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Research Article

Estimation of Fibrinogen Level among Sudanese Patients with Myocardial Infraction

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ABSTRACT

Myocardial infarction (AMI) is an irreversible myocardial injury and necrosis caused by serious and long-term ischemia. It is generally seen in middle aged men with high risk factors for coronary artery disease. Only 4% of patients with AMI are under 40 years of age. This was a cross sectional study conducted at AL SHAB hospital, Khartoum, Sudan, aimed to estimate the fibrinogen level among Sudanese patients with myocardial infarction. 50 patients attending Alshab Hospital and diagnosed with MI used as a case group and 50 apparently healthy individuals with no history of MI were selected as control group. 1.8 ml of blood samples has been collected in sodium citrate anticoagulant container for measurement of fibrinogen level by clauss method in coagulometer device. It is clearly significant increase in fibrinogen level in myocardial infarction patient (p.value 0.000). In addition, the prothrombin time and gender were insignificantly differences in (AMI) patients. In the other hand, age and smoking significantly increased as risk factor in myocardial infarction. This study concluded that fibrinogen level was significantly increased in Sudanese patients with myocardial infarction.

Keywords: Myocardial Infarction, Fibrinogen, Prothrombin Time, Coagulometer

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INTRODUCTION

Acute myocardial infarction (AMI) is an irreversible myocardial injury and necrosis caused by serious and long-term ischemia. It is generally seen in middle aged men with high risk factors for coronary artery disease. Only 4% of patients with AMI are under 40 years of age. Coronary anatomy is normal in 30% of young AMI patients. The presence of normal coronary anatomy is related to coronary vasospasm, embolism from endocardium or heart vessels and platelet aggregation or spontaneous lysis of thrombus^[1].

The morbidity and mortality rates of ACS are increasing, thus, Premature myocardial infarction with life threatening complications may become epidemic in some Asian and African countries Deaths per 1000 person-years in the quartile (P<0.001 for trend).^[2]

Pathogenicity

Instability of coronary atherosclerosis plaque, which is easily to rupture that, may induce platelet aggregation and lead to complete or incomplete coronary artery embolism. Further causes severe lumen stenosis and myocardial blood supply

shortage. At present, the treatment principle of ACS is early detection, early diagnosis and early treatment to achieve revascularization. In recent years, with the development in Chest Pain Center and interventional technology, ACS patients can receive timely treatment. However, research has found that some ACS patients would still develop major adverse cardiovascular events (MACEs) even after getting through the acute phase; MACEs can cause serious threats to the quality of life and even lead to death of patients. Therefore, predicting the short term prognosis for ACS patients is one of the hot issues that draw clinical attention. The pathological basis of ACS is thrombosis caused by abnormal fibrinolysis and blood coagulation and the pathological basis of MACE is the formation of sub-acute or chronic coronary embolism. In recent years, the researches confirmed that there was a correlation between the prognosis of patients with ACS and diverse biochemical markers. Its immunocompetence fragment can reflect the plasma concentration of cross linked fibrin polymer and its plasma level can effectively and specifically reflect the increase in blood circulating coagulation and the level of secondary fibrinolytic hyperactivity^[3].

AMI is diagnosed where there are at least two of following; chest pain longer than 30 minutes which does not respond to nitrates, in 12-lead electrocardiography, a new Q wave longer than 40 ms and/or ST segment elevation 0.1 mV on at least two extremity derivations or 0.2 mV on precordial derivation, a 1.5 times, or higher, increase in serum creatinophosphokinase-MB and TT, Fibrinogen well elevated.^[3]

Fibrinogen level

Fibrinogen is one of 13 coagulation factors responsible for normal blood clotting and made in the liver, also known as factor 1^[4]. When bleeding start the body initiates process called coagulation cascade or clotting cascade, this process cause coagulation factor to combine and produce a clot that will stop the bleeding. If the body hasn't enough fibrinogen or if the cascade isn't working normally clots will have difficulty forming, this can cause excessive bleeding.^[5]

Low fibrinogen levels can also cause thrombosis in coagulation activity. Thrombosis refers to the formation of blood clot inside of blood vessel. The clot blocks normal blood flow through the circulatory system. This can lead to serious medical condition such as heart attack and stroke^[6]. Numerous prospective epidemiological studies have reported positive associations between the risk of coronary heart disease (CHD) and plasma fibrinogen levels.^[7] Fibrinogen levels decreased considerably by lifestyle interventions that also affect levels of risk factors such as regular exercise, smoking discontinuation and moderate alcohol consumption, the measurement of fibrinogen level may help in disease prediction or prevention.^[8] This study aimed to estimate the fibrinogen level among Sudanese patients with myocardial infarction.

