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The Relation between Serum Uric Acid and Liver Function Test in Patients with Acute Coronary Syndrome in Tikrit Teaching Hospital

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Abstract

Introduction
Acute coronary syndrome is a term that compasses both unstable angina and myocardial infarction. Acute coronary syndrome may present as new phenomenon or against the back ground of chronic stable angina.
The aim:
To determine the frequency of hyperuricemia and abnormal liver enzymes in patients with acute coronary syndrome (ACS).
Patients & Methods
Cross sectional study has been done at the coronary care unit (CCU) and laboratory department in Tikrit Teaching Hospital, during the period from October 2013 to June 2014.The study was carried out on 100 patients selected randomly.
The patients were divided into four major groups according to their age. The patients were diagnosed by ECG, cardiac enzymes and clinical history and diagnosis. Blood samples were drawn from all patients and sent to the laboratory for liver enzymes, serum uric acid, serum albumin, fasting blood sugar, blood urea and serum creatinine.
Results
The present study founded that 80% of ACS patients have normal aminotransferase enzyme levels and ALP levels (no significant difference between the two enzymes).
Also our present study founded that 85% of ACS patients are having a normal uric acid level . the peak age frequency of ACS was between 51-70 years with higher frequency in males than females.
Conclusion
Aminotransferases (AST and ALT), ALP, S.albumin and S.uric acid are normal in the majority of patients with ACS, moreover the frequency of ACS is higher in males than females.

Keywords: Acute coronary syndrome, coronary care unit, Blood samples, ACS patients.

Introduction And Literature Review

Acute coronary syndrome is a term that compasses both unstable angina and myocardial infarction. Acute coronary syndrome may present as new phenomenon or against the back ground of chronic stable angina. This is dynamic process whereby the degree of obstruction either increase leading to complete vessel occlusion or regress by endogenous fibrinolysis.[1]

In unstable angina there is no detectable rise in cardiac enzyme and the initial diagnosis depend on clinical history and ECG. In contrast, myocardial infarction causes arise in the plasma concentration of enzymes and protein that are normally concentrated inside cardiac cells.[2]

Hyperuricemia is related to increased free radicals, stimulates inflammation and produces endothelial dysfunction.[3]

Most patients with acute coronary syndrome will need statins at high doses. The most frequent side effects related to the use of statins is myopathy, and rhabdomyolysis, but increased levels of transaminases are unusual.[4]

1.1- Heart structure :

The heart has four chambers through which the blood is pumped. The upper two are the right and left atria figure (1-1). The lower two are the right and left ventricles. Four valves are open and closed to let blood flow in only one direction when the heart beats:[5]

1. Tricuspid valve is between the right atrium and right ventricle.
2. The pulmonary valve is between the right ventricle and the pulmonary artery.
3. The mitral valve is between the left atrium and the left ventricle.
4. The aortic valve is between the left ventricle and the aorta.

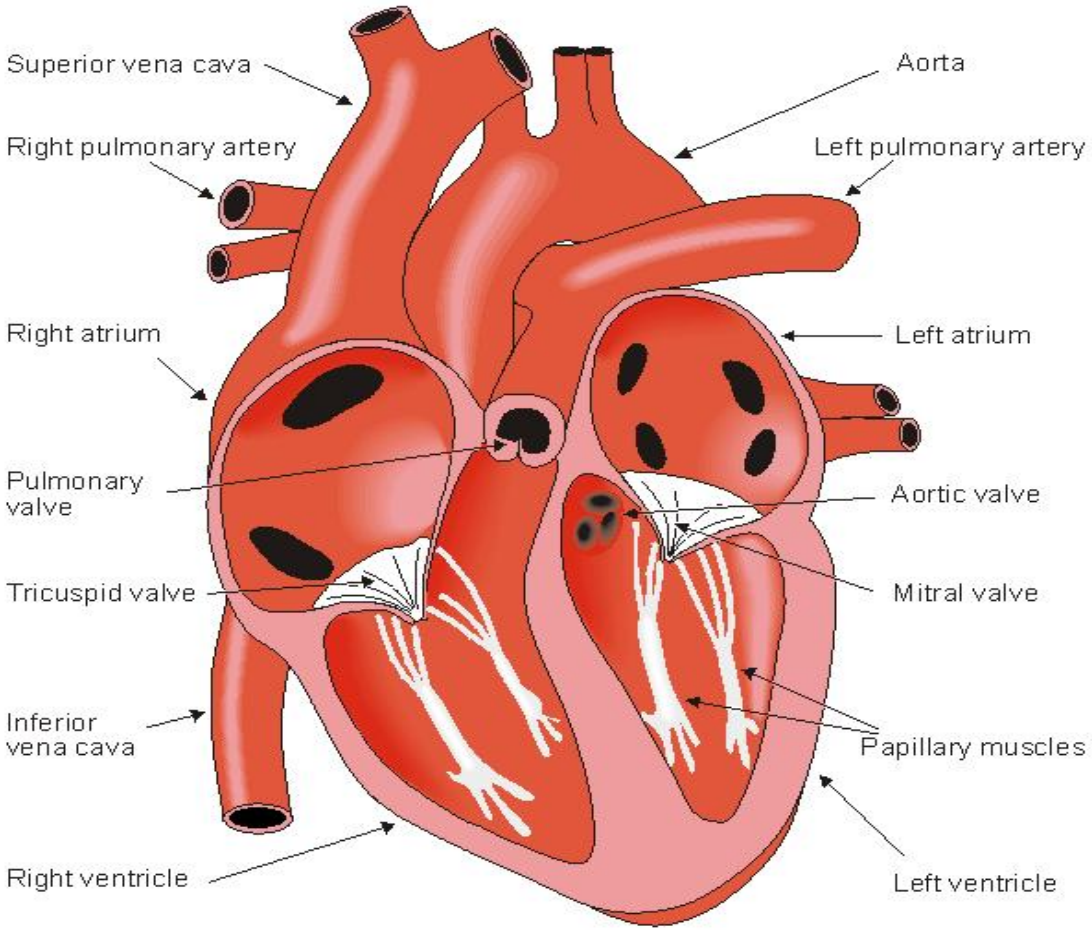

Figure (1-1): Structure of the heart[4]

1.2- Coronary circulation:

Figure (1-2) show the coronary circulation. The main left and right coronary arteries arise from the left and right coronary sinuses of the aortic root, distal to the aortic valve. Within 2.5 cm of its origin, the left main coronary artery divides into the left anterior descending artery (LAD) and the left circumflex artery (CX). The LAD gives branches to supply the anterior part of the septum (septal perforators) and the anterior, lateral and apical walls of the LV. The CX gives marginal branches that supply the lateral, posterior and inferior segments of the LV. The RCA gives branches which supply the RV, RA and the inferoposterior aspects of the LV. The posterior descending artery supplies the inferior part of the interventricular septum. This artery is a branch of the RCA in 90% of people(dominant right system) and is supplied by the CX in the remainder (dominant left system).The RCA supplies the SA node in 60% of individuals and the AV node in about 90%.[5,6]

The venous follows the coronary arteries drains into the coronary sinus in the Atrio-ventricular groove, and then to the RA. An extensive lymphatic system drains into vessels that travel with the coronary vessels and then into the thoracic duct. [1- 4]

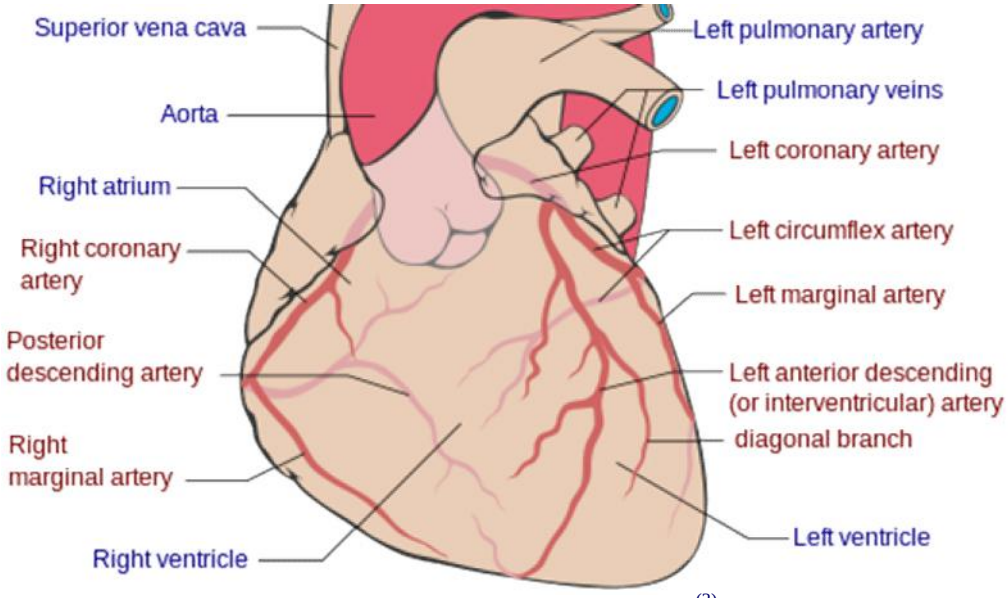

Figure (1-2) coronary circulation[3]

1.3- Atherosclerosis:

A name comes from the Greek words athero (meaning gruel or paste) and sclerosis (hardness). It involves deposits of fatty substances, cholesterol, cellular waste products, calcium and other substances in the inner lining of an artery. This buildup is called plaque. It usually affects large and medium sized arteries.[1- 5]

Atherosclerosis is a slow, complex disease that starts in childhood and often progresses when people grow older. In some people it progresses rapidly, even in their thirties. It's due to damage to the inner layer of the artery, which called the endothelium.[6, 7]

Three proven causes of damage to the arterial wall are: [8,9]

1. Elevated levels of cholesterol and triglycerides.
2. High blood pressure.
3. Tobacco smoke.

Deposition of fats, cholesterol, platelets, cellular debris, calcium and other substances in the arterial wall, these may stimulate artery wall to produce other substances that result in further buildup of cells. The arterial diameter shrinks and blood flow decreases, reducing the oxygen supply or diminished leading to coronary ischemic events.[6-10]

1.4- Acute coronary syndrome:

Patient with ischemic heart disease fall into to large groups: patients with chronic coronary artery disease (CAD) who most commonly present with stable angina and patients with acute coronary syndrome (ACS).[9]

Acute coronary syndrome may present as a new phenomenon or against the background of chronic stable angina. The culprit lesion is usually a complex ulcerated or fissured athermatous plaque with adherent platelet rich thrombus and local coronary artery spasm. This is a dynamic process whereby the degree of obstruction may either increase, leading to complete vessel occlusion, or regress due to the effect of platelet disaggregation and endogenous fibrinolysis.[9,10]

In acute MI , occlusive thrombus is almost always at the site of rupture or erosion of an athermanous plaque.[10]

1.4.1- Clinical features:

Pain is the cardinal symptoms of an acute coronary syndrome but breathlessness, vomiting, and collapse are common features. The pain occurs in the same sites as angina but is usually more severe and lasts longer; it is often described as a tightness , heaviness or construction in the chest. Most patients are breathless and in some this is the only symptom. Indeed, MI may pass unrecognized. Painless or silent MI is particularly common in older patient or those with diabetes mellitus.

