" PROGNOSTIC SIGNIFICANCE OF SERUM URIC ACID LEVEL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION "

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CERTIFICATE

This is to certify that this dissertation entitled "PROGNOSTIC SIGNIFICANCE OF SERUM URIC ACID LEVEL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION" submitted by Dr.M.Subramani to the faculty of General Medicine, The Tamil Nadu Dr.M.G.R Medical University, Chennai in partial fulfillment of the requirement for the award of M.D degree Branch I (General Medicine) is a bonafide research work carried out by him under my direct supervision and guidance.

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INTRODUCTION

Acute Myocardial Infarction is the leading cause of mortality in both developed and developing countries (Rogers WJ et.al[1]., Kesteloot H et.al[2].,)

Acute coronary syndromes are emerging out in epidemic proportions through out the world. Factors contributing to death following Acute Myocardial Infarction are many.

These factors relate mainly to electrical disturbances in the form of Arrhythmia (Carmeliet E[3], Thompson CA[4]) and mechanical disturbances in the form of pump failure (Hochman et. al[5]., Bertrand M et. al[6].).

Most sudden deaths in Acute Myocardial Infarction occur within one hour due to ventricular fibrillation and also due to left ventricular failure when there is an extensive injury. (Lewis EF et. al[7].)

Rest of the deaths following Myocardial Infarction occur within first one week and death cannot be predicted and occurs suddenly. Hence many trials have been conducted to identify markers that would be helpful to predict the risk of such adverse cardiac events.

Many trials have used serum Magnesium level,(Milionis HJ et.al[8].,) C-Reactive Protein levels, (Ridker PM, Morrow DA et.al[9].,) Malonyldialdehyde, (Pol Merkuriusz Lek[10]) white blood cell count (Comparan Nunez. A et. al[10].,) as a predictor for mortality and morbidity

following Acute Myocardial Infarction and risk of developing adverse cardiac events like sudden cardiac death and congestive heart failure

THIS STUDY IS ONE OF SUCH KIND IN THAT IT TRIES TO VALIDATE THE PROGNOSTIC ROLE OF SERUM URIC ACID LEVEL FOLLOWING ACUTE MYOCARDIAL INFARCTION. (Kojima S., Sakamoto, Am .J Cardiol . 2005 Aug, Sakai H University of Medical Science, Otsu, Japan, Niizeki T., J. Cardiology 2006 May, Joshua M, Circulation 2003: American Heart Association.)

Previous studies have established that serum uric acid levels reflect circulating xanthine oxidase activity and oxidative stress production following Acute Myocardial Infarction.

Free radicals produced in large amounts during myocardial ischemia and reperfusion take part in the degradation of cellular and subcellular membrane structures. The source of oxygen radicals in ischemic myocardium are Neutrophils recruited into the necrotic region as well as metabolic transformation of Hypoxanthine and Xanthine to Uric acid (Domonsky L et. al[10].)

Thus it is evident that elevated Uric acid levels is a good marker of oxidative stress and useful to assess the prognostic events in Acute Myocardial Infarction.

This forms the basis of the study.

AIMS OF THE STUDY

1. ***To assess the prognostic significance of serum Uric acid level in Acute Myocardial Infarction.***
2. ***To correlate levels of Uric acid in terms of short term mortality***
3. ***To correlate serum Uric acid levels with incidence of cardiac failure***
4. ***To validate the relation between Quantitative serum Uric acid level on admission and Killip's class status on Acute Myocardial Infarction.***
5. ***To know whether the incidence of Arrhythmias bears a relation with serum Uric acid level in Acute Myocardial Infarction.***

REVIEW OF LITERATURE

Ischemic Heart Disease in the generic designation for a spectrum of disorders resulting from imbalance between the myocardial need for oxygen and the adequacy of blood supply[11]. In 90-95% of cases the reduction in the coronary blood flow is related to atherosclerotic narrowing or the subepicardial coronary trunks. Coronary vasospasm alone or superimposed on atherosclerotic narrowing may contribute to the reduction of flow[12].

Depending upon the rate of development of the arterial narrowing and its ultimate severity, four basic clinico pathologic syndromes may result.

They are

1. ***Myocardial Infarction***
2. ***Angina pectoris.***
3. ***Chronic Ischemic Heart Disease***
4. ***Sudden Cardiac Death – which may be superimposed on any of the three conditions.***

MYOCARDIAL INFARCTION :

This is the catastrophic frequently fatal form of Ischemic Heart Disease that usually results from precipitous reduction or arrest of a significant portion of coronary flow.

