Biochemical Markers And Risk Factors In Acute Myocardial Infarction

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Abstract

This study included 100 patients with myocardial infraction 77 were males and 23 were females with their mean age (58 ± 19 years). While the control groups consist of 45 subjects. They were chosen from medical staff and relatives who were free from signs and symptoms of coronary heart disease 38 were males and 7 were females, with their mean age (56±11 years old). Blood samples were taken from the patients 24 hours after attack and urine samples were collected from the patients in the 3rd day after attack. Blood and urine samples were gathered from the control groups for comparison. The results shows that creatine kinase , relative index micro albuminurea and serum uric acid found to be in high level compared with control as well as creatine kinase – MB . While the serum albumin found to be scientifically lower in its concentration .

الخلاصة

في هذه الدراسة تم اختيار مرضى احتشاء العضلة القلبية لغرض تقييم قياس فعالية انزيم الكرياتين كاينيز الكلي , حيث وجد بأن هنالك زيادة معنويةفي فعالية المتناظر الانزيمي CK-MB وكذلك المعامل النسبي في RI بالمقارنة مع الاصحاء وكذلك وجود زيادة معنويةبالنسة للاناث مما ادى الى وجود زيادة في المعامل النسبي وكذلك زيادة في تركيز حامض البوليك بالنسبة للذكور مقارنة بالاناث .

Introduction

Acute myocardial infarction (AMI) is defined as the death or necrosis of myocardial cells. It is a diagnosis at the end of the spectrum of myocardial ischemia or acute coronary syndromes (ACS). [1]

Critical myocardial ischemia may occur as a result of increased myocardial metabolic demand and/or decreased delivery of oxygen and nutrients to the myocardium via the coronary circulation. An

interruption in the supply of myocardial oxygen and nutrients occurs when a thrombus is superimposed on an ulcerated or unstable atherosclerotic plaque and results in coronary occlusion [2] .

A more common clinical diagnostic classification scheme is based on ECG findings as a means of distinguishing between two types of AMI—one that is marked by ST- segment elevation and one that is without ST-segment elevation(subendocardial infarction). The distinction between an ST-segment elevation AMI and a non-ST- segment elevation AMI also does not distinguish a transmutable from a non-transmutable AMI. The presence of Q waves or ST-segment elevation in ECG is associated with higher early mortality and morbidity; however, the absence of these two findings does not confer better long-term mortality and morbidity [3].

In Iraq ,some studies concerned with AMI provide some data and give an idea about this , In one study , the researcher finds that AMI is the second leading cause of death [4] .Some statistics in Kerbala city obtained from the cardiac care unite (CCU) show that 1800 patients per year admitted to the hospital are suffering from ACS(these data obtained directly from statistics of the CCU in AL Hussein general hospital

Most if not all risk factors that are related to atherosclerosis and cardiovascular morbidity and mortality , including traditional and non traditional risk factors , were also found to be associated with endothelial dysfunction. Endothelial dysfunction is systemic disorder and a critical element in the pathogenesis of atherosclerosis and its complication[5].

Diagnosis

Signs and symptoms

AMI may have unique presentations in individual patients. The degree of symptoms ranges from non at all to sudden cardiac death. An asymptomatic AMI is not necessarily less severe than a symptomatic event, but patients who experience asymptomatic AMI are more likely to be diabetic. Despite the diversity of presenting symptoms of AMI, there are some characteristic symptoms (Table 1):

Table(1) Signs and Symptoms of acute myocardial infarction

Chest pain described as a pressure sensation, fullness, or squeezing in the midportion of the thorax
Radiation of chest pain into the jaw/teeth, shoulder, arm, and/or back
Associated dyspnea or shortness of breath
Associated epigastria discomfort with or without nausea and vomiting
Associated diaphoresis or sweating Syncope or near-syncope
without other cause
Impairment of cognitive function without other cause

Markers of Cardiac Damage

Among patients admitted to the hospital with a chest syndrome, fewer than 20 percent are subsequently diagnosed as having an AMI. Therefore, in the majority of patients, clinicians must obtain serum cardiac marker measurements at periodic intervals to either establish diagnosis or be useful for a rough quantization of the size of infarction. The availability of new serum cardiac markers with markedly enhanced sensitivity for myocardial damage enables clinicians to diagnose AMI in about an additional one third of patients who would not have fulfilled[(6)] .

As myocytes become necrotic, the integrity of the sarcolemmal membrane is compromised and intracellular macromolecules (serum cardiac markers) begin to diffuse into the cardiac interstitial and ultimately into the microvasculature and lymphatic in the region of the infarction [(7)]. The rate of appearance of these macromolecules in the peripheral circulation depends on several factors, including intracellular location, molecular weight, local blood and lymphatic flow, and the rate of elimination from the blood . Time course of serum markers of AMI are listed in table (2) below [(8)].