If syncope occurs, it is usually due to arrhythmia or profound hypotension. Vomiting and sinus bradycardia are often due to vagal stimulation and are particularly common in patients with acute inferior MI. Sudden death from ventricular fibrilation or a systole may occur immediately and often within the first hour. If the patient survive this most critical stage, the liability to dangerous arrhythmias remain but diminishes as each hour goes by.[1]

1.4.2- Diagnosis of acute coronary syndrome:

The assessment of acute chest pain depend heavily on an analysis of the character of the pain and its associated features, evaluation of ECG, and serial measurements of biochemical markers of cardiac damage, such as troponin I and T. patients with ST segment elevation or new bundle branch block require emergency reperfusion therapy. In patients with acute coronary syndrome without ST segment elevation, the ECG may show transient or persistent ST/T wave changes including ST segment depression and T – wave inversion. Evaluation of people with chest discomfort and potentially life-threatening heart problem commonly includes four steps:[11,12]

1) Clinical assessment by history, including risk factors for atherosclerosis.
2) Physical examination: general and specific systematic.
3) Electrocardiogram (ECG) to look for abnormalities caused by damage to the heart as in figures (1-3), (1-4), (1-5).
4) Blood tests to detect abnormal levels of certain enzymes in the blood stream, which well known as "cardiac markers" and many recent studies suggest further added enzymatic assessment.

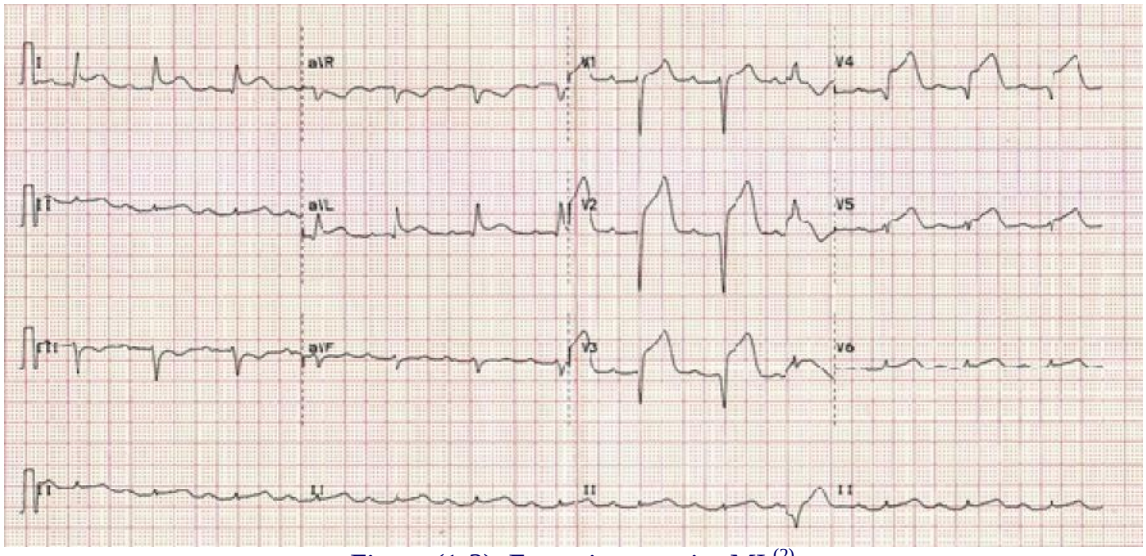

Figure (1-3): Extensive anterior MI.[2]

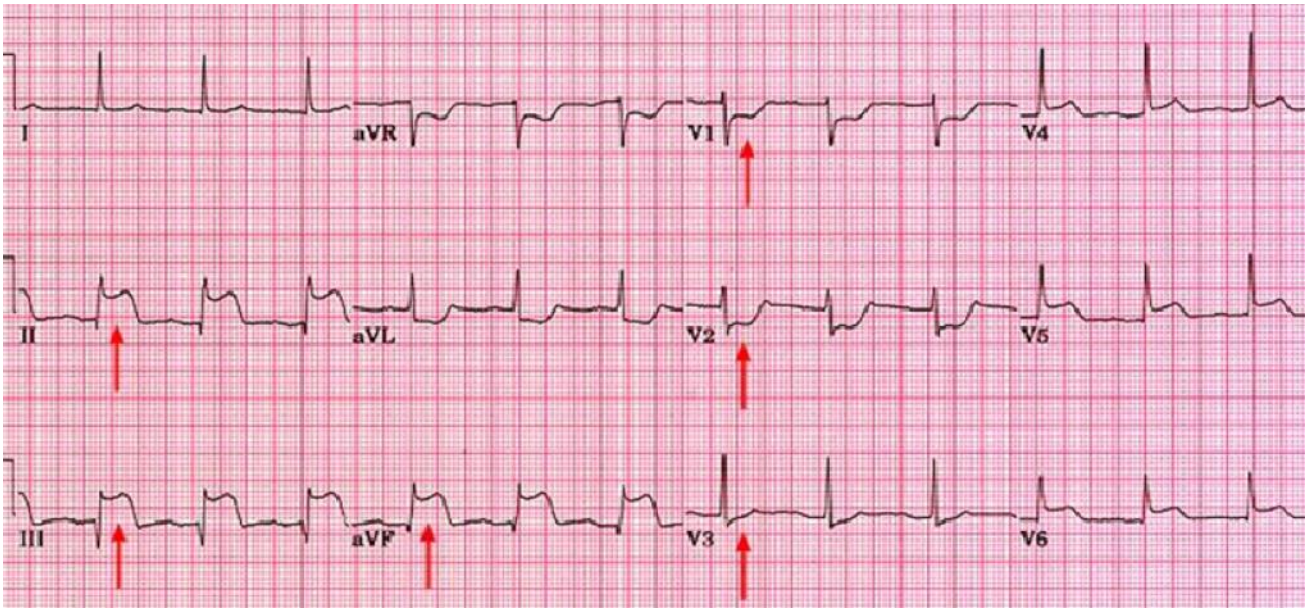

Figure (1-4): Inferior MI.[2]

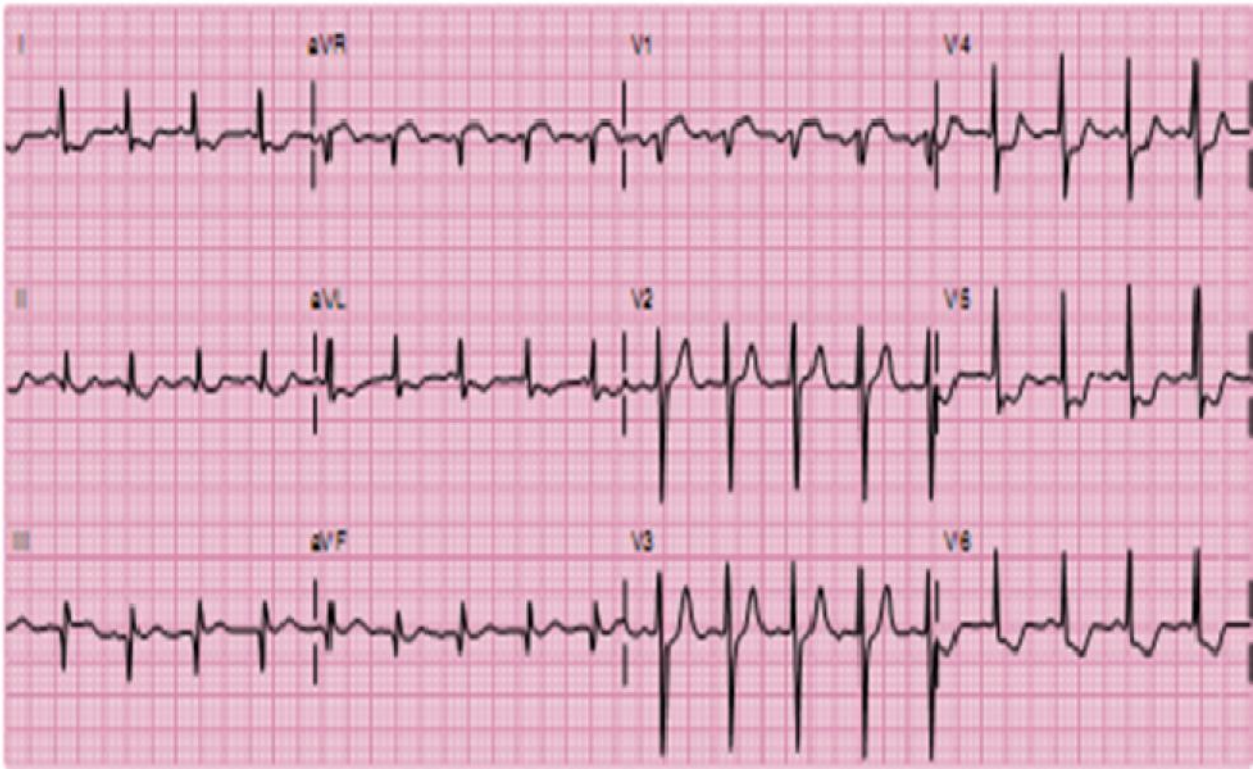

Figure (1-5): Unstable angina with previous inferior MI[2]

The plasma cardiac markers are creatine kinase (CK), a more sensitive and cardiospecific isoform of this enzyme (CK-MB), and the cardiospecific protein troponins T and I. admission and serial estimation are helpful because it is the change in plasma concentrations of these markers that confirm the diagnosis of acute MI.

CK start to rise at 4-6 hours, peaks at about 12 hours and fall to normal within 48-72 hours. CK also present in skeletal muscle and a modest rise in CK (but not CK-MB) may sometimes be due to an intramuscular injection, vigorous exercise or, a fall particularly in older people.[13,14]

The most sensitive markers of myocardial cell damage are the cardiac troponin T and I, which are released within 4-6 hours and remain elevated for up to 2 weeks.[1]

Other blood tests include leucocytosis is usual, reach a peak on the first day. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are also elevated.[13]

1.4.3- Management of acute coronary syndrome:

1 - Analgesia;

Intravenous opiates (initially morphine sulphate 10 mg or diamorphine 5mg and antiemetic (initially cyclizine 50mg or prochlorperazine 12.5mg) should be administered through an IV cannula and titrated against the response by giving repeated small aliquots until the patient is comfortable. Intra muscular injection should be avoided because the clinical effect may be delayed by poor skeletal muscle perfusion, and a painful hematoma may form following thrombolytic or anti-thrombotic therapy.[1]

2- Antithrombotic therapy:

2-1- Antiplatelet therapy: oral administration of 75-300mg aspirin daily improve survival, with 25% relative risk reduction in mortality. The first tablet (300mg) should be given orally within 12 hours and the therapy should be continued if there is no side effect. In combination with aspirin , the early (within 12 hours) use of clopidogrel 600mg, followed by 150mg daily for 1 week and 75mg daily thereafter confers further reduction in ischemic events.[1]

2-2- Anticoagulants: Reduces the risk of thromboembolic complication, and prevent reinfarction in the absence of reperfusion therapy or after successful thrombolysis.