In great majority of cases wide spread severe coronary atherosclerosis of the coronary arteries underly Myocardial Infarction. In addition some sudden event such as coronary thrombosis must unfavorably alter the precarious balance. Alternatively the myocardial supply can be suddenly reduced by a superimposed vasospasm. Congenital abnormalities such as anomalous origin of left anterior descending coronary artery from the pulmonary artery may cause myocardial ischemia and infarction. But it is very rare.

Coronary atherosclerosis creates a disparity between myocardial needs and supply. Myocardium extracts a high and virtually fixed fraction of oxygen from the coronary arterial blood. Atherosclerotic arteries can not dilate and so incapable of adjusting to the demands. Transient deficit of oxygen can be compensated by anerobic glycolysis with the production of lactate[13]. If the imbalance is not transient, it passes from the reversible ischemic injury to the irreversible ischemic necrosis. Depending upon the rate of development of the arterial narrowing and its ultimate severity, three basic clinico pathologic syndromes occur namely Angina pectoris, Acute coronary insufficiency & Myocardial Infarction.

Angina pectoris is a clinical syndrome resulting from transient reversible myocardial ischemia and is produced by any effort which increases the metabolic demands of the myocardium beyond the capacity of the coronary circulation. The anginal pain is due to

accumulation of certain metabolites that are formed in ischemic working muscle. It is diagnosed clinically by the typical history of the site, the character and duration of pain, the site of its radiation and by its characteristic precipitating and relieving factors. Here the Electrocardiogram will be usually normal. Ischemic changes can be demonstrated only by the stress Electrocardiogram.

Acute coronary insufficiency is a syndrome which is intermediate between Angina pectoris and Myocardial Infarction. In this condition, physiologically the coronary circulation is insufficient to meet the full demands to the myocardium even at rest, yet sufficient to prevent myocardial necrosis. Clinically it may be acute or sub acute in onset. The important feature is that the pain may occur even at rest and the duration of pain is prolonged than that of the anginal pain and precipitated on exertion and not relieved by rest. There will not be any evidence of myocardial cell necrosis. It can be diagnosed by the characteristic ischemic changes in the Electrocardiogram.

Acute Myocardial Infarction is a pathologic process resulting from the reduced perfusion of a segment of the myocardium such that irreversible injury occurs. The infarct may be subendocardial or transmural.

Subendocardial infarct refers to a multifocal, non-confluent areas of ischemic necrosis, often distributed circumferentially. This does not extend beyond. The inner one third to one half of the

thickness of the left ventricular wall. The patients with this type of infarction are more prone for cardiac arrhythmias. Coronary thrombosis is not found in more than 10% such cases[14].

Transmural infarct refers to a confluent area of ischemic necrosis extending at some point from the subendocardium to the epicardium or subepicardial fat. Coronary thrombosis is usually present in 90-95% of these cases.

EPIDEMIOLOGY :

The incidence of fatal Myocardial Infarction progressively rises with age to peak in the 55-65 years old group.

Myocardial Infarction occur in younger individuals, even in the third decade of life, particularly when predispositions to atherosclerosis, Hypertension , diabetes, familial hypercholestrolemia & other causes of hyperlipoproteinemia are present.

Virtually throughout life, males are at significantly greater risk than females, the differential progressively declining with advancing age. Except for those having some predisposing atherogenic condition, women are remarkably protected against Myocardial Infarction during reproductive life. Women using oral contraceptives have 3 to 4 fold greater risk than non users and this increased risk does not appear to be related to the duration of use[15].

CIGARETTE SMOKING:

Cigarette smoking particularly in combination with other risk factors has been shown to have a strong and consistent association with increased incidence of atherosclerosis, by increasing catecholamine stimulation which enhances platelet aggregation and peripheral lipid mobilization and decreasing the ratio of High Density Lipoprotein (HDL) to Low Density Lipoprotein (LDL) [16].

STRESS AND PERSONALITY :

Stress is associated with increased catecholamine secretion and surges mental stress may thus be a aggravating factor.

Type A individuals who are anxious, aggressive, impatient, competitive, always in a frustrate mood are more prone for IHD [17].

SEDENTARY LIFE STYLE :

Exercise conditioning when regularly employed, reduces the rate of fatal Heart disease [18].

It is proved that HDL level increases with exercise, & also augments fibrinolytic response and there by provide a potential protective mechanism against development of thrombi within coronary arteries [19].

DIABETES MELLITUS :

It has been shown that a diabetic patients serum can cause hyperplasia of smooth muscle cells. Furthermore, high blood sugar is often associated with obesity, hypertension, increased triglycerides, Low HDL, increased LDL and abnormal platelet adhesiveness. Diabetes is said to double the risk of ischemia in men and women 3-4 times. Silent Myocardial Infarction is thought to occur with increased frequency in diabetes and should be suspected whenever symptoms of left ventricular failure appear suddenly[20].

