (WBCs cell/mm³, Granulocytes %, Lymphocytes % and platelets cell/mm³) in Patient affected with MI and those healthy control groups according to gender.

The levels which were illustrated in following table (1) explained the means ±SE of all mentioned above parameters of both patient and control, the results of WBCs a significant increase at p<0.05 were achieved for people with MI of both sexes, males patient (8.01±2.1 cell/mm³) and females patient (8.06±1.6 cell/mm³) when compared with healthy persons of both sexes, males healthy (5.07±0.6 cell/mm³) and females healthy (5.01±1.4 cell/mm³), granulocyte value a significant increase at p<0.05 were achieved for people with MI of both sexes, males patient(85.12±9.7 %) and females patient(69.48±4.7 %) when compared with healthy persons of both sexes, males healthy (71.45±9.1%) and females healthy (84.06±11.7%), lymphocyte value a significant increase at p<0.05 were achieved for people with MI of both sexes, males patient(13.28±2.6 %) and females patient(14.74±3.1 %) when compared with healthy persons of both sexes, males healthy (27.07±7.2%) and females healthy (29.53±8.1%), and PLT males patient (181.30±12.8 cell/mm³) was non-significant difference at p>0.05 compared with males healthy (186.40±22.1 cell/mm³) ,when PLT females healthy value a significant increase at p<0.05 were achieved for people with MI (202.95±14.4 cell/mm³) compared with females healthy (185.60±13.4 cell/mm³).

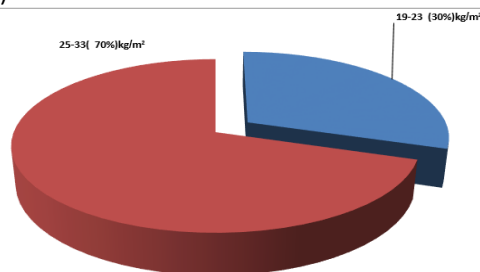


Figure (1): Shows the percentage ratio (%) of body mass index for patients affected with myocardial infarction.

Table (1): Showed the results of hematological parameters (WBC, Granulocytes, Lymphocytes and platelets) of patients affected with myocardial infarction according to gender.

Groups Parameters	Males	Females	LSD (0.05) (gender*group)
-------------------	-------	---------	---------------------------

	Patient	Control	Patient	Control	
	Mean ±S.E				
WBCs (cell/mm3)	* 8.01±2.1	5.07±0.6	* 8.06±1.6	5.01±1.4	0.345
Granulocyte (%)	* 85.12±9.7	71.45±9.1	* 69.48±4.7	84.06±11.7	1.878
Lymphocyte (%)	* 13.28±2.6	27.07±7.2	* 14.74±3.1	29.53±8.1	1.945
PLT (cell/mm3)	* 181.30±12.8	186.40±22.1	* 202.95±14.4	185.60±13.4	9.412

-All values were mean ±SE
 -Means with asterisk were significantly different (LSD) at p<0.05.
 -Means with no asterisk were non- significantly different (LSD) at p>0.05.

Levels of biochemical markers (fibrinogen mg/dl, troponin pg. /ml and C - reactive protein (CRP) mg/dl) of patients affected with myocardial infarction according to gender. Means which were illustrated in following table (2) explained the means ±SE of all mentioned above parameters of both patients and controls, showed a

significant decrease fibrinogen, troponin, and CRP (488.40±30.2 mg/dl, 31.90±4.6 pg/ml and 11.65±1.6 mg/dl respectively) in males and females (469.35±22.6 mg/dl, 16.69±2.4 pg/ml and 11.99±1.9 mg/dl respectively) at p<0.05 value was obtained for all parameters.

Table (2): Illustrate the biochemical markers (fibrinogen mg/dl, troponin pg/ml and C - reactive protein (CRP) mg/dl) of patients affected with myocardial infarction according to gender.

Groups Parameters	Males		Females	LSD(0.05) (gender*group)	
	Patient	Control	Patient	Control	
	Mean ±S.E				
Fibrinogen (mg/dl)	* 488.40±30.2	219.85±28.1	* 469.35±22.6	225.35±17.8	17.397
Troponin (pg/ml)	* 31.90±4.6	0.80±0.03	* 16.69±2.4	1.16±0.6	1.476
CRP (mg/dl)	* 11.65±1.6	5.01±0.6	* 11.99±1.9	4.95±0.2	0.740

-All values were mean ±SE
 -Means with asterisk were significantly different (LSD) at p<0.05.
 -Means with no asterisk were non- significantly different (LSD) at p>0.05.