MATERIALS AND METHODS

This is a cross sectional study, conducted at Alshab Hospital, Khartoum, Sudan during the period May 2019 to July 2019. All patients attending Alshab Hospital and diagnosed with MI during the aforementioned period were included. In addition to that, apparently healthy individuals with no history of MI were selected as control group. The study was approved by the ethical committee of Al shab Hospital, The data was collected using pre-designed structural questionnaire, the demographic and clinical data concerning each participant was obtained from the registry data base office, which included the following information: (Gender, age, weight, smoking, chronic disease, treatment, exercise and medical history). The laboratory data included hematological results and fibrinogen level findings. 2.8 ml of blood samples were collected in trisodium citrate anticoagulant container for fibrinogen level count.

Tests procedure

1. Thrombin time

75 μ l of thrombin solution added to 100 μ l of tested plasma in cuvette at 37°C and start reading of clotting time.

Sample diluted in 1:10 in imidazole buffer

Normal range: up to 10_12 second.

2. prothrombin time

100 μ l of thrombin solution was added to 100 μ l of tested plasma in cuvette at 37°C and reading of clotting time was recorded.

Normal range: up to 11_ 13.5second.

3 .Fibrinogen assay

The preparation of calibration/standard plasma dilution in Imidazole buffer was followed; 1:5(200%)-1:10(100%)-1:20(50%)-1:30(33%)-1:40(25%). Firstly 0.1ml of each dilution was incubated at 37°C for 120 seconds, then 0.075ml of thrombin solution was added and simultaneously start reading, the clot was observed and clot time was measured nearest to 0.1seconds. The polt calibration curve on log- log graph paper and the clot time versus the fibrinogen concentration in g/l the curve was obtained by the linear. The dilute control plasma or patient sample 1:10 in Imidazole buffer. The normal reference for fibrinogen is generally 1.5-3.5g/l (150—350mg/dl)

RESULTS

In the present study 50 of myocardial infarction patients were included. Among them, 35 were males, while 15 were females. In addition, 50 of apparently healthy individuals were selected as control group, 19 were males, while 31 were female. (fig 1). The most affected age group in the patients was more than 60 years followed by 51-60 years which constituted 52% and 26%, respectively (Table 1).

The hematological parameters revealed that, when compared the age group with thrombin time and fibrinogen level among the patient gave significant result ($P = 0.000$) (table 5) . Also, there was insignificant result when Comparison of age ($p = 0.866$), Weight ($p = 0.520$), PT ($p = 0.617$), INR ($p = 0.422$) (table 6), but significant in TT ($p = 0.002$) and Fibrinogen level ($p=0.008$) among gender of MI patients (table 6). When Comparison of PT ($p=0.229$), INR ($p=0.422$), TT ($p = 0.159$) and Fibrinogen level ($p = 0.146$) among patients used treatment of chronic disease (diabetes and hypertension) there was insignificant result (table7). Also when Comparison of PT ($p=0.068$), INR ($p = 0.134$) among smoker gave insignificant result, while the TT ($p = 0.000$), and Fibrinogen level ($p=0.000$) among smoker patients gave significant result (table 8). While, there was significant difference when correlation between weight and TT (second). In addition to that, there was significant difference between weight and fibrinogen levels (mg/dl).

Table (1): Age groups of affected patients

Age groups	frequency	Percent
Less than 30	2	4.0
31-40	1	2.0
41-50	8	16.0
51-60	13	26.0
More than 60	26	52.0
Total	50	100.0

Table (2): Frequency of smoking among affected patients

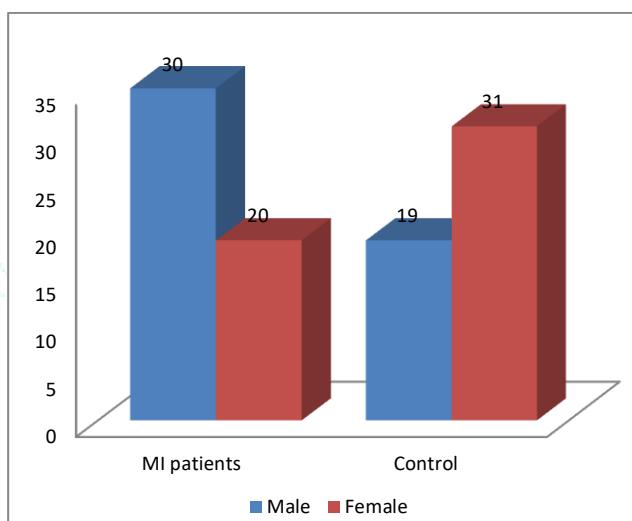
Smoking	Frequency	Percent
NO	33	66.0
Yes	17	34.0
Total	50	100.0