Anticoagulant can be achieved using unfractionated heparin, fractioned (low molecular weight) heparin or a pentasaccharide. Comparative clinical trials suggest that the pentasaccharides (subcutaneous fondaparinux 2.5mg daily) have best safety and efficacy profile, with low molecular weight heparin (subcutaneous enoxaparin 1mg/kg 12-hourly) being a reasonable alternative.[1]

Anticoagulant should be continued for 8 days or until discharge from hospital or coronary revascularization.[1,11]

3- anti-anginal therapy:

Sublingual glyceryl trinitrate (300-500 µg) is a valuable first aid measure in unstable angina or threatened infarction, and IV nitrate (GTN 0.6-1.2 mg/hour or isosorbide dinitrate 1-2mg/hour) are useful for the treatment of left ventricular failure and relief of recurrent or persistent ischemic pain.

Intravenous B-blockers (eg. atenolol 5-10mg or metoprolol 5-15mg given over 5mins) relieve pain, reduce arrhythmias and short term mortality in patient who present within 12 hours of onset of symptoms. They should be avoided if there is heart failure (pulmonary oedema), hypotension (systole BP <105mmhg) or bradycardia (heart rate < 65/min).

A dihydropyridine calcium channel antagonist (eg. Nifedipine or amilodipine) can be added to the B-blocker if there is persistent chest discomfort but may cause an unwanted tachycardia if used alone. Because of their rate –limiting action, verapamil and diltiazem are the calcium channel antagonist of choice if a B-blocker is contraindicated.[1]

4- Reperfusion therapy:

Non-ST segment elevation acute coronary syndrome:

Immediate emergency reperfusion therapy has no demonstrable benefit in patients with non-ST segment elevation MI and thrombolytic therapy may be harmful. Selected medium to high risk patients do benefit from in hospital coronary angiography and coronary revascularization but this does not need to take place in the 12 hours.[1]

ST segment elevation acute coronary syndrome:

Immediate reperfusion therapy restore coronary artery patency, preserve left ventricular function and improve survival. Successful therapy is associated with pain relief, resolution of acute ST elevation and sometimes transient arrhythmias (eg. Idioventricular rhythm).[3]

Primary percutaneous coronary intervention:

This is the treatment of choice for ST segment elevation MI. it is used in combination with glycoprotein IIb/IIIa receptor antagonist and

intracoronary stent implantation. In comparison to thrombolytic therapy, it is associated with a greater reduction in the risk of death, recurrent MI or stroke. Intravenous thrombolytic therapy remain the first line reperfusion treatment in many hospital, especially those in rural or remote area. When primary PCI cannot be achieved within 2 hours of diagnosis, thrombolytic therapy should be administered.(11)

Thrombolysis:

The appropriate use of thrombolytic therapy can reduce hospital mortality by 25-50% and this survival advantage is maintained for at least 10 years. The benefit is greatest in those patients who receive treatment within the first few hours (minutes mean muscle).

Alteplase (human tissue plasminogen activator or tPA) is a genetically engineering drug that is given over 90 minutes (bolus dose of 15mg, followed by 0.75mg/kg but not exceeding 50mg over 30 minutes and then 0.5mg/kg but not exceeding 35mg over 60 minutes).(1)

Its use is associated with better survival rates than other thrombolytic agents, such as streptokinase, but carries a slightly higher risk of intracerebral bleeding (10 per 1000 increased survival, but 1 per 1000 more non- fatal stroke).(11)

An overview of all the large randomized trials confirm that thrombolytic therapy reduces short term mortality in patients with acute MI if it given within 12 hours of the onset of symptoms and the ECG shows bundle branch block or characteristic ST segment elevation more than 1mm in the limb leads or 2mm in the chest leads. Thrombolytic therapy appear to be of little net benefit and may be harmful in those who present more than 12 hours after the onset of symptoms and in those with a normal ECG or ST depression.(11,12)

For some patients, thrombolytic therapy is contraindicated or fails to achieve coronary artery reperfusion. Early emergency PCI may be considered particularly where there is evidence of cardiogenic shock.(11)

1.4.4- Complication of acute coronary syndrome:

1- rrhythmias : many patients with acute coronary syndrome have some form of arrhythmia, in the majority of cases this is transient and of no hemodynamic or prognostic importance. Pain relief,

2- rest and the correction of hypokalaemia may help prevent them.(1)

Common arrhythmias in acute coronary syndrome are ventricular fibrillation, atrial fibrillation , ventricular tachycardia, atrial tachycardia, accelerated idioventricular rhythm, sinus bradycardia, ventricular ectopics, and atrioventricular block.(1,14)

2- Ischemia : patient who develop recurrent angina at rest or on minimal exertion following an acute coronary syndrome are at high risk and should be considered for prompt coronary angiography with a view to revascularization. (1,11,)

3- Acute circulatory failure: acute circulatory failure usually reflect extensive myocardial damage and indicates a bad prognosis. (1)

4- Pericarditis: this is only occur following infarction and is particularly on the second and third days. The patient may recognize that a different pain has developed, even it is at the same site, and that it is positional and tend to be worse or sometime only present on inspiration. A pericardial rub may be audible. Opiate based analgesia should be used. Post MI syndrome (Dressler's syndrome) is characterized by persistent fever, pericarditis and pleurisy, and is probably due to autoimmunity. The symptoms tend to occur a few weeks or even months after the infarct, prolonged or severe symptoms may require treatment with high dose aspirin, NSAIDs or even steroid. (1,11)

5- Mechanical complications: part of necrotic muscle in a fresh infarct may tear or rupture, with devastating consequences:

- Rupture of the papillary muscle can cause acute pulmonary oedema and shock due to the sudden onset of severe mitral regurgitation. The diagnosis is confirmed by echocardiography and emergency mitral valve replacement may be necessary.

- Rupture of interventricular septum cause left to right shunting through a ventricular septal defect. This usually presents with sudden haemodynamic deterioration accompanied by anew loud pansystolic murmur radiating to the right sternal border, but may be difficult to distinguish from acute mitral regurgitation. Doppler echocardiography and right heart catheterization will confirm the diagnosis. (1,9)

- Rupture of the ventricle may lead to cardiac tamponade and is usually fatal.

6- Embolism: thrombus often forms on the endocardial surface of the freshly infarct myocardium. This can lead to systemic embolism and occasionally causes a stroke or ischemic limb. [3,11]

7- Impaired ventricular function, remodeling and ventricular aneurysm:

Acute transmural MI is often followed by thinning and stretching of infarct segment (infarct expansion), this leads to increase in wall stress with progressive dilatation and hypertrophy of the remaining ventricle (ventricular remodelling). Infarct expansion occurs over a few days and weeks but ventricular remodelling can take years. ACE inhibitor therapy reduces late ventricular remodelling and can prevent the onset of heart failure. [1,3]

A left ventricular aneurysm develops in approximately 10% of patients with MI and particularly common when there is persistent occlusion of the infarct related vessel. Heart failure, ventricular arrhythmias, mural thrombus and systemic embolism are all recognized complications of aneurysm formation. Other clinical features include a paradoxical impulse on the chest wall, persistent ST elevation on the ECG, and sometimes an unusual bulge the cardiac silhouette on the chest X-ray. Echocardiography is usually diagnostic. Surgical removal of the left ventricular aneurysm carries a high morbidity and mortality but is sometimes necessary.[1,13]

1.5- Liver function tests:

Liver function tests include the measurement of serum bilirubin, aminotransferases, alkaline phosphatase, gamma-glutamyl transferase and albumin. Although abnormalities on LFTs are often non specific, the pattern are frequently helpful in directing further investigations. Also level of bilirubin, albumin and the prothrombin are related to clinical outcome in patients with severe liver disease reflected by there use in several prognostic score: the Child-Pugh and MELD score in cirrhosis, the Maddrey score in alcoholic hepatitis and the king`s college hospital criteria for liver transplantation in acute liver failure.[1]

1.5.1- Bilirubin :

The degree of elevation of bilirubin reflects the degree of liver damage. Bilirubin , a breakdown product of the porphyrin ring of heme- containing protein, is found in the blood in two fraction- conjugated and unconjugated. The unconjugated fraction also termed the indirect fraction, is insoluble in water and is bound to albumin in the blood. The conjugated (direct) bilirubin fraction is water soluble and can therefore be excreted by kidney. When measured by the original Van den Bergh method, the normal total serum bilirubin concentration is less than 17 µmol/L. up to 30% or 5.1 µmol/L of total is direct-reacting (conjugated) bilirubin.

Elevation of the unconjugated fraction of bilirubin is rarely due to liver disease. An isolated elevation of unconjugated bilirubin is seen primarily in hemolytic disorders and in a number of genetic conditions. [11]

1.5.2- Albumin:

Albumin is synthesized exclusively by hepatocytes. Serum albumin has along half life : 18-20 days with ~4% degraded per day. Because this slow turnover, the serum albumin is not a good indicator of acute or mild hepatic dysfunction. Only minimal changes in the serum albumin are seen in acute liver conditions such as viral hepatitis, drug related hepatotoxicity and obstructive jaundice. In hepatitis , albumin level less than 3 g/L should be raised the possibility of chronic liver disease. Hypoalbuminemia is more common in chronic liver disorders such as cirrhosis and usually reflect severe liver damage and decreased albumin synthesis. One exception is the patient with ascites in whom the synthesis may be normal or even increased, but level are low because of increased volume of distribution. [3]

1.5.3- Serum enzymes:

Serum enzyme tests can be grouped in to three categories (1) enzymes whose elevation in serum reflects damage to hepatocytes, (2) enzymes whose elevation in serum reflects cholestasis, and (3) enzyme test that do not fit precisely in to either pattern.[1,11]

The aminotransferases are sensitive indicators of liver cell injury and are most helpful in recognizing acute hepatocellular diseases such as hepatitis. They include the aspartate aminotransferase (AST) and the alanine aminotransferase (ALT).

AST is found in the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lung, leukocytes and erythrocytes in decreasing order of concentration.[11]

ALT is found primarily in the liver. The aminotransferases are normally present in the serum in low concentration. These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increase permeability. Liver cell necrosis is not required for the release of aminotransferases, and there is a poor correlation between the degree of liver cell damage and the level of aminotransferases. Any type of liver cell injury can cause modest elevation in the serum aminotransferases. Level of up to 300 u/L is nonspecific and may be found in any type of liver disorder. Minimal ALT elevation in asymptomatic blood donor rarely indicate severe liver disease, studies have shown that fatty liver disease is the most likely explanation. Striking elevation of aminotransferases more that 1000 U/L occur most exclusively in disorders associated with extensive hepatocellular injury such as (1) viral hepatitis, (2) ischemic liver injury, or (3) toxin – or drug induced liver injury. [6]

The pattern of aminotransferases elevation can be helpful diagnostically. In most acute hepatocellular disorder, the ALT is higher than or equal to the AST. An AST:ALT ratio more that 2:1 is suggestive while a ratio more than 3:1 is highly suggestive of alcoholic liver disease. The AST in alcoholic liver disease is rarely more than 300U/L and the ALT is often normal. A low level of ALT in the serum is due to an alcohol-induced deficiency of pyridoxal phosphate.[11]

The aminotransferases are usually not greatly elevated in obstructive jaundice. One notable exception occurs during the acute phase of biliary obstruction caused by the passage of a gallstone into the common bile duct. In this setting, the aminotransferases can briefly be in the 1000-2000U/L range. However, aminotransferases level decrease quickly and the liver function test rapidly evolves into typical cholestasis.[13]

Alkaline phosphatase,5-nucleotidase and gamma-glutamyl transpeptidase(GGT) are usually elevated in cholestasis. Alkaline phosphatase and 5-nucleotidase are found in or near the bile canalicular membrane of hepatocyte, while GGT is located in the endoplasmic reticulum and in bile duct epithelial cells. GGT elevation in serum is less specific for cholestasis than are elevation of alkaline phosphatase or 5-nucleotidase. Some have advocated the use of GGT to identify patients with occult alcohol use.