Test	Onset	Peak	Duration
Total CK ,CK-MB	3-1 2 hours	18-24 hours	36-48 hours
Troponins	3-12 hours	18-24 hours	Up to 10 days
Myoglobin	1-4 hours	6-7 hours	24 hours
Total LDH	6-12 hours	24-48 hours	6 to 8 days
GOT	6-12 hours	20 - 30 hours	2 to 6 days

Table (2) : Time course of serum markers of AMI

Relative index

In attempt to confer more cardiac specificity to CK-MB, a relative index is used and calculated according to the following equation :-

Relative index (RI) = (CK-MB / total CK) 100%

For mass assay relative index value exceeding 2.5% is associated with myocardial sources of CK-MB, and for activity assay relative index varies but it usually in the range above 5% is associated with myocardial sources of CK-MB as shown in the following tables(3)[7]

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Table (3) Relative index in AMI by CK-MB Mass assay

Mass assay		
Interpretation	CK-MB ng/ml	RI %
AMI excluded	<4	<2
AMI probable	4-5	2-2.5
AMI ensured	>5	>2.5

Table (4) Relative index in AMI by CK-MB activity assay[7]

Activity assay		
Interpretation	CK-MB U/L	RI %
AMI excluded	<19	<0-4
AMI probable	19-20	4-5
AMI ensured	>20	>5

Microalbuminuria

Microalbuminuria (MA) is defined as elevated albumin excretion in urine more than 30 mg/day and of below 300 mg/day. These values less than the value detected by the urine dipstick testing for the protein which become positive until protein excretion in the urine exceed 500 mg/day which is considered as overt proteinuria. MA was less than detected by routine urine dipstick testing for proteinuria thus; the routine urine dipstick is insensitive marker for MA [9]

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Materials and Methods

Patients

This study was done in the department of medical biochemistry, college of medicine, Babylon University. The collection of samples was conducted during the period from (September 2004) to (may 2005). Of 122 patients were taken from cardiac care unite (CCU) in AL-Hussein general hospital in Kerbala .

Blood sample

Ten milliliters of venous blood were drawn from each patient about 24h after attack of AMI(i.e. attack of chest pain). Slow aspiration of the blood sample via the needle of syringe to prevent hemolysis and from veins of cubital fossa and tourniquet apply 15cm above. All the samples were grossly hemolysed, were neglected and another sample was taken to separate the serum for analysis which divided into two parts ,The first part 1.5ml of serum was kept in the eppendrof tube which is used for measuring total CK and CK-MB, and stored at -20 C° .

The second part of serum 1ml was kept in the eppendrof tube and stored at 2-8 C° which is used to measure serum albumin, uric acid and serum total cholesterol. Similarly the blood samples were taken from the control group.

Urine samples

The urine samples were taken from patients in the CCU during 2^{nd} and 3^{rd} day after attack of AMI(i.e. attack of chest pain). A 20 ml of newly 24-hours collected urine samples were taken from urine bag for those who were catheterized or from 24-hours urine container for those who were not catheterized Similarly the urine samples were taken from the control group_.

Chemicals

The chemicals and kits that were used in this study were of the highest purity and used without any further purification .

Methods

Total CK

Serum total CK was measured by using kit supplied from Randox com. England .

CK - MB

Serum uric acid and total cholesterol of performed by using kits, supplied by Linear copay (spain).

Urinary albumin

The method of measuring urinary albumin was performed according to the method described by Asad in Mousel University in which urinary albumin was measured from 24hours collected urine [10] .

Serum albumin

The method used was described by Gerhardt and waldenstron(1976) .

Biostatistics analysis

The biostatistics used in this study depended on (SPSS) and (Excel) programs and obtained an important significant statistical association were student T-test and chi-square . At the level of high significance (P value < 0.05) and very high significant (P value < 0.001) .

Results and Discussion

The groups in this study are divided into two groups, patients group and control group, and each group subdivided into males and females. The males in both groups were more in number and older in age than females . The following table (1) contains groups with their number male and female, male to female ratio, their age and age range.

Table (1) Subjects characteristics

Groups	Male no.	Female no.	Total	Male to Female ratio	Mean age ±SD year	Age range year
Patients	77	23	100	3.3: 1	58±19	31-83
Controls	38	7	45	5.4: 1	56±11	45-75
Total	115	30	145	3.8: 1		

The age distribution in AMI shows a peak level in the age between (51-60) years represented by 32 patients and the least was in the age group above (81) years represented by 3 patients. And in control group the highest number in the age between (51-60) years represented by 23 subjects and the least was in the age group (71-80) years represented by 3 subjects as shown in the following figure (1) .