CORONARY BLOOD FLOW :

The blood flow in coronary arteries resembles that in other regions in being dependant on the blood pressure and on the vascular resistance of the arteries and the arterioles.

A distinctive feature of the coronary circulation is that the arteries are compressed by the contracting myocardium during systole. Consequently coronary blood flow occurs mainly during diastole[21].

The normal coronary circulation is dominated and controlled by the myocardial requirements for oxygen. This need is met by the heart's ability to vary coronary vascular resistance and therefore blood flow. Considerably while the myocardium extracts a high and relatively fixed percentage of oxygen.

The large epicardial vessels serve as conduits in healthy persons, although they are capable of constriction and relaxation they are referred as the conductance vessels.

The intramyocardial vessels normally exhibit striking changes in tone and are therefore referred as resistance vessels.

Hence with exercise and emotional stress, the changing oxygen needs affect coronary vascular resistance and in this manner regulate the supply of blood and oxygen (metabolic regulation).

These same vessels adapt to physiologic alterations in blood pressure in order to maintain coronary blood flow at levels appropriate to myocardial needs. (Auto regulation).

The frequencies of the critical narrowing of each of the three main arterial trunks and the associated myocardial lesions are as follows[22] :

a) Left Anterior descending coronary artery (40-50%)	***: Anterior wall of left ventricle near apex, anterior two thirds of Inter ventricular septum.***
b) Right coronary artery (30-40%)	***: Posterior wall of left ventricle, Posterior one third of inter ventricular septum***
c) Left circumflex coronary artery (15-20%)	***: Lateral wall of left ventricle.***

REVISED DEFINITION OF MYOCARDIAL INFARCTION: [23]

Criteria for acute evolving or recent MI :

Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI :

1. Typical rise and gradual fall (troponin) or more rapid rise and fall (CK- MB) of biochemical markers of myocardial necrosis with at least one of the following :

- ***a) Ischemic symptorns.***
- ***b) Development of pathologic Q waves on the ECG reading.***
- ***c) ECG changes indicative of ischemia (ST segment elevation or depression)***
- ***d) Coronary artery intervention (eg : coronary angioplasty)***

2. Pathological findings of acute MI .

Criteria for established MI :

Either of the following criteria satisfies the diagnosis for established MI :

1. ***Development of new pathological Q waves on serial ECG readings. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.***

2. ***Pathological findings of a healed or healing MI.***

Several researchers all over the world have been attempting for decades to establish those criteria that best define patients with a poorer prognosis. Taken in toto, the various studies and articles published in the literature may be classified conveniently into two major headings:

1. ***Criteria obtained at the initial physician contact including patient characteristics (eg : age, gender), details of history, the initial clinical examination findings .***
2. ***The laboratory parameters obtained on admission.***

CHEST PAIN :

Despite the recent advances in the laboratory diagnosis of Acute Myocardial Infarction (AMI), the history remains of substantial value in arriving at a diagnosis. A prodrome of chest discomfort can usually be elicited in 20 to 60% of patients with AMI. [24]

The pain of AMI resembles that of classic Angina pectoris, except that is more severe, occurs at rest or with lesser activity than usual, lasts longer (more than 30 minutes) is associated with more systemic symptoms (eg : diaphoresis, nausea) and not relieved by rest or nitrates. On occasion it radiates to the arms. Less common sites of radiation include the abdomen back, lower jaw, and neck. The pain may radiate as high as the occipital area but not below the umbilicus.

In an analysis of the atypical presentations of AMI, Bean et.al., lists the following : [25]

1. ***Congestive Heart failure.***
2. ***Classic angina pectoris (not severe or prolonged).***
3. ***Atypical locations of the pain.***
4. ***Central nervous system manifestations, resulting from a reduced cardiac output, resembling a stroke.***
5. ***Apprehension and nervousness.***
6. ***Sudden Mania and Psychosis.***
7. ***Syncope***
8. ***Over whelming weakness.***
9. ***Acute indigestion***
10. ***Peripheral embolism.***

To this list must be added those patients with "silent" AMI – who have had no symptoms at onset. Such presentations are commoner in diabetes and hypertensives, and both of these conditions are also associated with an increased mortality. [26]

PHYSICAL FINDINGS :

Most patients are anxious and restless, attempting unsuccessfully to relieve the pain by moving about in bed, altering their position, and stretching. Pallor associated with perspiration and coolness of the extremities occurs commonly. About one fourth of patients with Anterior Infarction have manifestations of sympathetic nervous system hyperactivity (tachycardia or hypertension) and upto one half with Inferior Infarction show evidence of para sympathetic hyperactivity (bradycardia or hypotension). [27]

The apical impulse may be difficult to palpate. S_3, S_4 gallop sounds, decreased intensity of first Heart sound and paradoxical splitting of second Heart sound may be there. A transient mid systolic or late systolic apical systolic murmurs may be heard in mitral area. Pericardial friction rub is heard at some time in the course of disease. The carotid pulse is often decreased in volume, reflecting reduced stroke volume. In most transmural MI patients, systolic pressure declines by approximately 10-15 mmHg from the pre infarction state.