Elevated serum gamma-glutamyl transferase (GGT) level has been proposed as a risk factor for coronary artery disease and is associated with poor clinical outcome in acute coronary syndrome (ACS). The normal serum alkaline phosphatase consists of many distinct isoenzymes found in the liver, bone, placenta and less commonly small intestine. Patients over age 60 can have a mildly elevated alkaline phosphatase, it is also nonpathologically elevated in children and adolescents undergoing rapid bone growth, because of bone alkaline phosphatase, and late in normal pregnancies due to the influx of placental alkaline phosphatase.[1]

Elevation of liver-diverted alkaline phosphatase is not totally specific for cholestasis and a less than threefold elevation can be seen in almost any type of liver disease. Alkaline phosphatase elevation greater than four times normal occur primarily in patients with cholestatic liver disorders, infiltrative liver diseases such as cancer and amyloidosis and bone conditions characterized by rapid bone turnover. In absence of jaundice or elevated aminotransferases, an elevated alkaline phosphatase of liver origin often but not always suggests early cholestasis and less often hepatic infiltration by tumor or granulomata.[12]

Other conditions that cause isolated elevations of the alkaline phosphatase include Hodgkin's disease , diabetes, hyperthyroidism, congestive heart failure, amyloidosis and inflammatory bowel disease.[11]

1.5.3- Coagulation factors:

With the exception of factor VIII, the blood clotting factors are made exclusively in hepatocytes. Their serum half lives are much shorter than albumin, ranging from 6 hours for factor VII to 5 days for fibrinogen. Because of their rapid turnover, measurement of the clotting factors is the single best acute measure of hepatic synthetic function and helpful in both diagnosis and assessing the prognosis of acute parenchymal liver disease.

Useful for this purpose is the serum prothrombin time, which collectively measures factors II, V,VII, and X. biosynthesis of factors II, VII, IX, and X depends on vitamin K. the prothrombin time may be elevated in hepatitis, cirrhosis as well as in disorders that lead to vitamin K deficiency such as obstructive jaundice or

fat malabsorption of any kind. Marked prolongation of the prothrombin time >5 second above control and not corrected by parenteral vitamin K administration is a poor prognostic sign in acute viral hepatitis and other acute and chronic liver disease.[11]

1.6- Uric acid metabolism:

Uric acid is the final breakdown of purine degradation in human. Urates, the ionized form of uric acid, predominate in plasma extracellular fluid and synovial fluid, with 98% existing as monosodium urate at PH 7.4.[11]

Plasma is saturated with monosodium urate at a concentration of 6.8mg/dl at 37c. At higher concentration plasma is therefore supersaturated, creating the potential for urate crystal precipitation. However, plasma urate concentration can reach 80mg/dl without precipitation, perhaps because of the presence of solubilizing substance. The PH of urine greatly influence the solubility of uric acid. At pH 5.0 urine is saturated with uric acid at concentration ranging from (6-15mg/dl). At pH 7.0 saturation is reached at concentration between (158-200mg/dl). Ionized form of uric acid in urine include mono- and disodium, potassium, ammonium, and calcium urates.[1,3]

The kidneys clear urate from the plasma and maintain physiologic balance by utilizing specific organic anion transporters (OATs) including urate transporter 1(URAT1) and human uric acid transporter (hUAT). (hUAT) and other OATs carry urate into the tubular cells from the apical side of the lumen. Once inside the cell, urate must pass to the basolateral side of the lumen in a process controlled by the voltage dependent carrier hUAT. Until recently, a four component model has been used to describe the renal handling of urate: glomerular filtration, tubular reabsorption, secretion and postsecretory reabsorption.[11,13]

Most children have serum urate concentration of (3.0-4.0mg/dl). Levels begin to rise in males during puberty but remain low in females until menopause. Mean serum urate values of adult men and premenopausal women are 360 and 415Mmol/L (6.0 and 6.8 mg/dl), respectively. After menopause values for women increase to approximate those of men.[14]

1.6.1- Hyperuricemia:

Hyperuricemia can result from increase production or decrease excretion of uric acid or from combination of the two processes. Sustained hyperuricemia predispose some individual to develop clinical manifestations including qouty arthritis, urolithiasis, and renal dysfunction. Hyperuricemia is defined as a plasma (or serum) urate concentration more than 408 Mmol/L (6.8mg/dl).

Hyperuricemia may be classified as primary or secondary depending on whether the cause is innate or is the result of an acquired disorder. The association between uric acid and cardiovascular disease was largely ignored until the mid-1950s and early 1960s, when it was rediscovered. Since then, a number of epidemiologic studies have reported a relation between serum uric acid levels and a wide variety of cardiovascular conditions, including hypertension, metabolic syndrome, coronary artery disease, cerebrovascular disease, vascular dementia, preeclampsia, and kidney disease.

The relation between uric acid and cardiovascular disease is observed not only with frank hyperuricemia (defined as more than 6 mg per deciliter [360 µmol per liter] in women and more than 7 mg per deciliter (420 µmol per liter in men) but also with uric acid levels considered to be in the normal to high range (>5.2 to 5.5 mg per deciliter 310 to 330 µmol per liter).[1,14]

However it is more useful to classify hyperuricemia in relation to the underlying pathophysiology, whether it result from increase production, decrease excretion, or a combination of the two.[6]

1.6.1.1- Gout:

1- Primary gout:

About one- third of the body uric acid pool is derived from dietary sources and two-third from endogenous purine metabolism. The concentration of uric acid in body fluid depend on the balance between it's synthesis and elimination by the kidneys(two-third) and gut (one-third). In over 90% of patients with primary gout, hyperuricemia results from an inherited defect in fractional uric acid excretion which impairs their ability to increase urate excretion in response to a purine load (under excretion). Some primary gout patients are intrinsic (over production) of uric acid through no identifiable cause. Very rare less than 1%

there may be an inherited defect in purine metabolism, which should be suspected particularly if gout develops under age 25, in patients with uric acid renal calculi, or if there is strong family history of early gout.[3]

Risk factors and associations for primary gout include metabolic syndrome, high alcohol intake and diets relatively high in red meat or fructose or relatively low in vitamin C or coffee.[13]

2- Secondary gout:

Secondary gout result from hyperuricemia due to renal impairment or chronic diuretic use. In diuretic-induced gout, nodal generalized OA is a further risk factor, especially in elderly women. This presumably relates to a non-specific predisposition to crystallization in osteoarthritic cartilage, possibly due to reduced levels of proteoglycan and other inhibitors of crystal formation. Lead poisoning is a rare cause of hyperuricemia and secondary gout.[6]

1.6.1.2- Clinical features:

1- Acute gout:

In almost all first attacks a single distal joint is affected. The first MTP joint is affected in over 50% of cases, other common sites in order of decreasing frequency, the ankle, midfoot, and knee, small joints of hands, wrist and elbow.

The axial skeleton and large proximal joints are rarely involved and never as the first site. Typical attacks have the following characteristics:

1- Extremely rapid onset, reaching maximum severity in just 2-6hours, often waking the patient in the early morning.
2- Severe pain, often describe as the worst pain ever.
3- Extreme tenderness, the patient is unable to wear a sock or to let bedding rest on the joint.
4- Marked swelling with overlying red, shiny skin.
5- Self-limiting over 5-14 days, with complete return to normality.[3]

2- Recurrent and chronic gout:

After an acute some people never have a second episode, in others the next episode occurs after years. In most, however, a second attack occurs within 1 year and the frequency of attacks gradually increases with time. Later attacks are more likely to involve several joints and be more severe. The joints most commonly involved are the same as those affected by acute attacks.[1]

Chronic tophaceous gout

Large monosodium urate monohydrate (MSU) crystal deposit produce irregular firm nodules (tophi) around extensor surfaces of fingers, hands, forearm, elbow, Achilles tendons and sometimes the helix of the ear. The white colour of MSU crystal may be evident and permit distinction from rheumatoid nodules. Large nodules may be ulcerated , discharging white gritty material and associating with local inflammation even in absence of secondary infection. Secondary gout may present with painful sometimes discharging tophi without preceding acute gout.[11]

1.6.1.3- Hyperuricemia and metabolic syndrome:

Metabolic syndrome is characterized by abdominal obesity with visceral adiposity, impaired glucose tolerance due to insulin resistance with hyperinsulinemia, hypertriglyceridemia, increase low density lipoprotein cholesterol, decreased high density lipoprotein cholesterol, and hyperuricemia.

Hyperinsulinemia reduces the renal excretion of uric acid and sodium. Not surprisingly, hyperuricemia resulting from euglycemic hyperinsulinemia may precede the onset of type 2 diabetes, hypertension, coronary artery disease and qout in individuals with metabolic syndrome.[6]

1.6.1.4- Investigations for hyperuricemia:

Definitive diagnosis requires identification of MSU crystal in the aspirate from the joint, bursa or tophus. In acute gout, synovial fluid shows increased turbidity due to greatly elevated cell count (more than 90% neutrophils). In chronic gout fluid is more variable but occasionally appears white due to high crystal load.
Although hyperuricemia is usually present, it does not confirm gout. Equally a normal serum uric acid especially during an attack, does not exclude gout since it fall as part of acute phase reaction.

Measurement of 24 hours urinary uric acid excretion on a low purine diet will identify an over-producer. Assessment of renal function, hypertension, blood glucose and serum lipid profile should be undertaken. During attack an elevated CRP and neutrophilia are

usual; the ESR is often modestly raised in tophaceous gout. X-ray can asses the degree of joint damage. In early disease they are usually normal, but changes of OA may develop with time, or may be present as a predisposing factor in secondary gout.[3]

1.6.1.5- Management of hyperuricemia:

1- The acute attack:

A fast acting oral NSAID plus PPI can give effective pain relief and is the standard treatment, together with local ice packs. Oral colchicine (a potent inhibitor of neutrophil microtubular assembly) is also very effective but often causes vomiting and severe diarrhea at high dose, a low dose regimen is therefore recommended. Joint aspiration can give instant relief and, when combined with an intra-articular steroid injection to prevent fluid reaccumulation, often effectively abort the attack.[1]

2- Long term management:

Once an acute attack has settled, predisposing factors should be corrected if possible. Weight loss and reduction of excess alcohol intake, especially beer may significantly reduce hyperuricemia. Diuretic should be stopped if possible. A very high purine diet (eg. See food, red meat, offal) should be tempered but there is no need for highly restrictive diet.[1]

Indications for urate-lowering therapy (ULT) are:
- Recurrent attack of acute gout.
- Evidence of bone or joint damage.
- Associated renal disease and or nephrolithiasis.
- Gout with greatly elevated serum uric acid.
- Tophi.