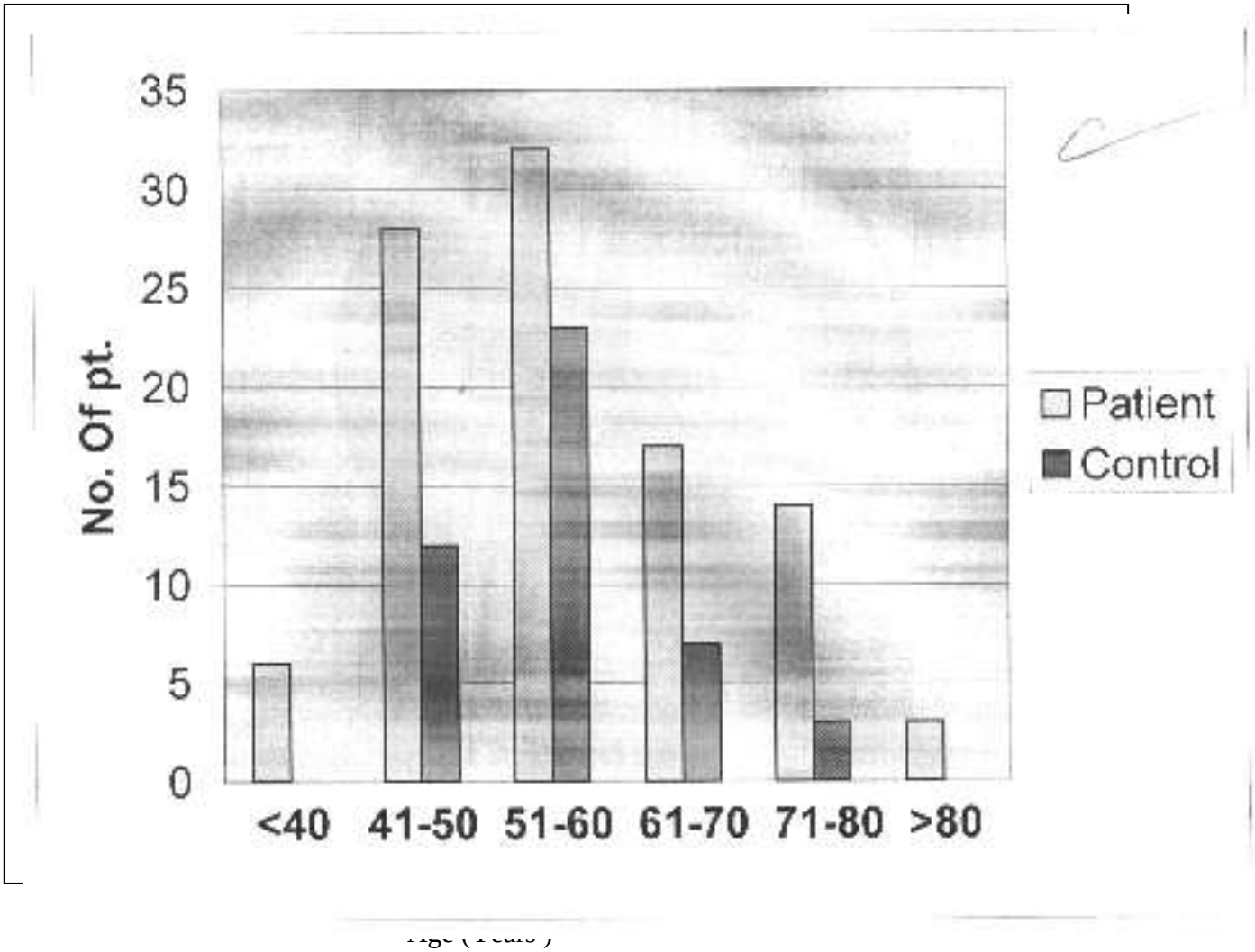

Figure (1) : Age distribution in AMI and control group .

Total CK activity

In this study the total CK activity measurement of the male patients (381 ± 138 U/L) and female patients (373.7 ± 139 U/L)found to be significantly very high when compared with control group(148 ± 46 U/L),(127.8 ± 14.3 U/L) for male and female respectively at the level of significantly($P<0.001$). Male patient has non significant higher activity compared with female patient ($P>0.05$), by student T test and Chi square. The sensitivity and specificity of total CK activity measurement for male and female (88.3%) (84.2%) (82.6%) (100%) respectively figure (2)