Table (3): Descriptive statistics for myocardial infarction patients

Variable	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	50	20	90	61.5	14.2
Weight (kg)	50	47	90	74.9	7.9
PT (seconds)	50	13.7	19.8	16.4	1.3
INR	50	0.9	1.4	1.1	0.13
TT (seconds)	50	17.5	25.0	20.9	2.2
Fibrinogen (mg/dl)	50	421	602	505.1	53.2

Table (4): Descriptive statistics for control

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	50	22	36	28.9	3.9
TT (seconds)	50	9.9	12.0	10.7	0.7
Fibrinogen (mg/dl)	50	238	290	260.3	15.8

**Fig (1): Frequency of gender among study population****Table (5): Comparison of age, TT and Fibrinogen level among population study**

Parameters	Population study (Mean \pm SD)		P. value
	MI patients (n=50)	Control (n=50)	
Age (years)	61.5 \pm 14.2	28.9 \pm 3.9	0.000
TT (seconds)	20.9 \pm 2.2	10.7 \pm 0.7	0.000
Fibrinogen (mg/dl)	505.1 \pm 53.2	260.3 \pm 15.8	0.000

Table (6): Comparison of age, Weight, PT, INR, TT and Fibrinogen level among gender of MI patients

Parameters	Gender (Mean \pm SD)		P. value
	Male (n=35)	Female (n=15)	
Age (years)	61.3 \pm 14.5	62.1 \pm 13.9	0.866
Weight (kg)	74.3 \pm 6.3	76.3 \pm 11.1	0.520
PT (seconds)	16.5 \pm 1.3	16.2 \pm 1.6	0.617
INR	1.1 \pm 0.13	1.1 \pm 0.15	0.422
TT (seconds)	21.5 \pm 2.2	19.7 \pm 1.6	0.002
Fibrinogen (mg/dl)	517.8 \pm 52.8	475.4 \pm 42.6	0.008

Table (7): Comparison of PT, INR, TT and Fibrinogen level among patients use treatment of chronic disease

Parameters	Treatment (Mean \pm SD)		P. value
	No (n=35)	Yes (n=15)	
PT (seconds)	16.2 \pm 1.4	16.7 \pm 1.2	0.229
INR	1.1 \pm 0.1	1.1 \pm 0.1	0.422
TT (seconds)	21.3 \pm 2.2	20.3 \pm 1.9	0.159
Fibrinogen (mg/dl)	512.3 \pm 54.4	488.3 \pm 48.1	0.146

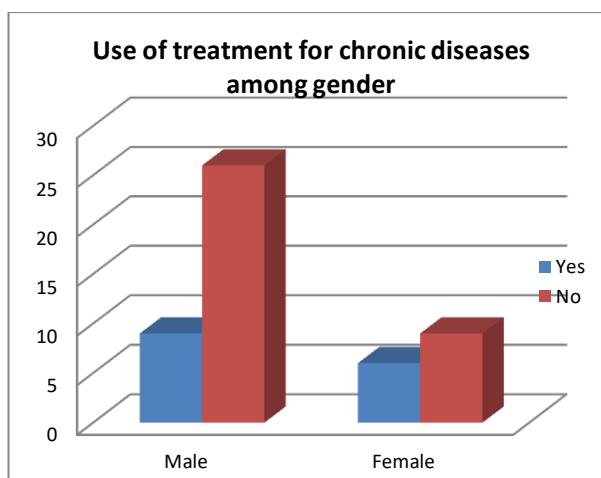


Fig (2): Frequency of use treatment for chronic diseases among gender

Table (8): Comparison of PT, INR, TT and Fibrinogen level among smoker

Parameters	Smoking (Mean \pm SD)		P. value
	No (n=33)	Yes (n=17)	
PT (seconds)	16.1 \pm 1.3	16.9 \pm 1.3	0.068
INR	1.1 \pm 0.12	1.1 \pm 0.13	0.134
TT (seconds)	20.0 \pm 1.7	22.7 \pm 1.9	0.000
Fibrinogen (mg/dl)	483.2 \pm 42.8	547.4 \pm 46.2	0.000