Results of hematological parameters (WBCs cell/mm3, Granulocytes %, Lymphocytes % and platelets cell/mm3) of patients affected with MI according to gender and age. Data that were illustrated in following table (3) explained the means ±SE of all mentioned above parameters of both patients and controls, showed the statistical differences among studied age groups all (40-49, 50-59, 60-69,70-79 years old) and high significant difference (LSD) values were obtained for

(WBCs ,granulocyte and lymphocyte) all groups compared to and PLT males in age groups (40-49, 50-59 and 70-79 years old) was low significant difference (LSD) while in age groups (60-69 years) was high significant difference (LSD), while PLT females in age groups (40-49 and 60-69 years) was high significant difference (LSD), while in age groups (50-59 and 70-79 years old) was low significant difference (LSD).

Table (3): Showed the results of hematological parameters (WBC, Granulocytes, Lymphocytes and platelets) of patients affected with myocardial infarction and control group according to gender and age.

Groups Parameters	Age (year)	Males		Females		LSD(0.05)
		Patient	Control	Patient	Control	
		Mean ±S.E				
WBC (m/mm ³)	40-49	* 7.77±1.2	4.79±0.3	* 8.00±0.1	5.37±0.9	0.156

	50-59	* 8.56±1.3	5.77±0.1	* 8.07±0.2	4.63±0.4	
	60-69	* 7.66±0.6	4.79±0.1	* 8.30±0.2	5.02±0.1	
	70-79	* 8.06±0.2	4.94±0.2	* 7.88±0.2	5.01±0.2	
Granulocytes (%)	40-49	* 83.54±12.4	70.84±11.4	* 83.14±14.3	70.10±10.1	4.936
	50-59	* 86.86±6.9	70.84±10.3	* 84.50±10.7	72.00±7.8	
	60-69	* 83.66±11.2	71.72±13.4	* 84.82±9.4	70.08±9.9	
	70-79	* 86.42±7.9	72.40±10.6	* 83.78±8.8	65.72±5.4	
Lymphocytes (%)	40-49	* 14.46±2.4	27.42±2.2	* 15.66±0.9	28.90±3.6	5.426
	50-59	* 11.34±2.1	27.56±1.6	* 13.90±1.1	27.00±4.2	
	60-69	* 14.74±1.9	27.08±1.4	* 14.18±1.5	28.92±2.7	
	70-79	* 12.58±1.7	26.20±1.7	* 15.22±1.6	33.28±2.9	
PLT (m/mm3)	40-49	* 200.40±20.5	197.60±20.6	* 204.20±22.3	166.80±11.6	12.464
	50-59	* 180.80±22.7	186.00±13.4	* 202.40±16.4	193.00±13.4	
	60-69	* 174.40±16.7	190.00±22.4	* 202.80±17.4	182.00±20.4	
	70-79	* 169.60±17.7	172.00±13.3	* 202.40±25.6	200.60±9.8	
-All values were mean ±SE -Means with asterisk were significantly different (LSD) at p<0.05. -Means with asterisk were non- significantly different (LSD) at p>0.05.						

Results of biochemical markers (fibrinogen mg/dl, troponin pg/ml and C - reactive protein (CRP) mg/dl) of patients affected with myocardial infarction and control group according to gender and age. The levels which were illustrated in following table (4) explained the

means ±SE of all mentioned above parameters of both patients and controls, They were a statistical differences among all studied age groups (40-49, 50-59, 60-69,70-79 years old) and significant difference (LSD) value was obtained for all groups that were illustrated in the following figures in this study.

Table (4): Illustrate the biochemical markers (fibrinogen mg/dl, troponin pg/ml and c-reactive protein (CRP) mg/dl) of patients affected with myocardial infarction healthy groups according to gender and age.