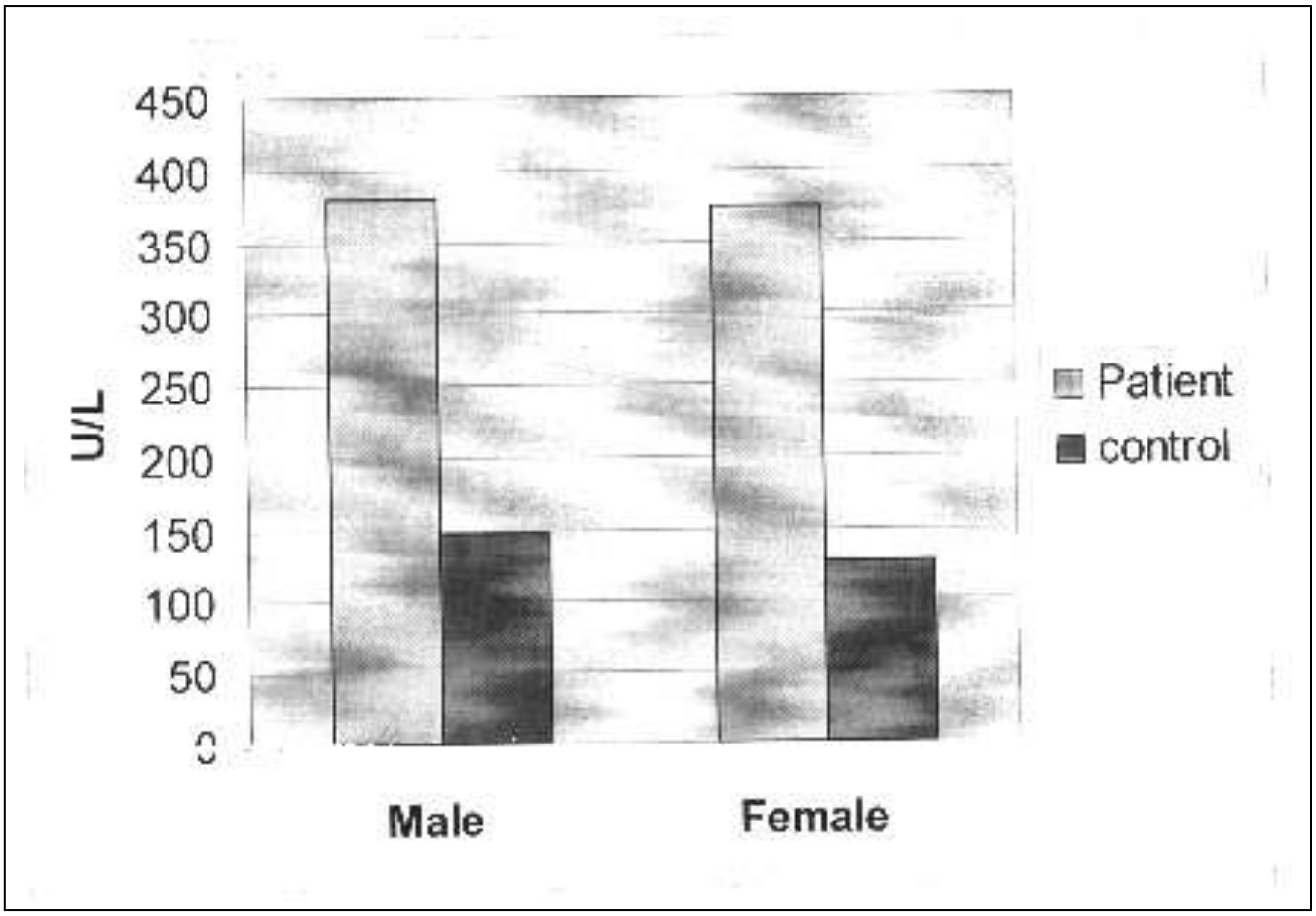

Figure (2) : Total CK activity among male and female in both groups .

CK-MB activity

In this study the CK-MB isoenzyme activity measurement for the male patients (39.8 ± 28.2 U/L) and female patients (32 ±19.8 U/L)found to be significantly very high when compared with control group (4.3 ± 2.8 U/L),(2.2 ± 1.1 U/L) for males and females respectively at the level of

significantly (P<0.001) ,Male patient has non significant higher activity compared with female patient (P>0.05) ,by student T test and Chi square as show in the figure (3)