SERUM CARDIAC BIOMARKERS :

These cardiac markers are released into the blood in large quantities from necrotic heart muscle after MI.

Creatinine phosphokinase (CK) rises within 4 to 8 hour and generally returns to normal by 48 to 72 hrs . An important draw back of

total CK measurement is its lack of specificity for STEMI (ST Elevation MI), as CK may be elevated with skeletal muscle trauma.

Creatinine phosphokinase MB isoenzyme (CK-.MB) has the advantage over total CK that is not present in significant concentrations in extra cardiac tissue and therefore is more specific. However, cardiac surgery, myocarditis, electrical cardioversion often result in elevated serum levels of CK-MB. A ratio (relative index) of CK-MB mass : CK activity ≥ 2.5 suggests but is not diagnostic of a myocardial rather than a skeletal muscle source for the CK – MB elevation. [28]

Cardiac specific troponin T (cTnT) and cardiac specific troponin I (cTnI) are not normally detectable in the blood of healthy individuals, but may increase after STEMI to levels > 20 times higher than the upper reference limit. They are now the preferred biochemical markers of MI. Levels of cardiac troponins remain elevated for 7 to 1o days after STEMI.

Myoglobin is released into the blood within a few hours of the onset of STEMI. But it lacks cardiac specificity, because it is rapidly excreted in the urine, So blood levels return to the normal range with in 24 hours of the onset of infarction.

Serum lipids are often determined in patients with STEMI. During the first 24 to 48 hours after admission, total Cholesterol and HDL cholesterol remain at or near baseline values, generally fall after 48

hours. The fall in HDL cholesterol after STEMI is greater than total cholesterol. Elevation of white blood cell count (Polymorphonuclear Leukocytosis) appears within a few hours and peaks at 2 to 4 days.

Erythrocyte Sedimentation Rate peaking during the first week and elevated for 1 or 2 weeks. Other markers like C-Reactive Protein, LDH, SGOT also elevated. [29]

CARDIAC IMAGING :

Two dimentional echocardiography, Doppler echocardiography , myocardial perfusing imaging with Thallium 201 or ^{99m}*Tc – Sestamibi scan useful in Acute MI. Radio nuclide ventriculography carried out with* ^{99m}*Tc labeled red blood cells frequently demonstrates wall motion disorders and ejection fraction in MI patients.* [30]

HEMODYNAMIC ABNORMALITIES:

In 1976, Swan, Forrester, and their associates measured the cardiac output and wedge pressure simultaneously in a large series of patients with acute Myocardial Infarction and identified four major hemodynamic subsets of patients. [31]

1. *Patients with normal perfusion and without pulmonary congestion (normal cardiac output and normal wedge pressure).*
2. *Patients with normal perfusion and pulmonary congestion. (normal cardiac output and elevated wedge pressure).*

3. ***Patients with decreased perfusion but without pulmonary congestion. (reduced cardiac output and normal wedge pressure).***
4. ***Patients with decreased perfusion and pulmonary congestion. (reduced cardiac output and elevated wedge pressure).***

This classification which overlaps with a crude clinical classification proposed earlier by Killip and Kimball, has proved to be quite useful, but it should be noted that patients frequently pass from one category to another with therapy and sometimes even spontaneously.

HEMODYNAMIC CLASSIFICATION OF PATIENTS WITH AMI BY KILLIP CLASSIFICATION :

Class	***Definition[31]***
I	*Patients with MI and no evidence of Heart failure.*
II	*Patients with MI, Early Heart failure as manifested by bibasilar rales, and at times S_3 gallop.*
III	*Patients with MI, features of pulmonary edema (Rales >1/2 lung fields)*
IV	*Patients with MI, cardiogenic shock.*

Subset	*Based on invasive monitoring Definition*[32]
I	*Normal hemodynamics* *PCWP <18, CI >2.2*
II	*Pulmonary Congestion* *PCWP >18, CI >2.2*
III	*Peripheral hypo perfusion* *PCWP <18,CI<2.2*
IV	*Pulmonary congestion and peripheral hypo perfusion* *PCWP>18, CI <2.2*

PCWP → Pulmonary Capillary Wedge Pressure

CI → Cardiac Index.

HEART FAILURE :

Heart failure is a state when the heart cannot maintain an adequate cardiac output or can do so only at the expense of an elevated filling pressure.

Heart failure is frequently due to coronary artery disease, tends to affect elderly people and often leads to prolonged disability.