Groups Parameters	Age (year)	Males		Females		LSD (0.05)
		Patient	Control	Patient	Control	
		Mean ±S. E				
Fibrinogen (mg/dl)	40-49	* 480.40±10.6	202.40±17.7	* 454.40±23.4	238.00±22.6	110.762
	50-59	* 487.40±24.1	242.80±19.6	* 475.60±26.7	226.80±30.4	
	60-69	* 481.20±34.2	221.80±18.5	* 497.40±18.7	232.00±37.2	
	70-79	* 504.60±41.2	212.40±22.1	* 450.00±13.9	204.60±17.6	
Troponin (pg/ml)	40-49	* 25.70±4.5	0.98±0.01	* 16.96±2.4	0.50±0.03	1.677
	50-59	* 34.96±7.9	0.38±0.02	* 16.52±0.6	0.84±0.01	
	60-69	* 35.76±6.7	1.06±0.07	* 16.40±2.7	1.36±0.2	
	70-79	* 31.16±4.5	0.76±0.03	* 16.88±3.7	1.92±0.1	
CRP (mg/dl)	40-49	* 12.54±2.1	5.70±0.9	* 12.58±1.2	4.88±0.9	1.522
	50-59	* 10.82±0.9	4.74±0.9	* 9.60±1.1	4.98±0.6	
	60-69	* 10.44±0.7	4.76±0.5	* 13.06±1.3	5.08±0.5	
	70-79	* 12.80±1.3	4.82±0.6	* 12.74±1.3	4.86±0.5	
-All values were mean ±SE -Means with asterisk were significantly different (LSD) at p<0.05. -Means with no asterisk were non- significantly different (LSD) at p>0.05.						

Levels of biochemical markers (fibrinogen mg/dl, troponin pg/ml, C - reactive protein (CRP) mg/dl) of patients affected with myocardial infarction according to body mass index (BMI Kg/m2). Means which were depicted in the table (5) indicated a

significant increase in the level of fibrinogen, troponin and CRP (493.00±14.4 mg/dl, 25.98±3.9 pg/ml and 12.92±0.7 mg/dl respectively) in patient at level p<0.01 compared to control (203.20±7.8 mg/dl, 1.20±0.3 pg/ml and 4.32±0.3 mg/dl respectively).

Table (5): Illustrate the biochemical markers (fibrinogen mg/dl, troponin pg/ml, c-reactive protein (CRP) mg/dl) of patients affected with myocardial infarction according to body mass index (BMI Kg/m2).

BMI groups Parameters	BMI (Kg/m2)		p≤0.05
	Patient (25-33)	Control (21+2)	
	Mean±S.E		
Fibrinogen(mg/dl)	493.00±14.4	203.20±7.8	≤0.0001**
Troponin (pg/ml)	25.98±3.9	1.20±0.3	≤0.0001**
CRP (mg/dl)	12.92±0.7	4.32±0.3	≤0.0001**

-All values were mean ±SE
-Results with two asterisk were significantly different at p≤0.0001.

Figure (2):- it had been shown there was a significant negative correlation (r = -0.99, sig = 0.0001) between granulocyte and lymphocytes in patients affected with MI.

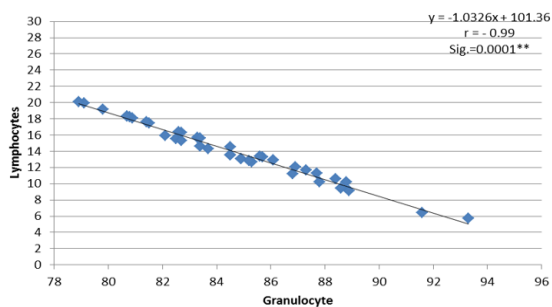


Figure (2): Correlation coefficient between granulocytes and lymphocytes.

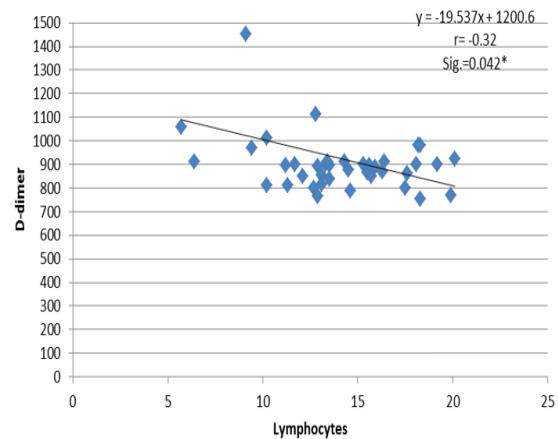


Figure (4-6): Correlation coefficient between lymphocytes and D-dimer

Table (6): the best cut off, sensitivity and specificity for prediction of the disease activity by parameters.