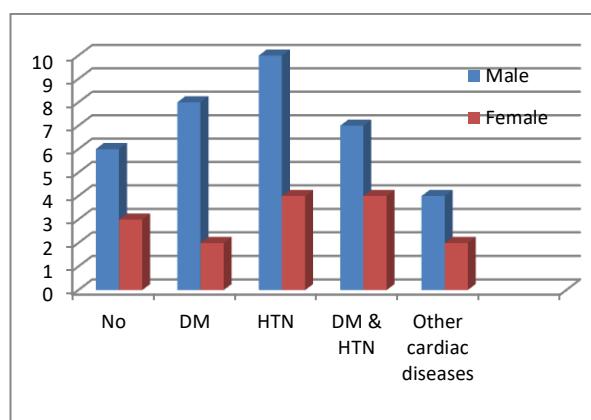


Fig (3): frequency of chronic diseases among gender

Table (9): Multiple Comparisons TT and Fibrinogen level according to risk factor of other diseases

Parameters	Sample (I)	Sample (II)	Mean of (I)	Mean of (II)	P value
TT (sec)	No	DM	22.9 ± 1.9	20.3 ± 2.3	0.007*
	No	DM & HTN	22.9 ± 1.9	20.2 ± 1.6	0.003*
	No	HTN	22.9 ± 1.9	20.9 ± 2.2	0.020*
	No	Other cardiac disease	22.9 ± 1.9	20.9 ± 1.9	0.066
	DM	DM & HTN	20.3 ± 2.3	20.2 ± 1.6	0.838
	DM	HTN	20.3 ± 2.3	20.9 ± 2.2	0.515
	DM	Other cardiac disease	20.3 ± 2.3	20.9 ± 1.9	0.548
	HTN	DM & HTN	20.9 ± 2.2	20.2 ± 1.6	0.374
	HTN	Other cardiac disease	20.9 ± 2.2	20.9 ± 1.9	0.933
Fibrinogen (mg/dl)	No	DM	555.3 ± 49.2	488.7 ± 55.4	0.005*
	No	DM & HTN	555.3 ± 49.2	484.4 ± 38.3	0.002*
	No	HTN	555.3 ± 49.2	501.0 ± 53.4	0.013*
	No	Other cardiac disease	555.3 ± 49.2	504.3 ± 44.2	0.055
	DM	DM & HTN	488.7 ± 55.4	484.4 ± 38.3	0.841
	DM	HTN	488.7 ± 55.4	501.0 ± 53.4	0.548
	DM	Other cardiac disease	488.7 ± 55.4	504.3 ± 44.2	0.541
	HTN	DM & HTN	501.0 ± 53.4	484.4 ± 38.3	0.405
	HTN	Other cardiac disease	501.0 ± 53.4	504.3 ± 44.2	0.890

* The mean difference is significant at the 0.05 level.

Table (10): Comparison of PT, INR, TT and Fibrinogen level according to Exercise

Parameters	Exercise (Mean ± SD)		P. value
	No (n=38)	Yes (n=12)	
PT (seconds)	16.4 ± 1.4	16.2 ± 1.1	0.623
INR	1.1 ± 0.1	1.1 ± 0.1	0.658
TT (seconds)	21.1 ± 2.2	20.4 ± 2.2	0.336
Fibrinogen (mg/dl)	508.6 ± 52.5	493.8 ± 56.2	0.408

Table (11): Correlations between Weight and TT

Correlations			
		Weight	TT
Weight	Pearson Correlation	1	-.063
	Sig. (2-tailed)		.663
	N	50	50
TT	Pearson Correlation	-.063	1
	Sig. (2-tailed)	.663	
	N	50	50