Cardiac output is a function of preload, afterload and myocardial contractility. The primary abnormality in Heart failure is impairment of ventricular function leading to a fall in cardiac output. This activates counter regulatory neurohormonal mechanisms that in normal physiological circumstances would support cardiac function, but in the setting of impaired ventricular function can lead to a deleterious

increase in both afterload and preload. A vicious circle may be established because any additional fall in cardiac output will cause further neurohormonal activation and increasing peripheral vascular resistance. [33]

Stimulation of the renin-angiotensin-aldosterone system leads to vasoconstriction, salt and water retention and sympathetic activation mediated by angiotensin II, which is a potent constrictor of arterioles both in the kidney and systemic circulation. Salt and water retention is promoted by release of aldosterone, endothelin (a potent vasoconstrictor peptide with marked effects on the renal vasculature) and in severe Heart failure. Anti Diuretic Hormone (ADH), Natriuretic peptides are released from the atria in response to atrial stretch, and act as physiological antagonists to the fluid conserving effect of aldosterone and extremely useful in diagnosis, prognosis and monitoring therapy.

After Myocardial Infarction, cardiac contractility is impaired and neurohormonal activation may lead to hypertrophy of non–infarcted segments with thinning, dilatation and expansion of the infarcted segment. (remodeling). This may lead to deterioration in ventricular function and worsening heart failure.

NEURO ENDOCRINE FACTORS KNOWN TO BE INCREASED IN PATIENTS WITH HEART FAILURE : [34]

Norepinephrine	*Endothelin*
Epinephrine	*β – endorphins*
Renin activity	*Calcitonin gene related peptide*
Angiotensin II	*Growth hormone*
Aldosterone	*Cortisol*
Arginine vasopressin	*Tumour necrosis factor - α*
Neuropeptide Y	*Neurokinin – A*
Vaso active intestinal peptide	*Substance – P*
Prostaglandins	*Adrenomedullin*
Atrial naturiuretic factor	

MECHANISMS OF CHRONIC CONGESTIVE HEART FAILURE DUE TO CORONARY ARTERY DISEASE: [35]

Severely depressed LV function :

MYOCARDIAL INFARCTION :

1. ***Large (usually Anterior) transmural infarct with severe depression of LV function (EF<30-35%) due to acute extensive loss of myocardium.***
2. ***Multiple infarcts with extensive myocardial fibrosis (not always clinically recognized) resulting in severe reduction in systolic function (Ischemic cardiomyopathy)***
3. ***Prior myocardial infarction with mitral regurgitation (systolic function mildly to severely decreased).***
4. ***LV aneurysm***
5. ***Late post MI systolic dysfunction, known as LV remodeling.***

MYOCARDIAL ISCHEMIA :

1. ***Extensive regions of hibernating LV myocardium – viable but ischemic (low coronary blood flow) zones of LV systolic dysfunction often accompanied by reversible and irreversible dysfunction fibrosis or scar.***

2. ***Ischemic papillary muscle dysfunction resulting in mitral regurgitation.***

<u>Normal or mildly depressed LV function:</u>

1. ***Diastolic dysfunction related to ischemia and or LV hypertrophy / fibrosis.***
2. ***Severe mitral regurgitation***
3. ***Ventricular septal defect (rare)***

<u>Any of above superimposed on cardiac distress related to other etiologies :</u>

1. ***Valvular heart disease***
2. ***Preexisting non ischemic cardiomyopathy.***

MORTALITY :

Studies involving large number of patients have revealed wide variations in the time elapsed between symptom onset and arrival at the hospital. Researchers have investigated for a relationship between this delay and inhospital mortality. However there are certain complexities in their relationship as follows .

Most sudden deaths in AMI occur due to ventricular Arrhythmias and this risk is maximum in the first hour after symptom onset. With each subsequent hour, the risk decreases, giving rise to the paradoxical situation where a patient who presents late to the hospital

has a lesser risk of sudden death than one who presents early for treatment. 40-60% of patients have some degree of left ventricular dysfunction at presentation if untreated, this may go on to a cardiogenic shock, the commonest cause of inhospital death in AMI. This implies that the patient who presents sufficiently early for shock to be treated or prevented has a better prognosis .

Established beyond reasonable doubt that the patient who presents early enough for thrombolysis has large benefits from reperfusion, vastly improving the prognosis.