Parameter	Sensitivity	Specificity	AUC	Cut off	95% confidence	p-value
Fibrinogen	0.93	0.63	.816	253	0.715-0.917	≤0.0001
Troponin	0.825	0.700	.813	1.650	0.716-0.910	≤0.0001
CRP	0.825	0.625	0.724	6.150	0.612-0.837	0.001

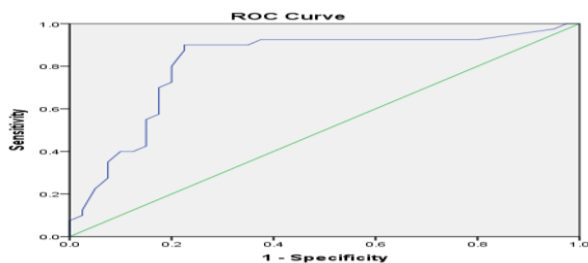


Figure (3): ROC curve for prediction of the disease activity by fibrinogen.

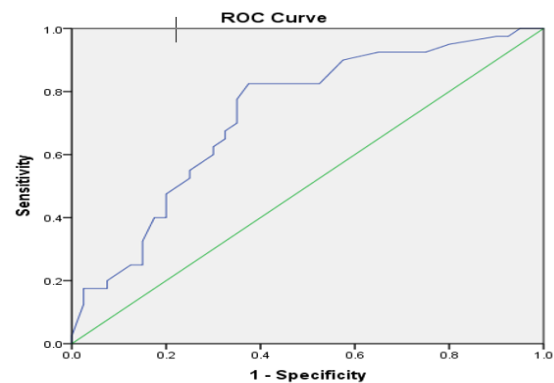


Figure (5): ROC curve for prediction of the disease activity by CRP.

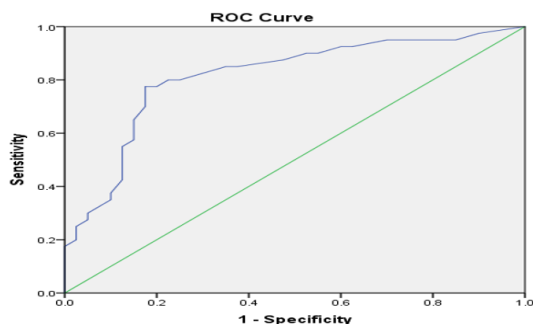


Figure (4): ROC curve for prediction of the disease activity by troponin.

5. Discussion

Data that are observed in the present study had been recorded a significant elevation (p<0.05) in the levels of WBCs in all patients group affected with MI compared to those control group. Data recorded a significant negative correlation (r = -0.99, sig = 0.0001) between granulocyte and data that there was a significant negative correlation (r = -0.32, sig = 0.042) recorded between lymphocyte and D-dimer of patient who had MI and a significant positive correlation (r=0.33, sig= 0.035) occurring between granulocytes and d-dimer levels.

The levels of leukocytes is associated with myocardial infarction and can determine the prognosis of MI, and

there is found that leukocytes increases in patients suffering from MI [13].

One of the most prominent indicator associated with coronary artery disease is both total WBCs and differential WBCs, in addition, there is association between WBCs count and mortality rate in patients with acute ischemic heart disease [14].

The development and progression of atherosclerotic cardiovascular diseases is related with inflammatory processes, with this relation, there is increase levels of inflammatory markers such as CRP, IL-6, and TNF- α , there for there is a positive relationship occurring between WBCs and risk incidence of cardiovascular events [15]. The white blood cells are accompanied with severity of coronary artery disease [16].

Data that are observed in the present study had been recorded non-significantly different ($p > 0.05$) in the levels of PLT in all patients group affected with MI compared to those control group. Data recorded a significant negative correlation ($r = -0.66$, $\text{sig} = 0.0001$) between PLT and troponin, and a significant positive correlation ($r = 0.36$, $\text{sig} = 0.021$) recorded between Hb and PLT.