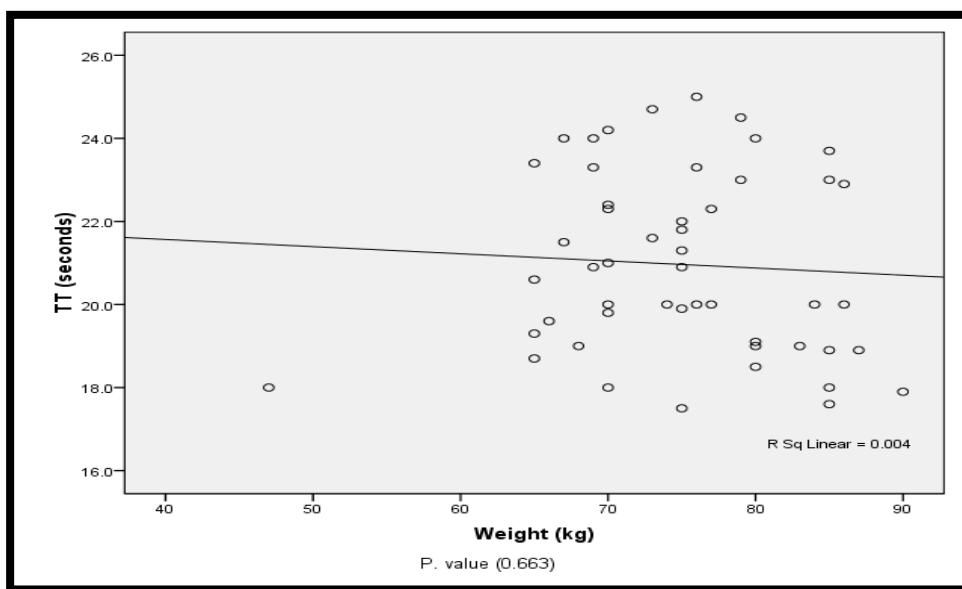


Fig (4): Correlations between Weight and TT

Table (12): Correlations between Weight and Fibrinogen level

Correlations			
		Weight	Fibrinogen
Weight	Pearson Correlation	1	-.053
	Sig. (2-tailed)		.716
	N	50	50
Fibrinogen	Pearson Correlation	-.053	1
	Sig. (2-tailed)	.716	
	N	50	50

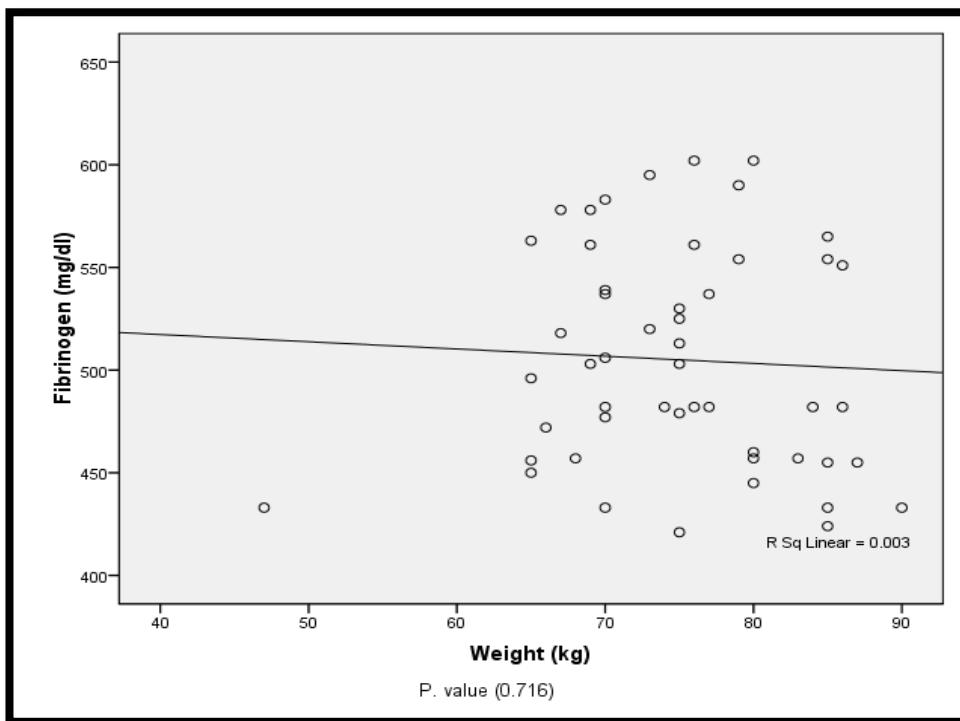


Fig (5): Correlations between Weight and Fibrinogen level

DISCUSSION

In the present study the results revealed the following: The descriptive statistics for myocardial infarction patients; mean of age (years) 61.5 and (Std deviation 14.2), mean of weight (kg) 74.9 (std deviation 7.9), mean of PT (second) 16.4 (std deviation 1.3), mean of INR 1.1 (std deviation 0.13), mean of TT (second) 20.9 (std deviation 2.2) and mean of fibrinogen (mg/dl) 505.(std deviation53.2). Also, the Descriptive Statistics for control; mean of age (years) 28.9 (std deviation 3.9), TT (second) 10.7 (std deviation 0.7) and mean of fibrinogen (mg/dl) 260.3 (std deviation15.8). The frequency of gender among study population; for the patients the males more than females, while in the control the females more than males.