Raitt et.al., have shown that each 30 minute delay is associated with a 1% increase infarct size. [36] *Julian D.G analyzing the results of five mortality trials, concluded that gaining about one hour prior to thrombolysis decreases mortality by about 17%.*[37] *Even for patients presenting at later than this window period of 6 hours, thrombolysis can be beneficial, compared to those that do not receive such treatment. Yusuf et al., showed a 22% reduction in mortality for those treated at 12-24 hours. The ISIS – 2 trial extended the concept of beneficial late perfusion with its results revealing a significant benefit beyond 6-12 hours, and even 12-24 hours.*[38] *These findings are confirmed by the ISIS- 3 and EMERAS trials.* [39] *The newer agents such as t–PA, Urokinase or even emergency coronary angioplasty may achieve better late reperfusion than Streptokinase.* [40]

GENDER RELATED DIFFERENCES IN PROGNOSIS :

Unlike in previous years, the incidence of AMI in women is increasing. AMI in women has certain peculiarities. Women are mostly older than men at presentation and are more likely to have atypical pain, Hypertension, Diabetes, unstable angina, hyperlipidemia, congestive cardiac failure or silent infarctions are all commoner in women. Women more frequently have non – Q AMI and tend to present later to hospital. [41] ***Of interest after STEMI, younger women but not older women have higher rates of inhospital mortality than men of the same age.***

<u>The pathogenic mechanisms different in women include :</u> [42]

- ***A greater incidence of vasospastic and micro circulatory angina.***
- ***Different plaque components (more cellular and fibrous tissue).***
- ***Different endothelial tone due to hormonal influences.***
- ***Different hemostasis (higher fibrinogen and factor VIII levels.***

DIABETES AND ITS EFFECTS ON PROGNOSIS :

The early pioneering studies an AMI, especially those by killip and Norris suggested that the presence of diabetes had a significant effect on the mortality. The famous Framingham Heart study indicated that diabetes increased the risk of death in women, but not men, after a

first AMI. They tend to have larger infarcts, and show a greater incidence of shock, cardiac failure and metabolic problems.[43]

HYPERTENSION AND ITS EFFECT ON PROGNOSIS :

The GISSI – 2 trial one of the largest ever series of AMI patients (11,843 patients, of which 3306 were hypertensive) investigated the prognostic value of hypertension in those receiving thrombolysis. Their results show a significantly higher mortality for hypertensives LV failure and recurrent ischemic events were also more common among hypertensives. [44]

PULSE, BLOOD PRESSURE AND ITS EFFECT ON PROGNOSIS:

The SPRINT study group, reporting in October 1995, found an increasing mortality with increasing heart rates at admission from less than 70 to more than 90 / minute. At even higher heart rates, the increasing trend of mortality was confined to those with heart failure. A combination of a rate more than 90 with a systolic pressure less than 120 mmHg was a powerful predictor of inhospital mortality.

Patients develop cardiogenic shock when more than 40% of the myocardium is destroyed. Beyond the immediate phase, cardiogenic shock is the commonest cause of mortality. The hospital mortality for cardiogenic shock is in the region of 60-80%. The incidence of ventricular arrhythmias and heart block was found to be higher in

these patients. (Killip et.al.,) By multivariate analysis of their cohort of 845 patients. Hands et.al., found that the predictors of cardiogenic shock included age >65, ejection fraction <35%, peak CK-MB value more than 160 IU/ L and a history of diabetes or prior infarction. [45]

PROGNOSTIC PARAMETERS AT HOSPITAL ADMISSION IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION : [46]

Parameters	*Effect on prognosis*
Age	*Prognosis worsens with increasing age*
Sex	*Women have a worse prognosis than men*
Heart Rate	*Heart rate >100/mt indicates a poor prognosis*
Cardiogenic shock	*A very high early mortality*
Congestive Heart failure	*Indicates a poor prognosis even when treated successfully*
ST segment deviation	*The more ST segment deviation or Q wave formation, the larger the infarct and the worse prognosis.*
Enzymes	*Not admission levels, but evolving rise in cardiac enzymes estimate infarct size.*
Troponin levels	*Elevated admission troponin – I or troponin – T indicates a worse prognosis even in the absence of rising CPK or CK-MB.*

URIC ACID BIOCHEMISTRY :

Uric acid is the final breakdown product of Purine metabolism. Most mammals have the ability to catabolize purines to allantion, a more water soluble end product.

Purines such as adenosine and guanine from the breakdown of ingested nucleic acids or from tissue destruction are converted into uric acid primarily in the liver. Uric acid is transported in the plasma from the liver to the kidney, where it is filtered by the glomerulus. Reabsorption of 98-100% of the uric acid in the glomerular filtrate occurs in the proximal tubules. Small amounts of uric acid are secreted by the distal tubules into the urine. This route accounts for about 70% of the daily uric acid excretion. The remainder is excreted into the GI tract and degraded by bacterial enzymes. Uric acid is produced only in tissues that contain xanthine oxidase, primarily the liver and small intestine.