Allopurinol is the drug of choice. It is xanthine oxidase inhibitor, which reduces the conversion of hypoxanthine and xanthine to uric acid. The recommended starting dose is 100mg daily, but 50mg in older patient or if renal function is impaired.

The reduction in tissue uric acid level that follow initiation of ULT can partially dissolve MSU crystals and trigger acute attacks. The patient should be warned of this and told to continue ULT even if an attacks occurs. The risk can be minimized by using a low starting dose or by concurrent administration of oral colchicine or an NSAID for the first few months.[3]

Febuxostat is a recently introduced xanthine oxidase inhibitor that is useful in patients in whom allopurinol is not tolerated or contraindicated. It is commonly provokes attack at the recommended starting dose (80mg daily) so prophylaxis with colchicine or NSAID is advised for the initial 6 months.

Uricosuric drugs such as probenecide or sulfinpyrazone can be effective but require several doses each day and maintenance of a high urine flow to avoid uric acid crystallization in renal tubules.[1,11]

Aims of the study:

To determine the frequency of hyperuricemia and abnormal liver enzymes in patients with acute coronary syndrome.

Objectives of the study:

1- Assess the liver function test in patients with acute coronary syndrome.

2- Measure the serum uric acid, blood urea, serum creatinine and fasting blood sugar in patients with acute coronary syndrome.

3- Make clinical and laboratory assessment of the patients for other diseases that may affect liver function test or serum uric acid.

Patients and Methods

2.1- patients:

Cross sectional study has been done at the coronary care unit (CCU) and laboratory department in Tikrit Teaching Hospital, during the period from October 2013 to June 2014.

The study was carried out on 100 patients selected randomly. The patients were divided into four groups according to their age:

Group one from 30 – 40 years (6 patients).
Group two from 41 – 50 years (16 patients).
Group three from 51 – 60 years (30 patients).
Group four from 61 years and more (48 patients).

The diagnosis of acute myocardial infarction depends on detect any one of following: [1]

• Detect of rise and/or fall of cardiac markers, symptoms of ischemia, ECG changes and development of pathological Q waves.
• Sudden unexpected cardiac death.
•Pathological finding of an acute MI.

All patients were subjected to:

1. Full history was taken according to certain formula designed as special questioner prepared for this study including risk factors of ischemic heart diseases, history of gout, dietary habit and alcohol.

2. Full clinical examination; general and systematic.

Blood investigations were done for all patients to identify the exclusion criteria which might affect liver function test & serum uric acid. These investigations include the followings:

- Complete blood picture with ESR and blood film to exclude thrompocytopenia that may associate with liver cirrhosis and leucopenia which may complicate portal hypertension and hyperslenism, whereas leucocytosis may occur in cholangitis, alcoholic hepatitis and liver abscesses.
- Coagulation screen including PT & INR.
- Viral screening for hepatitis viruses.
- Blood urea, serum creatinin, to exclude patients with renal failure.

Exclusion criteria were:

1- patients with liver diseases.
2- Patients with renal failure or chronic renal diseases.
3- Patients on statin therapy because it's well known effect on liver function.
4- Patients on diuretics.
5- Patients with previous rheumatological diseases.
6- Patients with malignancies.

Ten ml of blood was collected from all patients at time of admissionand sent to the laboratory for measurement of serum uric acid, bilirubin, AST, ALT, albumin, troponin, alkaline phosphatase and blood urea with serum creatinine.

2.2 - Methods:

2.2.1-ECG:

Twelve leads standard ECG (Philips PageWriter TC30 Cardiograph ECG Machine India) was done for all patients for diagnose and classification of the acute coronary syndrome as follows:

1-STEMI (ST- segment elevation MI):

Previously referred to transmural infarction or Q wave myocardial infarction, in which ST segment elevation at the J point in two contiguous leads at least 0.1mv in limb leads, or at least 0.2 mV in chest leads, these typically due to complete occlusion of the coronary artery and may exhibit initially as peaked or hyperacute T waves.

The distribution of leads with ST-elevation can identify the myocardial location and the culprit coronary artery as in table (2-1):

Table (2-1): Location of MI according to ECG changes.[2]

Location of MI	Leads detecting ECG changes	Involved artery
Inferior infarction	II, III, aVF	RCA
Anterior infarction	V3,4	LAD
Anteroseptal infarction	V1 – 4	LAD
Lateral infarction	I, aVL, V5,6	CRC
Extensive anterior infarction	I, aVL, V1 – 6	LAD
Posterior infarction	Prominent R in V1 – 4	RCA or CRC
Right ventricular infarction	ST elevation in V1 or V4R in setting of inferior MI	RCA

2- NSTEMI (non ST-segment elevation MI):

Previously termed as subendocardial infarction or non Q wave MI, occurs as a result of subtotally occlusive thrombus or thrombus that was initially totally occlusive but not sustained, enabling partial or complete lysis to occur within minutes or hours of its formation. They are associated with deep persistent ST depression and symmetrical T wave inversions on the surface ECG.

3- Unstable angina:

It is characterized by at least one of the following:

a- Occurs at rest or minimal exertion and usually lasts less than 20 minutes (if nitroglycerin is not administered)

b- Being severe and of new onset (i.e., within 1 month)

c- Occurs with a crescendo pattern (more severe, prolonged, or increased frequency than previously).

Unstable angina associated with reversible ST-segment depression and T wave inversions on the surface ECG.

2.2.2- Total and direct bilirubin: using BIOLABO kit which is the product of BIOLABO Company, made in France. Were measured by sulafinilic acid method, reaction between bilirubin and diazotized sulafinilic acid which leads to a compound, the azobilirubin, coloured in very acid or basic medium. To enable the assay of TB it is necessary to break the link between unconjugated bilirubin and albumin. this step is done by adding dimethylsulfoxide (DMSO). The absorbance of azobilirubin thus is proportional to the concentration of bilirubin and is measured at 550nm (530-580).Normal value (0.18-0.94 mg/dL).[15]

2.2.3- Serum albumin:using BIOLABO kit which is the product of BIOLABO Company, made in France.Were measured by BCG method for quantitative determination of albumin in human serum and plasma. In buffered solution at pH 4.2 bromocresol green binds albumin to form a coloured compound which absorbance, measured at 630 nm is proportional to the albumin concentration in the specimen. Normal value (3.5-5 g/dL).[15]

2.2.4- ALT and **AST:** using SPECTRUM kit from SPECTRUM Company product by Egyptian Company for biotechnology(S.A.E). were measured by colorimetric method (Reitman and Frankel) for determination of serum aminotransferases by monitoring the concentration of pyruvatehydrazone formed with 2,4-dinitrophenyl-hydrazine. Normal value (10-40 U/L).[16]

2.2.5- Serum creatinine:using BIOLABO kit which is the product of BIOLABO Company, made in France.Serum creatinine was measured by using kinetic method. Colorimetric reagent (jaff reagent) of craetinine with alkaline picrate measured kinetically at 490 nm, without any pretreatment step. Normal value (0.68-1.36 mg/dL)[15]

2.2.6- Serum cardiac troponin I: was measured by using one-step troponin I test which is a chromatographic immunoassay for the qualitative determination of troponin I in human whole blood, serum or plasma. When specimen is added to sample pad it moves through the conjugate pad and mobilizes gold anti-cTnI (cardiac troponin I) conjugate that is coated on the conjugate pad. The mixture move along the membrane by capillary action and reacts with anti-cTnI that is coated on the test region. If cTnI is present, the result is the formation of a colored band in the test region. If there is no cTnI in the sample the area will remain colorless. The sample continues to move to the control area and forms a pink color, indicating the test is working and the result is valid.

Assay procedures:

1- Read package insert carefully before testing. Allow the test devices, whole blood, serum or plasma to equilibrate to room temperature (15-30c) prior to testing. Do not open pouches until ready to perform the assay.

2- Remove the test devices from the foil pouch and use it as soon as possible.

3- Place the test device on a clean and level surface. Hold the dropper provided vertically and transfer 3 drops of specimen (100Ml) to the specimen well(s) in the test device.

4- Wait for the red line(s) to appear. The result should be read between 10 to 15 minutes.[17]

2.2.7-Serum uric acid: using RANDOX reagent for serum uric acid which is the product of RANDOX laboratories in United States.

Enzymatic colorimetric method was used for quantitative determination of uric acid in serum, plasma and urine. This product is suitable for manual use and on the RANDOX monza analyzer. Uric acid is

converted by uricase to allantoin and hydrogen peroxide which under the catalytic influence of peroxidase, oxidizes 3,4-Dichloro- 2-hydroxybenzenesulfonic and 4-aminophenazone to form a red-violet quinoneimine compound. Normal value in male (2.0-7.0 mg/dL) while in female (2.0-6.0 mg/dL).[18]

Statistical analysis and data management:

The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Chi (χ^2) square test of association was used to compare proportions of different factors among sample groups. Unpaired Student t test, one –way and two ways ANOVA was used to compare means of numerical variables. P value of ≤ 0.05 was regarded as statistically significant.

Results

Table (3 – 1) show the distribution of patients according to their age which reveals that 61% of the patients with ACS were between 51 – 70 years old, 22% were between 31 – 50 years old and 17% were above 70 years old.

Table(3 – 1):Age distribution of patients with ACS

Age	Cause of ACS		Total
	unstable angina	MI	
31-50 years	9	13	22
	33.3%	17.8%	22.0%
51-70 years	16	45	61
	59.3%	61.6%	61.0%
> 70 years	2	15	17
	7.4%	20.5%	17.0%
Total	27	73	100
	100.0%	100.0%	100.0%

X2= 4.18,df=2,p value >0.05 NS

Acute coronary syndrome was found to be more common in male than female 58% versus 42%, but this difference was not significant statistically (p value >0.05), table (3 – 2).

Table(3 – 2):Sex distribution of patients with ACS

Sex	Cause of ACS		Total
	unstable angina	MI	
Male	14	44	58
	51.9%	61.1%	58.6%
Female	13	29	42
	48.1%	38.9%	41.4%
Total	27	73	100
	100.0%	100.0%	100.0%

X2= 0.694,df=1,p value >0.05 NS

The mean of the patient's age was 60.02 years, the mean of ALT, AST, ALP, S.albumin, S.uric acid, B. urea, and S. creatinine were within normal range, but the mean of fasting blood sugar was high as shown in table (3 – 3).

Table (3 – 3):The mean value of studied parameters of patients with ACS.

Variables	Mean	Std. Deviation	Median
B. urea (mg/dl)	38.80	5.27	40.00
Creatinine (mg/dl)	1.16	0.20	1.20
Fasting blood sugar (mg/dl)	175.84	56.77	187.00
S.uric acid (mg/dl)	0.35	0.19	0.30
AST (U/L)	39.94	27.30	39.00
ALT (U/L)	35.78	11.37	37.50
ALP (U/L)	82.70	15.65	79.50
S.albumin (g/dl)	4.11	0.43	4.10

There was no significant difference in the mean of all studied parameters between those with myocardial infarction and unstable angina as seen in table (3–4).