To explain whether the platelets count influences or can be associated with MI, it was documented that platelets count was lower and mean of platelets volume (MPV) recorded a significant increase in those patients with MI, also, it was found from the obtained findings of the previous study that indicated these changes may be persist or changed after MI and these changes do not distinguish between thrombotic and the non-thrombotic MI [17].

The ischemic and bleeding disorders are mostly associated with platelets, it is well know that thrombocytes have essential roles in thrombotic events or damage to plaque of atherosclerotic lesion which represents the prominent factor in mechanism of acute myocardial infarction, as well as, there are several mechanisms enhance and evoke platelets formation and activation through systemic inflammation and degree of myocardial damage [18].

There is a recent study indicated that platelets contribute in development the MI pathogenesis, the take part in the formation of thrombus and of that micro thrombi, inflammatory mediators, immune modulators, and vasoconstrictive agents, however, increase inflammatory events and thrombotic risk factors are associated with increase formation and platelet activities [19].

The results of the present study recorded non-significant increase of PLT in patients of MI and this results might resulted from increased thrombotic events are related with triggering of new production of platelets from bone marrow as well as the increase levels of pro-inflammatory mediators can accelerated of platelets production.

The results of the present study indicated a significant elevation ($p < 0.05$) in all tested groups of patient affected with MI of both sexes and related with BMI. ROC analyses of the disease activity by fibrinogen, AUC result was (.816).

These findings were consistent with recent study who carried out by [20], which elaborated that increased plasma fibrinogen and a cute phase proteins in atherosclerotic cardiovascular disease such as myocardial

infarction and angina pectoris.

Another study pointed out there is an association between cardio vascular events conventional high risk factors and also predisposing factor of coronary artery disease and the results of this study showed higher levels of fibrinogen levels as a pro inflammatory biomarker in addition, it is essential role in clotting mechanism.

There is growing evidence indicates an association between levels of fibrinogen and risk of thrombosis of more concern of early CAD of women than of other clotting factors of hemostatic mechanism including stable factor (VII) and anti-hemophilic factor (VIII), tPA-1, and tPAI-1, moreover, increase concentration of fibrinogen during inflammatory processes is often associated with IL-6, however, fibrinogen level is higher in women and increase IL-6 production that can exacerbates incidence of CAD [21].

The relationship between visceral obesity and levels of fibrinogen are associated with increased incidence of inflammatory processes, hypertension, and prothrombotic status and these effects are occurred in children and elderly [22].

Inflammatory mediators (IL-6) triggers fibrinogen production by hepatocytes and then after the higher levels of fibrinogen can increase risk of thrombotic events [23].

The relationship between age and clotting and fibrinolytic system was studied, it had been found there is a positive correlations occurring between old ages and levels of D-dimer and fibrinogen so that this study concluded that hyper coagulable activities progress at old ages [24].

Results of the present study had been recorded a significant elevation ($p < 0.01$) in the levels of troponin in all patients group affected with MI compared to those control group. Data recorded a significant positive correlation ($r = 0.71$, $\text{sig} = 0.0001$) between Hb and troponin and a significant positive correlation ($r = 0.63$, $\text{sig} = 0.0001$) between RBCs and troponin. ROC analyses of the disease activity by troponin, AUC result was (.813).

The results of the present study are consistent with study of Negahdary et al. [25] that focused on the levels of troponin, a cardiac biomarker and explained elevation levels of troponin in patients with MI and other cardiac diseases.

Furthermore, study of Eidizadeh et al. [26] confirmed that in spite of troponin is important diagnostic factor for MI, but this study was confirmed that no recommendations or instructions concerne to the two types of troponin, including troponin I (cTnI) and troponin T (cTnT) in diagnostic severity of disease also, this study demonstrated that a sex dependent of these parameters by using ROC analysis improved and increase sensitivity with specificity of those troponin types.

In regard the age, it had been found that high sensitive troponin T values recorded significant heightening in men with age over 40 years old compared to those men who have ages less than 40 years old in patients with MI, as well as, it was found women have lower level of hTnT when they compared to those men with the matched ages [27].

Also another studies investigated the effects of age of

levels of troponin and found that the old age especially more than 60 years old have higher levels of troponin when they are affected with a cute MI compared to those counter parts of healthy one [28, 29].