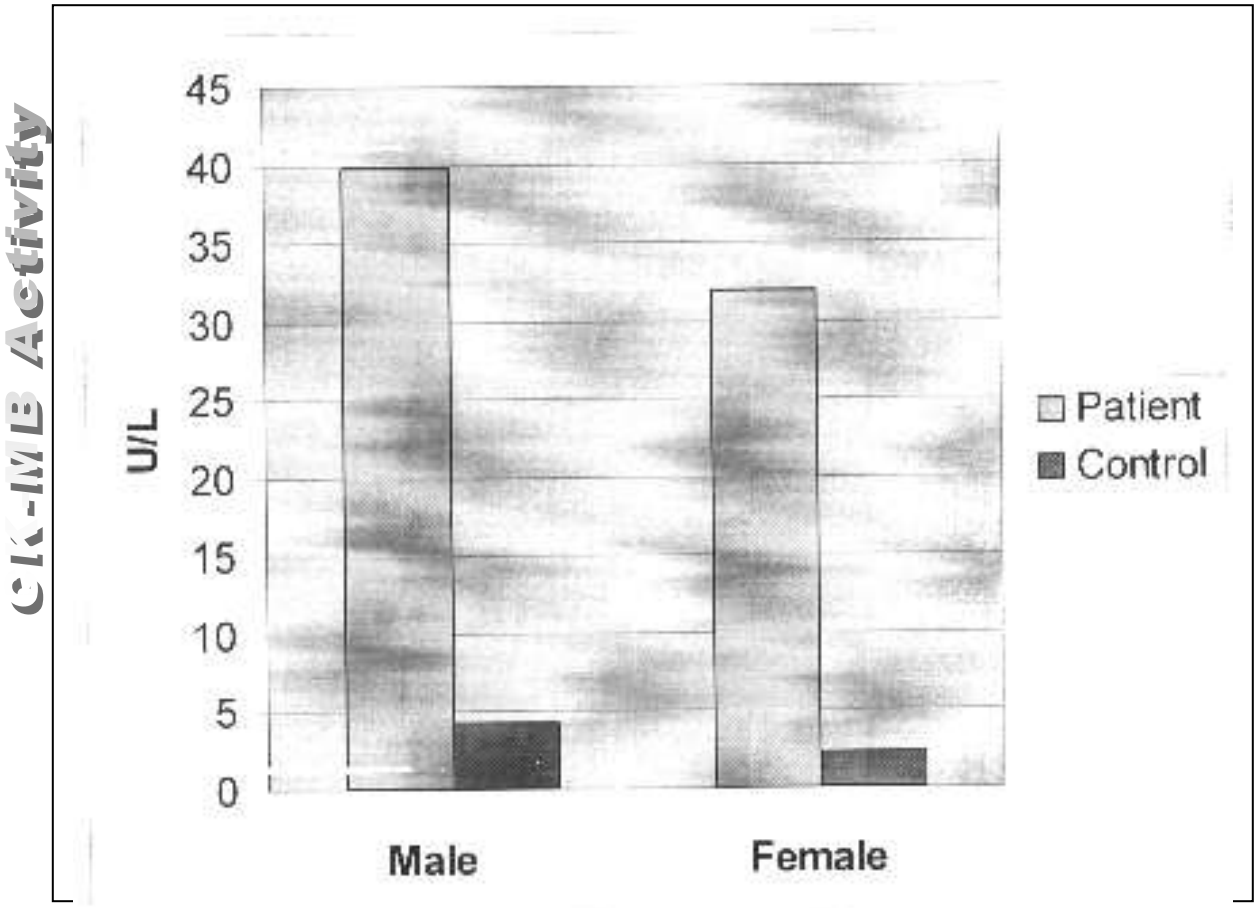

Figure (3) : CK-MB activity among male and female in both groups .

Relative index

Relative index(RI) was calculated by the following equation (CK-MB/ total CK) 100%.

In this study Rl for male patients (13.3 ± 8.3%)and female patients (12.9 ± 7.3%) ,lt was found to be significantly very high percentage when compared with males and females of control group (2.8 ± 2.5),(i.7 ± 0.9)respectively(p<0.001). Male patient has non significant higher percentage compared with female patient (P>0.05) ,by student T test and Chi square ,as shown in figure (4) . The sensitivity and specificity of Rl for male and female (96.3%) (99.2%) (95.2%) (100%) respectively.

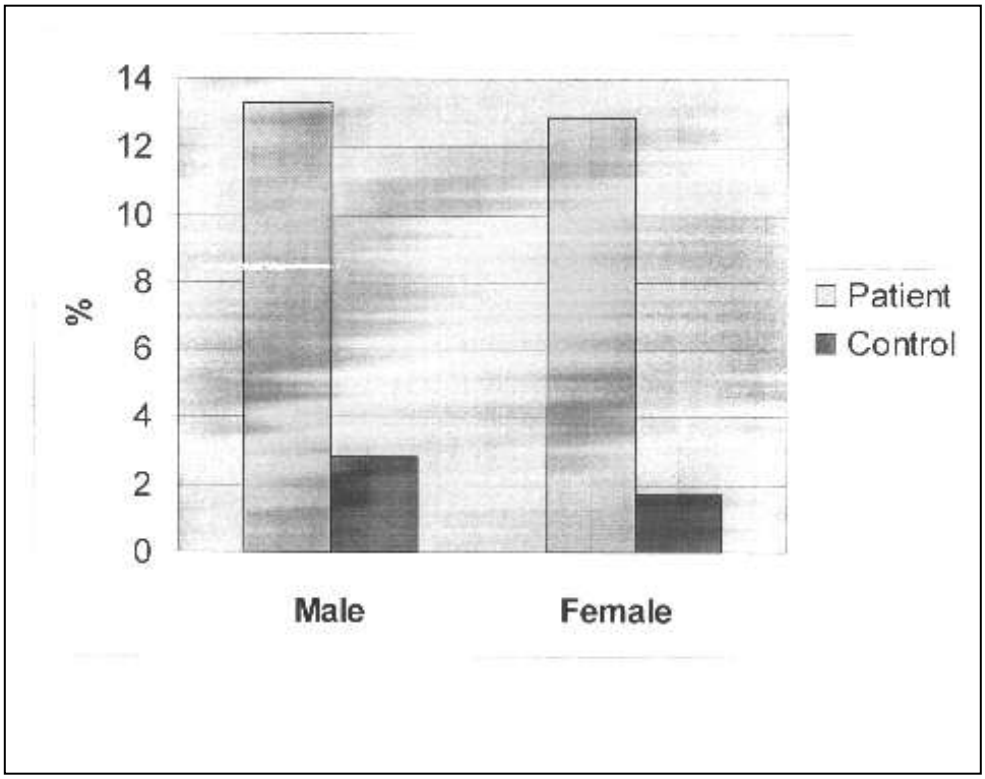

Figure (4) : Relative index among male and female in both groups .

Urinary albumin

In this study the urinary albumin measurement of the male patients(138 ± 89.3 mg/day) and female patients(142.9 ± 75.3 mg/day)found to be significantly high when compared with control group (23 ± 6 mg/day),(20 ± 5.1 mg/day) for males and females respectively at the level of significantly($P<0.05$). Female patient has non significant higher concentration compared with male patient ($P>0.05$) ,by student T test and Chi square as shown in the figure(5).