Table (3 – 4): The Mean of studied parameters according to study groups

Variables	unstable angina n=27		MI n=73		P value (df,t)
	Mean	Std. Deviation	Mean	Std. Deviation	
B.urea (mg/dl)	38.93	5.13	38.71	5.36	>0.05 NS (98,0.179)
S.creatinine (mg/dl)	1.17	0.18	1.15	0.21	>0.05 NS (98,0.457)
Fasting blood sugar (mg/dl)	181.33	44.74	176.37	60.84	>0.05 NS (98,0.387)
AST (U/L)	46.93	32.60	43.36	25.25	>0.05 NS (98,0.579)
ALT(U/L)	36.04	12.30	37.73	11.06	>0.05 NS (98,0.656)
S.uric acid (mg/dl)	0.35	0.16	0.38	0.20	>0.05 NS (98,0.824)
ALP (U/L)	81.30	17.10	83.74	15.15	>0.05 NS (98,0.891)
S.albumin (g/dl)	4.11	0.41	4.15	0.44	>0.05 NS (98,0.435)

AST was more than 40 U/L in 22% patients, 17% of them had MI and 5% had unstable angina, as seen in figure (3 – 1), statistically this difference was not significant.

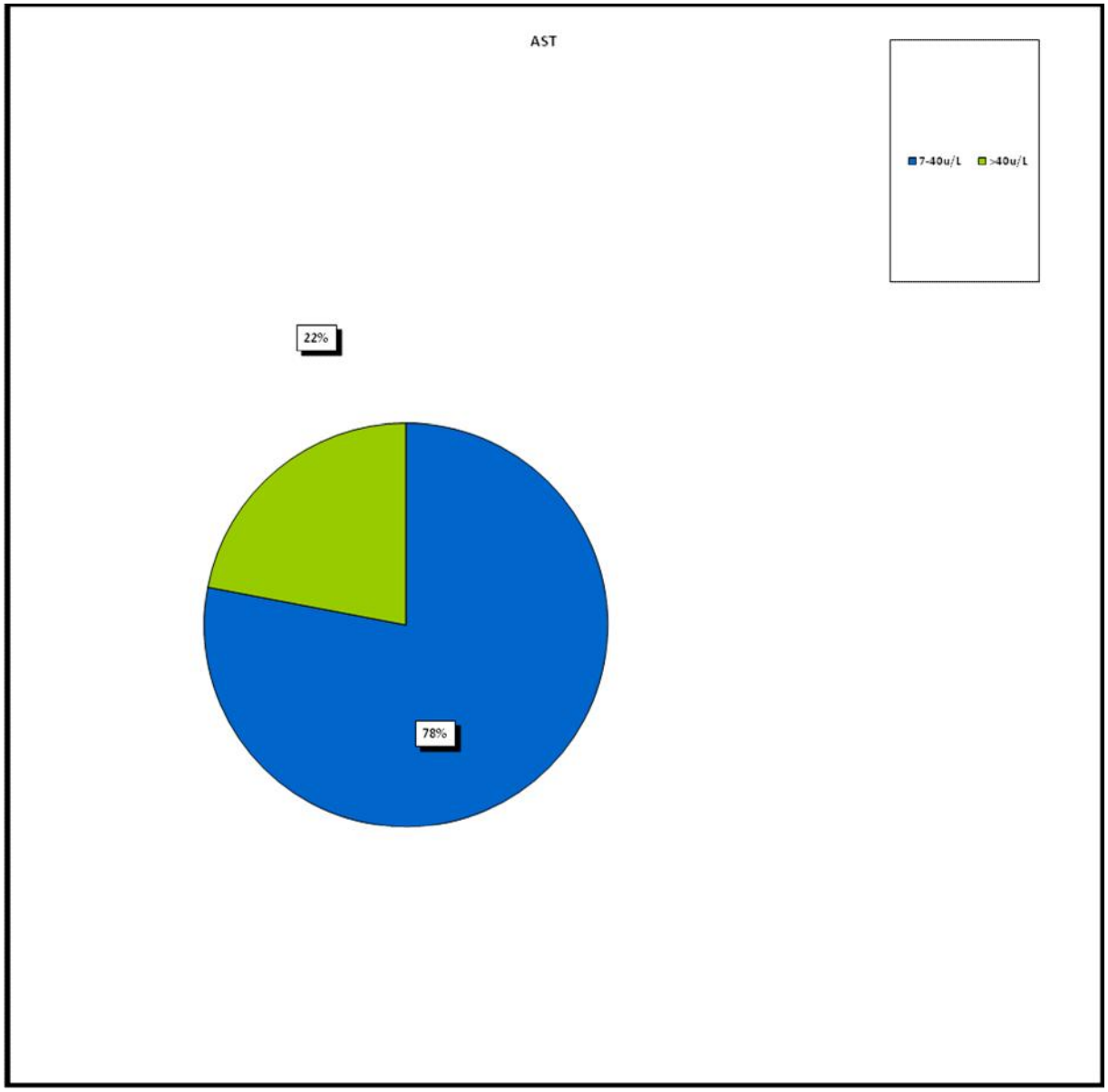

Figure (3 – 1): The levels of AST among study sample

ALT was more than 40 U/L in 20% patients, 15% of them had MI and 5% had unstable angina, as seen in figure (3 – 2), alsostatistically this difference was not significant.

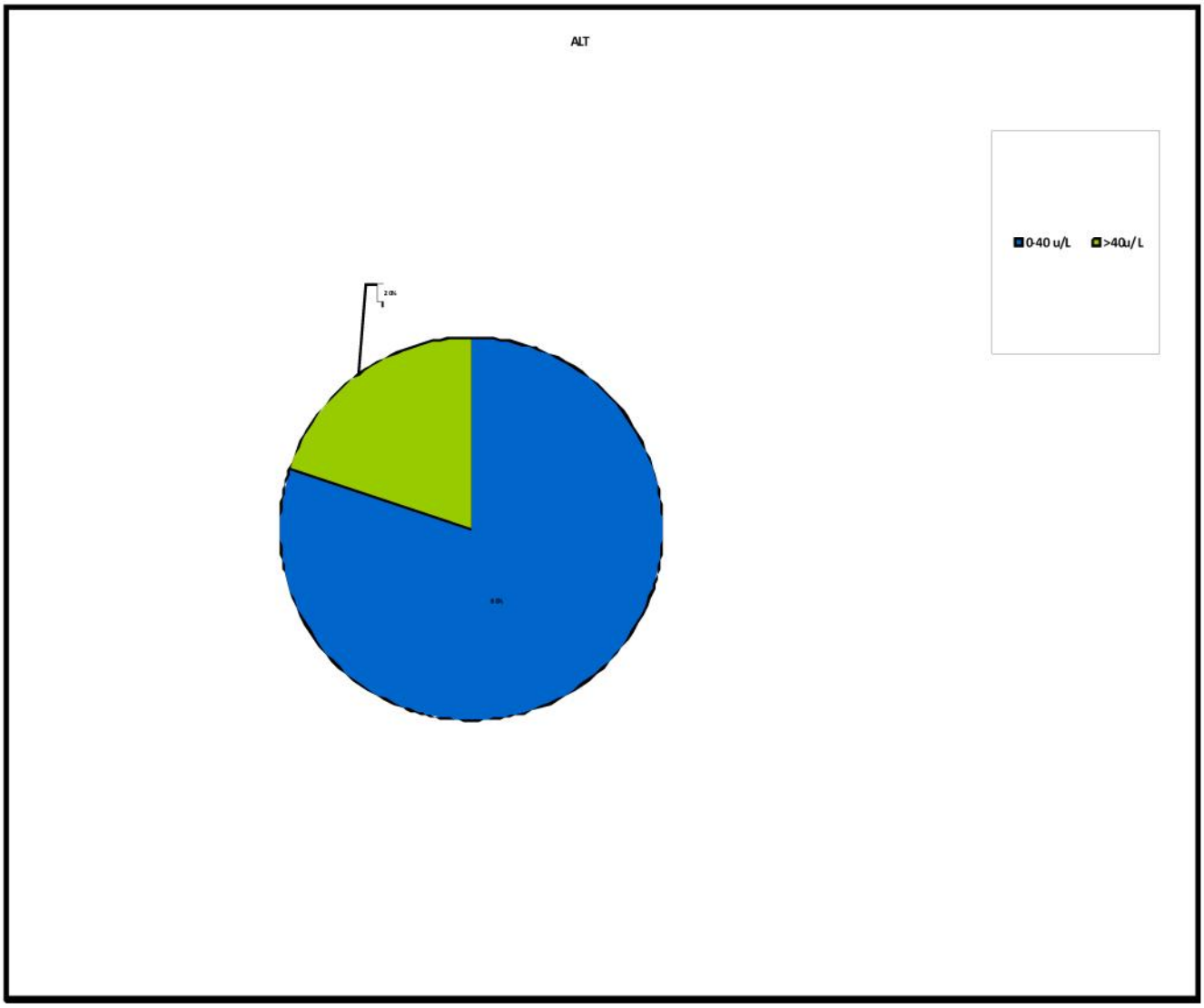

Figure (3 – 2): The levels of ALT among study sample

Serum uric acid was normal in 85 patients (85%) of the patients, one patient (1%) with borderline level, and high in 14 patients (14%) as shown in figure (3 – 3), 11 patients with high s. uric acid had MI and 3 patients had unstable angina. S.uric acid was significantly higher in those with MI than unstable angina, (p value < 0.05).

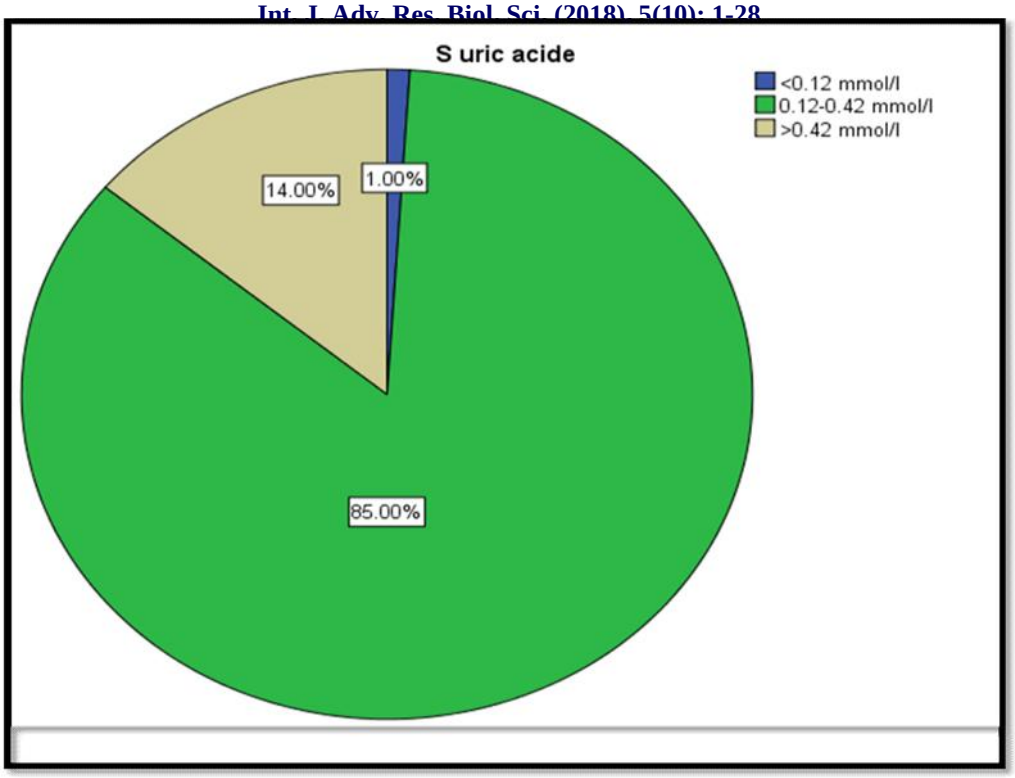

Figure (3 – 3): The levels of S. Uric acid among study sample

Serum alkaline phosphatase and serum albumin were normal in all patients.