Nearly all of the uric acid in plasma is present as monosodium urate. At the pH of plasma, Urate is insoluble; at concentrations greater than 6.4 mg/dl the plasma is saturated. As a result, urate crystals may form and precipitate in the tissue. In the urine at pH<5.7, uric acid crystals may form.

HUMANS CATABOLIZE PURINES TO URIC ACID :[47]

Humans convert the major purine nucleosides adenosine and guanosine to the excreted end product uric acid via the intermediates and reactions. Adenosine is first deaminated to inosine by adenosine deaminase. Phosphorolysis of the N-glycosidic bonds of inosine and guanosine, catalyzed by purine nucleoside phosphorylase releases ribose 1 – phosphate and a purine base. Hypoxanthine and guanine next form xanthine in reactions catalysed by xanthine to uric acid in a second reaction catalyzed by xanthine oxidase and guanase respectively. Xanthine is then oxidised to uric acid in a second reaction catalyzed by xanthine oxidase. Thus xanthine oxidase provides a potential locus for pharmacologic intervention in patients with hyperuricemia.

Net excretion of total uric acid in normal humans averages 400-600 mg/24hr. In mammals other than higher primates, the enzyme uricase cleaves uric acid, forming the highly water soluble end product allantion. However, since humans lack uricase, the end product of purine catabolism in man is uric acid. Amphibians, birds and reptiles also lack uricase and excrete uric acid and guanine as end products of purine catabolism.

Humans catabolize purines to week acid uric acid. (pk 5.8) which depending on urinary pH, exists as the relatively insoluble acid (at acidic pH) or its more soluble sodium urate salt. Urate crystals are

diagnosic of gout, a metabolic disorder of purine catabolism. Other disorders include Lesch – Nyhan syndrome, von Gierkes disease and hypouricemias.

HYPERURICEMIA :

It can result from increased production or decreased excretion of uric acid or from a combination of the two processes. Hyperuricemia is defined as a plasma concentration of > 7mg/dl in males and > 6mg/dl in females.

CLASSIFICATION OF HYPERURICEMIA BY PATHOPHYSIOLOGY :[48]

URATE OVERPRODUCTION :

- ***Primary idiopathic***
- ***HPRT deficiency***
- ***PRPP synthetase Over activity***
- ***Hemolytic processes***
- ***Lymphoproliferative Diseases***
- ***Myeloproliferative Diseases***
- ***Glycogenesis III, V, VII,***
- ***Rhabdomyolysis***
- ***Exercise***
- ***Alcohol***
- ***Obesity***
- ***Purine rich diet***
- ***Polycythemia vera***
- ***Psoariasis***
- ***Pagets disease***

DECREASED URIC ACID EXCRETION:

- ***Primary idiopathic***
- ***Renal insufficiency***
- ***Polycystic kidney disease***
- ***Diabetes insipidus***
- ***Hypertension***
- ***Acidosis***
  - ***Lactic acidosis***
  - ***Diabeticketo acidosis***
- ***Starvation ketosis***
- ***Berylliosis***
- ***Sarcoidosis***
- ***Lead intoxication***
- ***Hyperparathyroidism***
- ***Hypothyroidism***
- ***Toxaemia of pregnancy***
- ***Bartters syndrome***
- ***Down syndrome***
- ***Drug ingestion***
- ***Salicylates (>2g/d)***

Diuretics
Alcohol
Levodopa
Ethambutol
Pyrazinamide
Cyclosporine

COMBINED MECHANISM :

- ***Glucose - 6 – Phosphatase deficiency***
- ***Fructose – 1 – Phosphate aldolase deficiency***
- ***Alcohol***
- ***Shock***

Note : HPRT : Hypoxanthine Phospho Ribosyl Transferase

PRPP : Phospho Ribosyl Pyro Phosphate.

Accelarated purine nucleotide degradation can also cause hyperuricemia i.e with conditions of rapid cell turnover, proliferation or

cell death, as in Leukemic blast crisis, cytotoxic theraphy for malignancy, hemolysis or rhabdomyolysis. Hyperuricemia can result from excessive degradation of muscle ATP after strenuous physical exercise or status epilepticus.

Hyperuricemia of Myocardial Infarction, smoke inhalation and acute respiratory failure may also be related to accelerated breakdown of ATP.