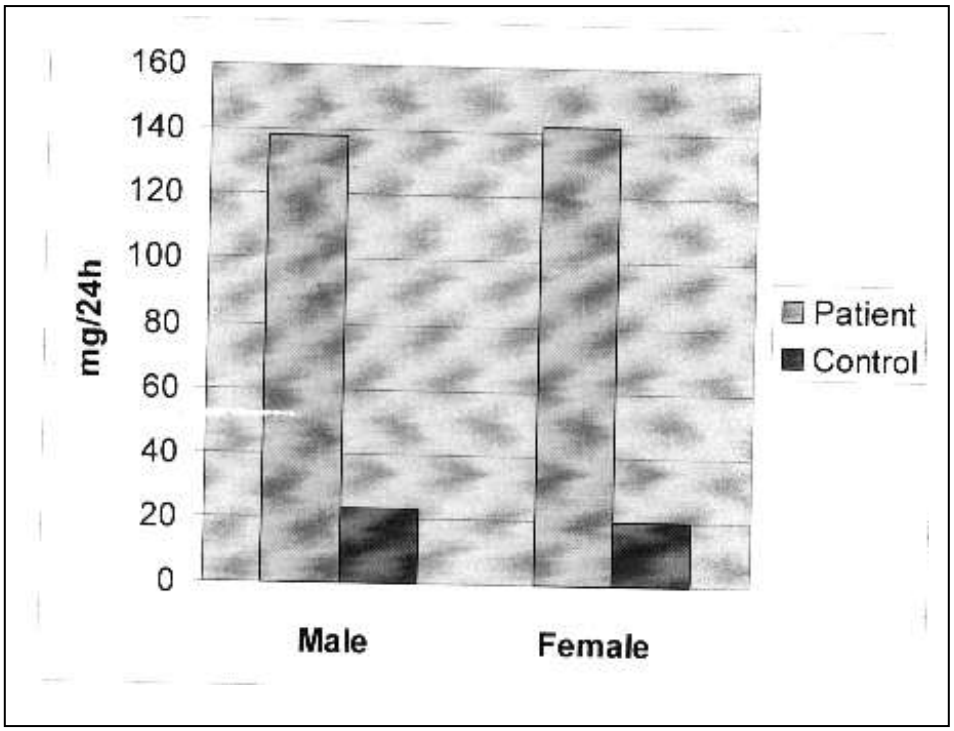

Figure (5) : Urinary albumin concentration among male and female in both groups .

Serum albumin

In this study the serum albumin concentration measurement of the male patients (3.2 ± 0.9 g/dl) and female patients (3.2 ±1 g/dl)found to be significantly low when compared with control group (4.2 ± 0.5 g/dl),(4.1 ± 0.9 g/dl) for male and female respectively at the level of significantly ($P<0.05$), No significant difference serum albumin concentration in male and female patient ($P>0.05$),by student T test and Chi square as shown in the figure (6) .

Albumin Con.