The mean of fasting blood sugar was higher than normal and 22 patients (22%), (16 patients with MI and 6 patients with unstable angina), had blood sugar in diabetic range as seen in figure (3 – 4), the difference was not significant statistically.

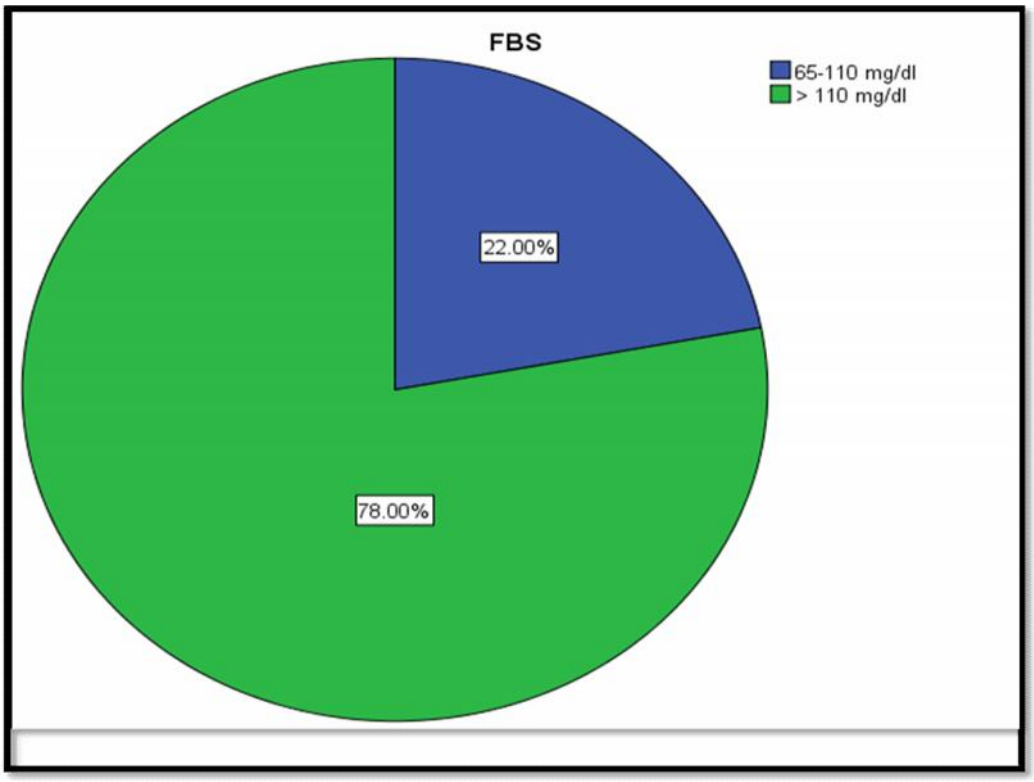

Figure (3 – 4): Fasting blood sugar among study sample

Serum troponin was positive in 73 patients (73%) (All the patients with MI), while serum troponine was negative in 27 patients (27%) (All patients with unstable angina) as seen in figure (3-5).

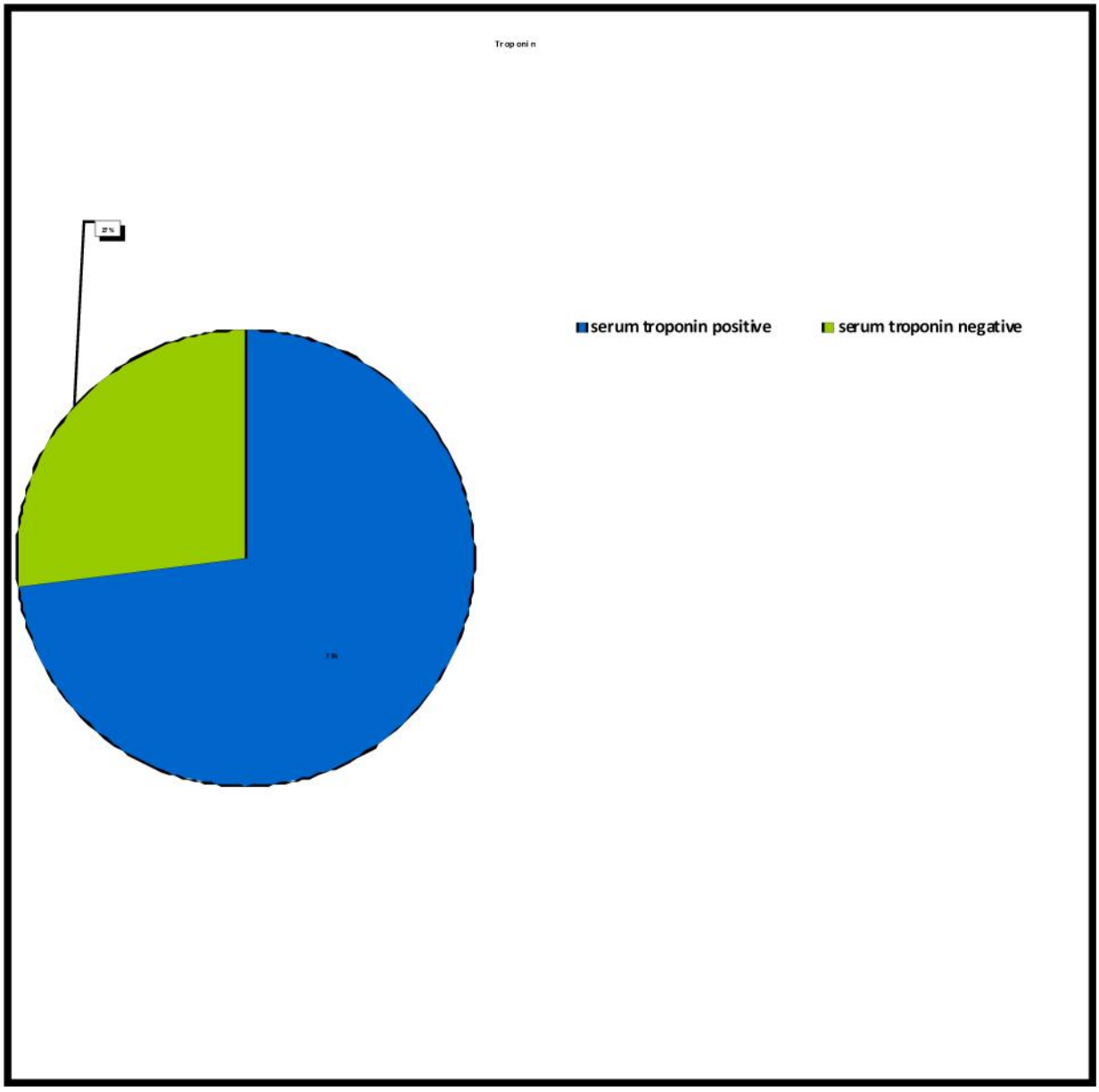

Figure (3 – 5) serum troponin among study samples

Regarding the age, blood urea was higher in those above 70 years, but statistically there was no significant difference, while S.uric acid was significantly higher in those between 51 – 70 years old, as seen in table (3– 5).

Table (3 – 5): The Mean level of studied parameters according to age

Variables	Age group	N	Mean	Std. Deviation	P value (df,F)ANOVA
B.urea (mg/dl)	31-50 years	22	37.59	6.07	>0.05 S (2,4.9)
	51-70 years	61	38.23	4.48	
	> 70 years	17	42.24	5.70	
S.Creatinine (mg/dl)	31-50 years	22	1.11	0.17	>0.05 NS (2,0.69)
	51-70 years	61	1.16	0.20	
	> 70 years	17	1.19	0.26	
Fasting blood sugar (mg/dl)	31-50 years	22	166.82	52.73	>0.05 NS (2,0.68)
	51-70 years	61	178.79	57.33	
	> 70 years	17	187.94	60.70	
S.uric acid (mg/dl)	31-50 years	22	0.30	0.07	<0.05 S (2,4.09)
	51-70 years	61	0.41	0.22	
	> 70 years	17	0.32	0.11	
AST (U/L)	31-50 years	22	33.64	6.43	>0.05 NS (2,2.5)
	51-70 years	61	48.62	33.32	
	> 70 years	17	42.71	12.82	
ALT (U/L)	31-50 years	22	32.50	5.14	>0.05 NS (2,2.7)
	51-70 years	61	38.23	12.90	
	> 70 years	17	40.00	9.91	
ALP (U/L)	31-50 years	22	77.14	14.58	>0.05 NS (2,2.2)
	51-70 years	61	85.28	15.61	
	> 70 years	17	82.88	15.96	
S.albumin (g/dl)	31-50 years	22	4.07	0.37	>0.05 NS (2,0.6)
	51-70 years	61	4.18	0.45	
	> 70 years	17	4.11	0.43	

As shown in table (3 – 6) there was no significant difference in the mean of studied parameters between male and female patients.

Table (3 – 6): The Mean of studied parameters according to sex

Variables	Male n=58		Female n=42		P value (df,t)
	Mean	Std. Deviation	Mean	Std. Deviation	
B. urea (mg/dl)	38.50	4.23	39.00	6.49	>0.05 NS (98,0.6)
S.creatinine (mg/dl)	1.14	0.19	1.18	0.22	>0.05 NS (98,1.08)
Fasting blood sugar (mg/dl)	176.31	60.05	179.39	52.50	>0.05 NS (98,0.288)
AST (U/L)	43.57	23.60	45.49	32.39	>0.05 NS (98,0.322)
ALT (U/L)	36.60	9.47	38.37	13.75	>0.05 NS (98,0.687)
S.uric acid (mg/dl)	0.37	0.20	0.38	0.18	>0.05 NS (98,0.356)
ALP (U/L)	82.41	14.75	84.29	17.06	>0.05 NS (98,0.498)
S.albumin (g/dl)	4.09	0.43	4.21	0.43	>0.05 NS (98,1.3)

Discussion

In this study 22% of patients with ACS had AST higher than 40 u/l. similarly 20% of these patients had ALT levels more than 45u/l. Wong found in a prospective study included 612 patients screened for liver enzymes and then underwent a coronary angiography, elevated liver enzymes was present in 84.6% of those with stable IHD and 64.1% of those ACS, which confirmed a strong association between elevated liver enzymes and coronary artery disease.[19] These results didn't agree with the current study due to several factors:-

1- About 30-37% of patients in Wong study were alcoholic and this might disturb liver functions.
2- Some patients included in that study suffered from fatty liver disease.
3- Demographic and metabolic factors.
4- Many people have asymptomatic elevated liver enzymes.
5- Selection bias and the sample size were much larger than the current study.