Concerning body mass index, recent study investigated whether BMI effect on cardiovascular events and cardiac biomarker, and this study was established that cardiac troponin, atrionatriuritic peptide, and pro natriuretic peptide were positively associated with body mass index [30].

Data obtained from the present work had been established significant increase of inflammatory cytokine (CRP) in all patients groups according to sex, age, and BMI compared to those of healthy control groups. ROC analysis of the disease activity by TPA-1, AUC result was (0.724).

It is well known that inflammation can evoke and increase initiation and development of coronary artery disease, there for, the levels of CRP is at higher level with severity of cardiovascular diseases, it increases tow fold in patients with CAD compared to healthy subjects, so that CRP consider the powerful indicator to evaluate the severity of MI [31].

On the basis of molecular point view, the increase adhesion molecules (CAM) and activation of inflammatory cells can co-operate to induce release of inflammatory mediators and pro coagulant molecules, these event eventually enhance thickening of atherosclerotic lesions and progress of acute coronary disease in particular MI [32, 33].

As well as, during myocardial infarction occurs activation for inflammatory mediators and this process is accompanied with heart damage and repairing mechanism, so that increase inflammatory mediators can lead to several cardiac damage and dysfunction [34].

Study of [35], was designed to determine the association between high sensitive CRP concentrations and myocardial infarction patients, this study was found increase levels of CRP in patients with MI in matching with those healthy people, at the same time it concluded that the major response of inflammation for tissue damage and CRP is prognostic factor to this response.

In regards, the relationship between body mass index and c-reactive protein, it had been documented that obesity represents chronic low level of inflammatory condition and this is recognized by elevation of specific inflammatory parameter that is c-reactive proteins, these facts were confirmed by study which indicated a significant positive correlation occurring between CRP and BMI [36].

References

1. Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: from myocardial infarction to chronic disease. *Cardiovascular research*. 2017;113(14):1708-18. <https://doi.org/10.1093/cvr/cvx183>
2. Jardins TD. *Cardiopulmonary Anatomy and Physiology: Essentials of Respiratory Care*. Delmar, Cengage Learning; 2013.
3. Chung DW, Harris JE, Davie EW. Nucleotide sequences of the three genes coding for human fibrinogen. In: *Fibrinogen, thrombosis, coagulation, and fibrinolysis*. Springer, 1990. p. 39-48. https://doi.org/10.1007/978-1-4615-3806-6_3
4. Kant J, Fornace A, Saxe D. I Simon, M.; McBride, OW; Crabtree, GR Evolution and organization of the fibrinogen locus on chromosome 4: Gene duplication accompanied by transposition and inversion. *Proc Natl Acad Sci USA*. 1985;82:2344-8.
5. Tamura T, Arai S, Nagaya H, Mizuguchi J, Wada I. Stepwise assembly of fibrinogen is assisted by the endoplasmic reticulum lectin-chaperone system in HepG2 cells. *PLoS One*. 2013;8(9):e74580. <https://doi.org/10.1371/journal.pone.0074580>
6. Frangogiannis NG. The inflammatory response in myocardial injury, repair, and remodelling. *Nature Reviews Cardiology*. 2014;11(5):255-65.
7. Ørn S, Manhenke C, Ueland T, Damås JK, Mollnes TE, Edvardsen T, Aukrust P, Dickstein K. C-reactive protein, infarct size, microvascular obstruction, and left-ventricular remodelling following acute myocardial infarction. *European heart journal*. 2009;30(10):1180-6. <https://doi.org/10.1093/eurheartj/ehp070>
8. Reindl M, Reinstadler SJ, Feistritz H-J, Klug G, Tiller C, Mair J, Mayr A, Jaschke W, Metzler B. Relation of inflammatory markers with myocardial and microvascular injury in patients with reperfused ST-elevation myocardial infarction. *European Heart Journal: Acute Cardiovascular Care*. 2017;6(7):640-9. <https://doi.org/10.1177/2048872616661691>
9. Prabhu SD, Frangogiannis NG. The biological basis for cardiac repair after myocardial infarction: from inflammation to fibrosis. *Circulation research*. 2016;119(1):91-112. <https://doi.org/10.1161/CIRCRESAHA.116.303577>
10. Valentine CM, Tcheng JE, Waites T. Translating the translation: what clinicians should know about the Fourth Universal Definition of Myocardial Infarction. *American College of Cardiology Foundation Washington DC*; 2018. p. 2668-70.
11. De Lemos JA, Newby LK, Mills NL. A proposal for modest revision of the definition of type 1 and type 2 myocardial infarction. *Circulation*. 2019;140(22):1773-5. <https://doi.org/10.1161/CIRCULATIONAHA.119.042157>
12. Daniel WW, Cross CL. *Biostatistics: a foundation for analysis in the health sciences*. Wiley, 2018.
13. Ferrari JP, Lueneberg ME, da Silva RL, Fattah T, Gottschall CAM, Moreira DM. Correlation between leukocyte count and infarct size in ST segment elevation myocardial infarction. *Archives of Medical Science-Atherosclerotic Diseases*. 2016;1(1):44-8. <https://doi.org/10.5114/amsad.2016.60759>
14. Yan X-N, Jin J-L, Zhang M, Hong L-F, Guo Y-L, Wu N-Q, Zhu C-G, Dong Q, Li J-J. Differential leukocyte counts and cardiovascular mortality in very old patients with acute myocardial infarction: a Chinese cohort study. *BMC cardiovascular disorders*. 2020;20(1):1-12. <https://doi.org/10.1186/s12872-020-01743-3>
15. Rana J, Boekholdt S, Ridker P, Jukema J, Luben R, Bingham S, Day N, Wareham N, Kastelein J, Khaw KT. Differential leucocyte count and the risk of future coronary artery disease in healthy men and women: the