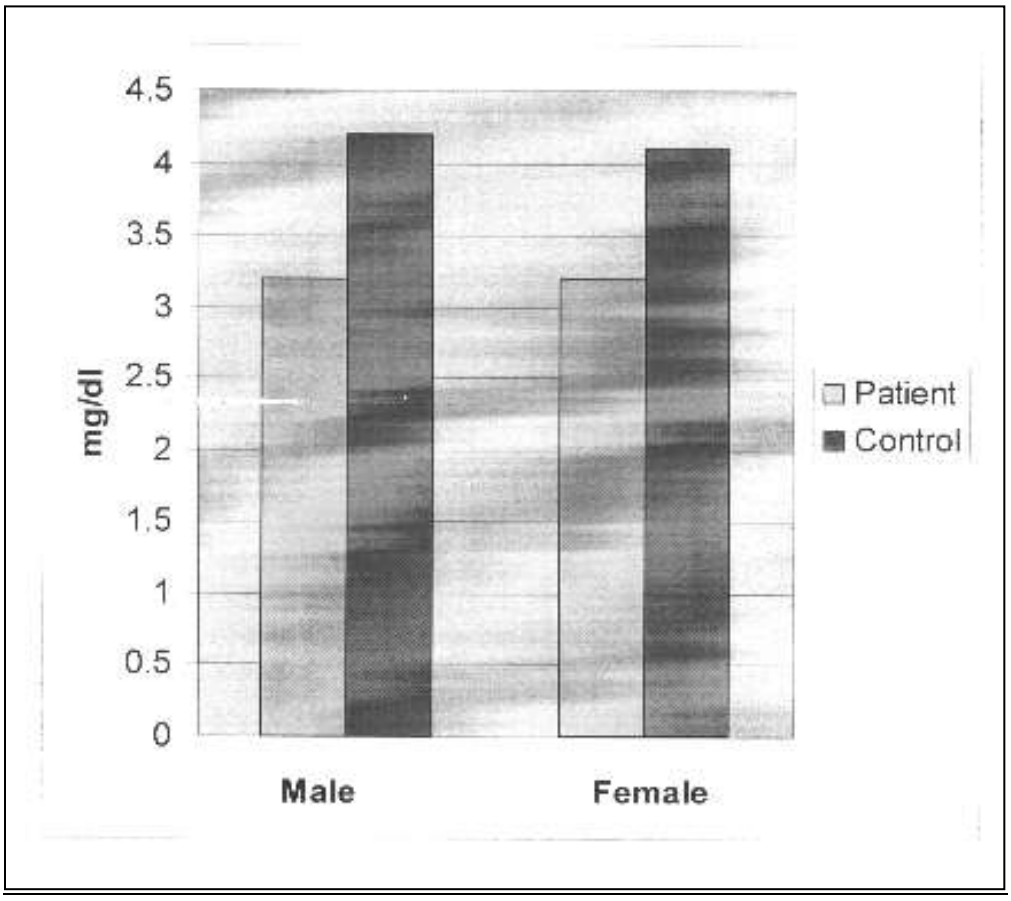

Figure (6) : Serum albumin concentration among male and female in both groups .

Serum uric acid

In this study the serum uric acid concentration measurement of the male patients (6.9 ± 1.7 mg/dl) and female patients (6.7 ± 1.7 mg/dl)found to be significantly high when compared with control

group (4.9 ± 2.2 mg/dl),(4.2 ± 1.6 mg/dl) for males and females respectively at the level of significantly (P<0.05) ,Male patient has non significant higher concentration compared with female patient (P>0.05) ,by student T test and Chi square as shown in the figure(7) .

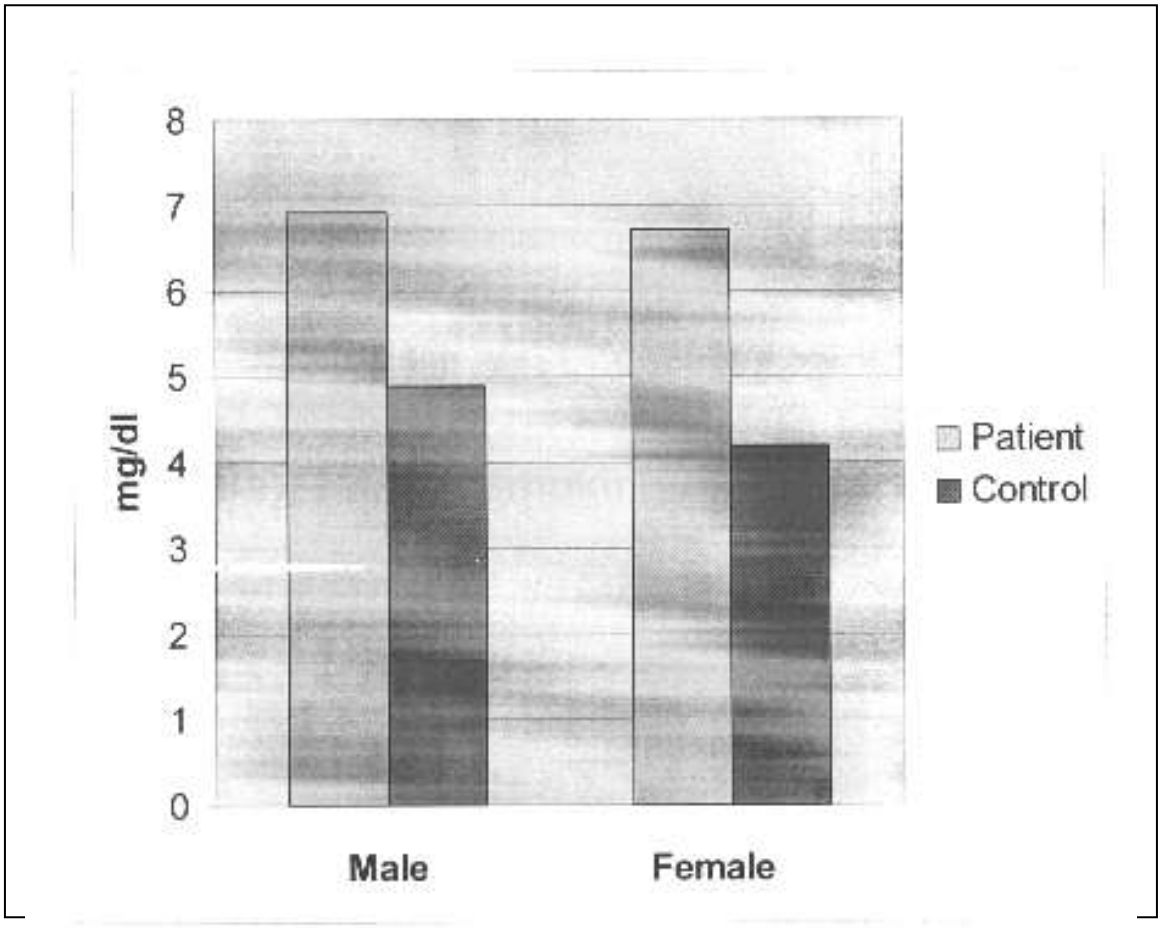

Figure (7) : Serum uric acid concentration between male and female in both groups .