Moreover many studies reveal a good relationship between acute coronary syndrome and elevated liver enzymes.[20-23]
A studyon 140 patients with IHD found that chronic coronary artery disease is a most often accompanied by elevated plasma concentrations of liver enzymes.[24,25]

Kubo *et al*. reported a slight AST elevation (65 U/L) in 90 patients with a new attack of IHD and this was consentient with the results of the current study.[26] However, many other studies support the findings of the present study.[27,28]

Seeto *et al*. stated in a study that systemic hypotension or shock because of ACS alone did not lead to liver dysfunction. The majority of patients in his study with elevated liver enzymes had severe underlying cardiac disease that led to congestion of the liver.[29]

Other study concluded that right-sided heart failure from inferior myocardial infarction resulting in hepatic venous congestion, may predispose the liver to hepatic injury induced by a hypotensive event. They report in their study that probable causes of cardiac induced elevated AST and ALT are hepatic congestion from venous hypertension and decreased oxygen delivery from a decreased cardiac output.[30]

A retrospective chart review demonstrated that liver function abnormalities increased with decreasing cardiac index (CI=cardiac output divided by the body surface area) and increasing central venous pressure (CVP).[31]

Another study on liver enzymes in patients with various presentations of ACS found that about 30% of the patients have 2-folds increase in liver enzymes and the most common abnormalities were elevation of the cholestatic liver enzyme profile, which includes ALP, GGT, bilirubin, and hypoalbuminemia; each of these was significantly more common (all $p<0.001$) than the increase of a hepatic profile (increased ALT and AST).It was found that the elevation of each of the cholestatic LFTs was significantly associated with the degree of tricuspid incompetence in inferior myocardial infarction. Patients with moderate or severe tricuspid regurgitation(TR) due to inferior myocardial infarction had significantly greater ALP, GGT, and bilirubin than those with no or mild TR.[32]

These variations in liver function test in different studies can be explained by many causes as:

1- The source of elevated enzymes may be cardiac rather than hepatic.
2- Many patients with ischemic heart diseases suffer from type 2 diabetes mellitus which is a very strong risk factor for IHD and many studies confirmed elevated AST and ALT in type 2diabetes mellitus.[33,34]
3- There are a several risk factors for ischemic heart disease that associated with hepatic dysfunction and produce a range of liver enzyme changes. These risk factors include alcohol, obesity, aging process, type 2diabetes and hyper-triglyceridemia.[35]
4- Many drugs used in the management of ACS are metabolized in the liver and can cause modest elevations in liver enzyme like statins,ACE-I, diuretics, and warfarin.[36]

Other studies found that there is strong correlation between liver enzymes and CK-MB elevations in ACS and their independent prognostic value for clinical outcomes suggest that AST and ALT levels reflect the severity and clinical significance of infarcts. They reported that about 62% of patients with ACS admitted to CCU got elevations in AST and ALT(2-3 folds) with high CK-MB. This relationship is not surprising for AST, whose role as a biomarker in MI and concentration in cardiac tissue is well known, despite its common label as a 'liver enzyme.' The pattern of AST elevation over time, with peaks approximately 24 h after presentation and quick resolution thereafter, largely resembles the curve of CK-MB and suggests primarily acardiac source of AST release.[37,38]

Indeed, unlike chronic heart failure, in which the pattern of liver enzyme elevation is largely one of cholestasis,[39,40] acute heart failure and ischemic heart disease most often result in a pattern of high transaminases.[41-43]

However, several observations suggest a primary cardiac source of transaminase release in ACS. First, no clear association between degree oftransaminase elevation and severity of ACS was observed, this would be expected if AST and ALT elevations were due to hepatic injury.

Second, the different patterns observed for the rise and fall of AST and ALT can be explained by their differing serum half-lives following release from a common source (AST half-life of 17±5 h; ALT half-life of 47±10 h).[44] Third, previous studies of smaller acute MI patient populations have shown similar patterns of both AST and ALT release.[45]Fourth, ischemic hepatitis or 'shock liver' is generally defined as massive but rapidly reversible elevations of serum transaminases in the setting of systemic shock in the absence of other causes of acute hepatitis.[46,47] Massive elevations in transaminases are generally considered 20–25 times the upper limit normal,[48,49] levels which far exceed those observed in the present study. Finally, if transaminase elevation was because of hepatic injury, then it would be expected that patients with pre-existing liver disease would have more severe elevations in liver enzymes and worse outcomes. In this study analysispatients with history of liver disease were excluded from the study.

Collectively, these suggest that AST and ALT elevations in STEMI are primarily due to myocardial injury.

The current study shows no significant association between hyperuricemia and ACS. S.uric acid in the majority(`85%) of the study sample was within normal range(up to 0.42mmol/l) and only small percentage(15%) had S.uric acid level higher than normal.

The link between gout and atherosclerosis has been observed for more than 100 years.[50]

While the link between acute MI and hyperuricemia is well known. One of the large-scale epidemiologic studies of this link was reported by Abbott *et al*. who found that 37 patients among 94 men with ACS (39%) had gout unrelated to diuretic use, compared with 509 patients out of 1,764 men without gout (29%). After risk adjustment it was found that an excess risk of 60% for coronary artery diseases among patients with gout as compared with those without gout. In their analyses, the investigators excluded cases of diuretic-induced gout and adjusted for potential confounding by age, systolic blood pressure, total cholesterol level, alcohol intake, BMI, and diabetes mellitus.[51-55]

In other study on 130 coronary artery disease events. Among them, 31 subjects were getting hyperuricemia after admission to CCU after exclusion of past history of gout or drug- induced hyperuricemia.[56]

Recently, analysis of patients with gout in a general practice database showed that the cumulative incidence of cardiovascular disease (angina pectoris, MI) was higher in individuals with hyperuricemia (26%) than in controls matched for age, sex, and physician practice (20%).[57,58]

The differences in results regarding hyperuricemia between the present study and that studies can be due to confounding factors in their cases make their results are higher such as prior diuretic use, renal function status of their patients, smoking, family history, aspirin use, and genetic factors.

There was a recent study showed a significant modest association between hyperuricemia and IHD events, and the overall risk of IHD death increased 12% for each increase of 1mg/dL of uric acid.[59]

In the subgroup analysis, hyperuricemia appeared to significantly increase the risk of IHD deaths in women (approximately 70 %), but not in men. Although this gender differences require further research, these results support previous findings of a stronger association between hyperuricemia and cardiovascular disease in women.[60-63]

Several observational studies reported that gout was associated with multiple risk factors for cardiovascular disease and with cardiovascular morbidities and mortalities.[64-66]

Whether gout directly or indirectly through hyperuricemia increases the risk of cardiovascular disease remains uncertain, but current data suggest more aggressive cardiovascular risk management in patients with gout. Nevertheless, larger clinical trials with a longer follow-up period are still needed to determine the safety and efficacy of urate lowering therapy such as allopurinol in cardiovascular disease.[67]

5. Conclusion and Recommendations

5.1-Conclusions:-

1- Acute MI was more common in the age group (51-70) while unstable angina was more common in patients younger than 50 years.
2- ACS was more common in males than female.
3- Aminotransferases (AST and ALT) are within normal limits in majority of patients of ACS.
4- The serum uric acid is not elevated in the most patients of ACS.
5- Most ACS patients have normal limit of serum albumin and ALP.
6- The source of elevated liver enzymes in ACS disease is cardiac rather than hepatic in origin due to enzyme release after myocardial damage.

5.2- Recommendations:-

1- Further studies to evaluate the effects of statins and antiplatelet used in ACS on the liver enzymes.
2- Further studies to assess the effect of liver enzyme disturbance in ACS on long term prognosis.
3- Further studies to assess the effect of treatment of hyperuricemia on the cardiovascular diseases.
4- Further studies to explain the relationship between hyperuricemia and disturbed liver enzymes with chronic complications of ischemic heart diseases.

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العلاقه بين حامض اليوريك في مصل الدم واختبار وظيفة الكبد في مرضى متلازمة الشريان التاجي الحاده في مستشفى تكريت التعليمي

الخلاصـــة

المقدمة

[redacted] متلازمة الشريان التاجي الحادة هو المصطلح الذي يتضمن كل من الذبحة الصدرية غير المستقرة واحتشاء عضلة القلب.

متلازمة الشريان التاجي الحادة قد تظهر بشكل ظاهرة جديدة أو ضد اساسية الذبحة المستقرة المزمنة.

الهدف

[redacted] الهدف من هذه الدراسة هو لتحديد تردد فرط حمض اليوريك في الدم والاظطرابات التي تحصل بأنزيمات الكبد في المرضى الذين يعانون من متلازمة الشريان التاجي الحادة .

المواد والمرضى

هذه الدراسه هي دراسة مقطعية قد تمت في وحة التاجية (CCU) وقسم المختبر في مستشفى تكريت التعليمي، خلال الفترة مرين الاول 2013 إلى حزيران 2014. هذه الدراسه أجريت على100 مريضا تم اختيارهم بشكل عشوائي.

[redacted] ى أربع مجموعات رئيسية وفقا لسنهم. تم تشخيص المرضى من قبل تخطيط القلب(ECG)، إنزيمات القلب والتاريخ الطبي . تم سحب عينات دم من جميع المرضى وإرسالها إلى المختبر لأنزيمات الكبد، حمض اليوريك في الدم، الزلال في الدم، السكر في الدم ،اليوريا في الدم والكرياتينين في مصل الدم.

النتائج

وجدت الدراسه الحاليه انه80% من مرضى المتلازمة التاجيه الحاده كانت لديهم انزيمات الكبد في الدم وقلوية الفوسفاتيز ضمن الحدود الطبيعيه(لا يوجد اختلاف مهم بين هذه الانزيمات).

كذلك دراستنا الحاليه وجدت انه 85% من مرضى المتلازمهالتاجيه الحاده لديهم نسب طبيعيه من حامض اليوريك بالدم.

ذروة عمر التردد لمرضى المتلازمهالتاجيه الحاده مابين 51-70 سنهمع تردد الذكور اكثر من الاناث.

الاستنتاج

انزيمات الكبد الالانين(AST وALT), قاعدية الفوسفتيز, الالبومين وحامض اليوريك في الدم ضمن الحدود الطبيعيه في اغلبية مرضى المتلازمهالتاجيه الحاده, بالاضافه الى ذلك نسبة تردد المتلازمهالتاجيه الحاده في الذكور اكثر من الاناث.

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