- EPIC-Norfolk Prospective Population Study. *Journal of internal medicine*. 2007;262(6):678-89. <https://doi.org/10.1111/j.1365-2796.2007.01864.x>
16. Hong L-F, Li X-L, Luo S-H, Guo Y-L, Liu J, Zhu C-G, Qing P, Xu R-X, Wu N-Q, Jiang L-X. Relation of leukocytes and its subsets counts with the severity of stable coronary artery disease in patients with diabetic mellitus. *PLoS One*. 2014;9(3):e90663. <https://doi.org/10.1371/journal.pone.0090663>
 17. Amraotkar AR, Song DD, Otero D, Trainor PJ, Ismail I, Kothari V, Singh A, Moore IV JB, Rai SN, DeFilippis AP. Platelet count and mean platelet volume at the time of and after acute myocardial infarction. *Clinical and Applied Thrombosis/Hemostasis*. 2017;23(8):1052-9. <https://doi.org/10.1177/1076029616683804>
 18. Roh JW, Lim S, Hwang Y, Lee KY, Choo EH, Choi IJ, Hwang B-H, Kim CJ, Park M-W, Kim D-B. Ischemic and bleeding events associated with thrombocytopenia and thrombocytosis after percutaneous coronary intervention in patients with acute myocardial infarction. *Journal of clinical medicine*. 2020;9(10):3370. <https://doi.org/10.3390/jcm9103370>
 19. Hałucha K, Rak-Pasikowska A, Bil-Lula I. Protective Role of Platelets in Myocardial Infarction and Ischemia/Reperfusion Injury. *Cardiology Research and Practice*. 2021;2021. <https://doi.org/10.1155/2021/5545416>
 20. Surma S, Banach M. Fibrinogen and Atherosclerotic Cardiovascular Diseases—Review of the Literature and Clinical Studies. *International Journal of Molecular Sciences*. 2021;23(1):193. <https://doi.org/10.3390/ijms23010193>
 21. Kryczka KE, Kruk M, Demkow M, Lubiszewska B. Fibrinogen and a triad of thrombosis, inflammation, and the renin-angiotensin system in premature coronary artery disease in women: A new insight into sex-related differences in the pathogenesis of the disease. *Biomolecules*. 2021;11(7):1036. <https://doi.org/10.3390/biom11071036>
 22. Hafez M, El-Masry S, Musa N, Fathy M, Hassan M, Hassan N, El Hussein M, Tareef M. Relationship between visceral obesity and plasma fibrinogen in obese children. *Journal of Pediatric Endocrinology and Metabolism*. 2016;29(3):289-96. <https://doi.org/10.1515/jpem-2015-0264>
 23. Hulshof A-M, Hemker HC, Spronk HM, Henskens YM, Ten Cate H. Thrombin–Fibrin (ogen) Interactions, Host Defense and Risk of Thrombosis. *International journal of molecular sciences*. 2021;22(5):2590. <https://doi.org/10.3390/ijms22052590>
 24. Ochi A, Adachi T, Inokuchi K, Ogawa K, Nakamura Y, Chiba Y, Kawasaki S, Onishi Y, Onuma Y, Munetsugu Y. Effects of aging on the coagulation fibrinolytic system in outpatients of the cardiovascular department. *Circulation Journal*. 2016;CJ-16-0530. <https://doi.org/10.1253/circj.CJ-16-0530>
 25. Negahdary M, Namayandeh SM, Behjati-Ardekani M, Ghobadzadeh S, Dehghani H, Soltani MH. The importance of the troponin biomarker in myocardial infarction. *J Biol Today's World*. 2016;5(1):1-12.