Total CK, CK - MB, relative index

In this study , total CK activity found to be increasing during AMI but this increment is

neither sensitive nor specific for AMI, this increment is due to the injury of cardiac muscle with rupture of cell membrane and the release of it's cytoplasmic proteins which include (GOT, CK,LD!!), The poor circulation in the ischemic area which results in gradual clearance of these proteins (mainly by lymphatic system), and gradual increase in circulating these proteins lead to the elevation beyond the reference range within (4-12hours) after AMI ,and this contributed to the CK-MB isoenzyme [11].

Elevated total CK activity can be assumed to be due to CK-MM isoenzyme which obtained from skeletal muscle damage, except in AMI and sever unstable angina in which elevated total CK activity assumed to be due to CK-MB and partially CK-MM isoenzyme [11].

AMI diagnosis can not be based on the total CK only because of high negative and positive predictive value as the increment of total CK is not more than 2 to 3 folds in small infarction and in the patients with low muscle mass [12].

To get the true diagnosis of AMI, small elevation of CK-MB isoenzyme accompanied by relative index value more than 5% give confirmative diagnosis of AMI[13].

The main objective for the use of the CK-MB in this study is to establish the diagnosis of AMI in the suspected cases CK-MB isoenzyme found to be more sensitive and specific indicator for AMI , Milzman,etal , show that at 0-4 hours after AMI , CK-MB isoenzyme activity sensitivity and specificity (58.9%) (90.5%) and after 24 hours (92%) (95.3%) respectively, and this is consistent with our results[14].

Urinary albumin excretion.

The urinary albumin excretion in this study has non significant difference between males and females, in which female patients with AMI show higher urinary albumin than male patients, and this finding agree with Gosling P. in which he found albumin excretion was slightly higher in women than the men and don't give an explanation for this result[15]and our finding in contrast with which they found that prevalence of microallbuminuria was one fold higher in males than females, and this is explained by the vasculature more sensitive in males to give risk factor than in female, and increase urinary albumin excretion is considered as a marker of damage of vascular endothelium . microalbuminuria as very early stage of diabetic nephropathy[16].

If urinary albumin excretion begins to increase late in the atherosclerotic process ,microalbuminurea may be a marker of prevalent sub clinical atherosclerosis as suggested [17]. And if urinary albumin excretion is already increased early in the atherosclerosis process, microalbuminurea may reflect an endothelial dysfunction and perhaps an augment atherogenic susceptibility to other risk factors [18] .

Serum albumin concentration.

It was found that lower serum albumin concentration is associated with an increased risk for AMI among both sexes . This finding has been suggested that the relation between serum albumin and ischemic heart disease may vary across sex age and level of serum cholesterol[19], Corti and Colleagues found an association between serum albumin and ischemic heart disease among older women but not older men [20].

Our finding shows that no significant difference in serum albumin Concentration between women and men [21].In the NHANEST study Gillum and Makuc reported an increased risk of IHD and cerebral stroke increased with low serum albumin concentration [22] [23]. LUC Djousse found that patient with AMI and low serum albumin concentration not have causal role for IHD but could be an indicator of an underlying other disorders[24].

Serum uric acid.

Serum uric acid found to be higher in the females but it is within upper normal limit in the males with AMI , several studies have demonstrated the mechanism by which uric acid could be directly injurious to the endothelium and cardiovascular function [24][25] and these micro injuries caused accumulation of platelets in the sites of these micro injuries which may lead to form very small clots, others studies show that raised serum uric acid concentration in both male and female are powerful predicator for CVS risk but the mechanism remained unclear [26] Kojima suggests that hyperuricemia after AMI is associated with the development of heart failure. Serum uric acid level is a suitable marker for predicating AMI-related future adverse events, and the
combination of Killip's class and serum uric acid level after AMI is a good predicator of mortality in patients who have AMI[27].

Risk factors.

In this study we found that AMI occur at older age and in the males more than younger age and females , these findings related to the rate of development of atherosclerosis , which appear in the patient who have susceptibility of atherosclerosis in early life but become clinical significant when patient become older age [28].

The reason why atherosclerosis is more in males, is that females have a protective mechanism against atherosclerosis due to the effect of estrogen hormone and after menopause women loss this

effect so atherosclerosis developed and took long time to become clinically significant in compares with corresponding males in same age[29] .

The smoking had adverse effects on the coronary arteries which causes the following:-

1. Decrease HDL.
2. Increase LDL.
3. Vasoconstriction.
4. Increase fibrinogen, and clot formation. So the smoking had direct effect in the development of AMI [30].

Hypertension shows important association with AMI in our study in agreement with Gaze that show direct association of systolic and diastolic hypertension with AMI [29].

Family history of ischemic heart disease is significantly low with AMI and this is in contrast with Gamm , who found that atherosclerosis runs in members of the same family especially in first degree relatives , Some conditions are directly inherited such as familial hypercholesterolemia and familial combined Hyperlipidemia [29] .

Hypercholesterolemia has significant association with AMI as it has strong association with atherosclerosis that lead to AMI[30].

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