There was significant difference of age (years) in myocardial infarction patients when compared with control group (mean $61.5 \pm SD$) (p.value 0.000) and the most affected age group above 60, that is consistent with other study which reported; acute myocardial infarction is generally caused by thrombus arising secondary to the rupture of the atherosclerotic plaque in coronary artery and usually affects adults over 40. Only 4% of AMI patients are under 40. [9,10] Also, there was significant difference of TT (second) in myocardial infarction patients when compared with control group (mean $20.9 \pm SD$) (p.value 0.000), that is agree with other study also showed a significant difference of thrombin time in patients with acute phase of MI. [11] Regarding the fibrinogen level our results showed; there was a significant

difference of fibrinogen (mg/dl) in myocardial infarction patients when compared with control group (p.value 0.000), that is consistent with other study also reported that; the serum fibrinogen levels are a risk factor for premature AMI.[12,13] In the present study there was insignificant difference of age (years) in gender of myocardial infarction patients male when compared with female (p.value0.866). One of previous study agreed with our finding and reported that; the decline among women to be less consistent than that observed in men. [14] Also, there was insignificant difference of weight (kg) in gender of myocardial infarction male (mean $74.3 \pm SD$) when compared with female (mean $76.3 \pm SD$) (p.value 0.520). In compare with other study said that; overweight is often regarded as one of the most important modifiable cardiovascular risk factors, but its association with cardiovascular health over a lifespan remains incompletely understood. Not all studies have demonstrated adverse effects of overweight. [15]

There was insignificant difference of PT (second) and INR in gender of myocardial infarction male when compared with female (p.value 0.617) (p.value 0.422). That is agreed with other study which reported that; prothrombin time (PT) and activated partial thromboplastin time(a PTT) didn't show any significance among patients with AMI and disagreed with other study showed; both PT and a PTT are significantly increased in AMI patients on anticoagulation therapy. [16,17] Also, there was insignificant difference of PT (second) and INR in myocardial infarction patients not used

treatment for the chronic disease when compared with other used treatment (p.value0.229) (p.value0.422). In addition to that; there was insignificant difference of PT (second) and INR in myocardial infarction patient who didn't smoke when compared with smoking patients (p.value0.068). In the other hands our results revealed that; there was significant difference of fibrinogen levels (mg/dl) and TT (second) in myocardial infarction male when compared with female (p. value 0.00) & (p. value 0.002). Also, there was insignificant difference of fibrinogen levels (mg/dl) and TT (second) in myocardial infarction patients that didn't use treatment when compared with used treatment (p.value0.159) & (p.value0.146) Indeed , the frequency of use treatment for chronic diseases among gender of study population; male didn't use treatment more than female. There was significant difference of fibrinogen levels (mg/dl) and TT (second) in myocardial infarction patients who did not smoke when compared with smoking patients (p.value0.000). Many studies confirmed that; Smoking is the most important and commonest risk factor in young patients. [18,19]

In the present study the frequency of chronic diseases (hypertension, diabetes mellites and cardiac disease) among gender; male are more than the female in the study population, also there was significant difference for TT when compared patients of myocardial infarction with no risk factor (chronic diseases) with the patient with chronic diseases (DM P.V 0.007, HT P.V 0.003), while there was insignificant results when compered the two groups in the patients with the cardiac diseases

For the fibrinogen levels there was a significant difference when compered between the patients with chronic disease with the patients without chronic diseases (p value 0.002 for DM and p value 0.013 for HT) and in significant difference in the patient with cardiac disease (p.value0.066). Many studies agreed with our results and revealed the same risk factors for AMI including age, smoking, cholesterol, physical inactivity, arterial hypertension, diabetes. [18,20,21]

Finally there was insignificant difference of PT (second), INR, TT (second) and fibrinogen levels (mg/dl) when compered between the patients that were made exercise and the other were not. also, there was significant difference when correlation between weight and TT and fibrinogen levels that is in agreed with other study revealed that ; both overweight and obesity increased the incidence of AMI [22], another study showed that; an independent relationship between them. [23]

CONCLUSIONS

Fibrinogen level was significantly increased in myocardial infarction patients, also here were significant differences related to age group, smoking and weight , however PT, INR insignificantly increased in myocardial infarction patient and there were insignificant differences related to exercise.

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