 26. Eidizadeh A, Fraune L, Leha A, Wachter R, Asif AR, Binder L. Inconsistent Findings of Cardiac Troponin T and I in Clinical Routine Diagnostics: Factors of Influence. *Journal of clinical medicine*. 2021;10(14):3148. <https://doi.org/10.3390/jcm10143148>
 27. Isiksacan N, Biyik I, Opan S, Caglar FN, Erturk M, Yazan S, Kasapoglu P, Karabulut D, Kocamaz N, Yildirim MR. Effect of age and gender differences on high-sensitive troponin T measurement in the diagnosis of acute myocardial infarction. *Journal of Laboratory Medicine*. 2019;43(1):35-40. <https://doi.org/10.1515/labmed-2018-0326>
 28. Ichise T, Tada H, Sakata K, Kawashiri M-a, Yamagishi M, Hayashi K. Impact of aging on high-sensitivity cardiac troponin T in patients suspected of acute myocardial infarction. *Internal Medicine*. 2017;56(16):2097-102. <https://doi.org/10.2169/internalmedicine.8510-16>
 29. Sedighi SM, Prud'Homme P, Ghachem A, Lepage S, Nguyen M, Fulop T, Khalil A. Increased level of high-sensitivity cardiac Troponin T in a geriatric population is determined by comorbidities compared to age. *IJC Heart & Vasculature*. 2019;22:187-91. <https://doi.org/10.1016/j.ijcha.2019.02.015>
 30. Suthahar N, Meems LM, Groothof D, Bakker SJ, Gansevoort RT, van Veldhuisen DJ, de Boer RA. Relationship between body mass index, cardiovascular biomarkers and incident heart failure. *European journal of heart failure*. 2021;23(3):396-402. <https://doi.org/10.1002/ejhf.2102>
 31. Bouzidi N, Messaoud MB, Maatouk F, Gamra H, Ferchichi S. Relationship between high sensitivity C-reactive protein and angiographic severity of coronary artery disease. *Journal of geriatric cardiology: JGC*. 2020;17(5):256. <https://doi.org/10.11909%2Fj.issn.1671-5411.2020.05.003>
 32. Razi MM, Abdali N, Asif SM, Azharuddin M. Association of inflammatory cytokines/biomarkers with acute coronary syndrome and its correlation with severity and hospital outcome. *Journal of Clinical and Preventive Cardiology*. 2017;6(2):44.
 33. Ma C-Y, Xu Z-Y, Wang S-P, Peng H-Y, Liu F, Liu J-H, Ren F-X. Change of inflammatory factors in patients with acute coronary syndrome. *Chinese Medical Journal*. 2018;131(12):1444-9.
 34. Świątkiewicz I, Magielski P, Kubica J, Zadourian A, DeMaria AN, Taub PR. Enhanced inflammation is a marker for risk of post-infarct ventricular dysfunction and heart failure. *International journal of molecular sciences*. 2020;21(3):807. <https://doi.org/10.3390/ijms21030807>
 35. Milano SS, Moura Ovd, Bordin AAS, Marques GL. C-reactive protein is a predictor of mortality in ST-segment elevation acute myocardial infarction. *International Journal of Cardiovascular Sciences*. 2018;32:118-24.
 36. Farooq SN, Ahmed A, Mustafa MA, Rizvi MIS. High sensitivity C-reactive protein level increases with rise in body mass index and not affected by perceived stress in young Saudis. *Annals of Medical and Health Sciences Research*. 2017;7(4).