Secondary causes of hyperuricemia : [49]

1. *Obesity*
2. *Dyslipidemia (Usually type 4) with raised VLDL and normal cholesterol levels; hypercholestrelemia with increased LDL cholesterol and Low HDL cholesterol.*
3. *Hypertension*
4. *Insulin resistence with hyperinsulinemia and impaired glucose tolerance.*
5. *Ischemic Heart Disease.*

OXIDATIVE STRESS :

There is evidence that oxidative stress is increased both systemically and in the myocardium of patients with Heart failure.[50] *Increased oxidative stress may be due to reduced antioxidant capacity of the increased production of reactive oxygen species, which may be*

a consequences of mechanical strain on the myocardium or stimulation by neuro hormones and inflammatory cytokines. Possible sources of increased production of reactive oxygen species include the mitochondria, xanthine oxidase and NADPH oxidase.[51] Reactive oxygen species can stimulate myocyte hypertrophy, reexpression of fetal gene programs and apoptosis in cardiac myocytes in culture.[52]

There is no evidence that uric acid is toxic to myocardium. Hyperuricemia may be a marker of coincident cardiac disease, but not a causal risk factor. The increased plasma uric acid concentration observed in patients with ischemic heart disease could arise from upregulated vascular adenosine synthesis associated with ischemia and the subsequent degradation of adenosine to uric acid. The relationship of urate to endothelial function is complex. Plasma uric acid accounts for 60% of the free radical scavenging activity in human plasma. It interacts with peroxynitrite to form a stable Nitric oxide donar, so promoting vasodilaiton and reducing the potential for peroxynitrite induced oxidative damage. Conversely it could have an adverse effect on endothelial function by promoting leukocyte adhesion to the endothelium.[53]

URIC ACID PREDICTS CLINICAL OUTCOMES IN HEART FAILURE :

Insights Regarding the Role of Xanthine Oxidase and Uric Acid in Disease Pathophysiology :

In the current issue of circulation, Anker and Colleagues[54] report that elevated levels of uric acid predict mortality and the need for heart transplantation in patients with congestive heart failure. Serum concentrations of uric acid added important prognostic information alone and when combined with measures of cardiac function (ejection fraction) and patient functional status (maximal oxygen consumption with exercise) and were independent of renal function, serum sodium, Blood urea, diuretic usage, and patient age.

A consideration of the mechanism of uric acid production and metabolism offers insight into the relationship between uric acid levels and Heart failure outcomes. Moreover, uric acid levels may reflect xanthine oxidase pathway activity, which has the potential to myocardial energetics and myofilament calcium sensitivity.[55]

POTENTIAL MECHANISMS FOR INCREASED URIC ACID IN HEART FAILURE :

Uric acid is a metabolic byproduct of purine metabolism. Serum uric acid may increase in the failing circulation because of increased generation, decreased excretion, or a combination of the 2 factors.

There are several possible contributors to increased uric acid production in Heart failure, including increased abundance and activity of xanthine oxidase, increased conversion of xanthine dehydrogenase to xanthine oxidase, or increased xanthine oxidase substrate resulting from enhanced ATP breakdown to adenosine and hypoxanthine. As uric acid is excreted primarily by the kidney, decreased renal perfusion could lead to increased uric acid levels. To the extent that Heart failure leads to tissue ischemia and a rise in serum lactate, renal uric acid excretion can be further impaired as lactate competes with urate via an organic anion exchanger in the proximal tubule. [56]

PATHOPHYSIOLOGICAL ROLE OF THE XANTHINE OXIDASE PATHWAY IN HEART FAILURE:

The elevation in serum uric acid may reflect increased xanthine oxidase pathway activity and in turn the generation of superoxide and resultant oxidative stress via the xanthine oxidase system. [57] *Xanthine oxidase is upregulated within the heart in both experimental and human heart failure. Much had previously been made of the difficulty in identifying xanthine oxidase within the hearts of certain mammalian species, including humans,* [58] *nevertheless, it is clear that xanthine oxidase, which is produced in highest abundance in the liver and gut may circulate in the blood and adhere to endothelium in distant sites. Moreover, xanthine oxidase is expressed in cardiac myocytes, as*

shown by immunohistochemistry and may participate in intracrine signaling.

PATHOPHYSIOLOGICAL ROLE OF URIC ACID IN HEART FAILURE :

Beyond xanthine oxidase activity, recent experimental studies suggest that uric acid itself may have a role in cardiovascular and renal pathophysiology. This might seem surprising, as uric acid can function as an antioxidant both by itself and by promoting superoxide dismutase activity,[59] and might therefore be considered potentially protective. However, uric acid potently stimulates vascular smooth muscle cell proliferation in vitro, an effect mediated by stimulation of mitogen-activated protein kinases, cyclooxygenase –2, and platelet derived growth factor.[60]

CLINICAL UTILITY OF URIC ACID MEASUREMENTS :

From a clinical perspective, the current study raises the issue of whether serum uric acid levels should be routinely measured in Heart failure patients.[61] Indeed this is likely to be a controversial issue, and one which will require evaluation in the context of measurement of brain natriuretic peptide (BNP), a serum marker that also possesses prognostic and diagnostic value in Heart failure patients. Much in the same way as BNP has been evaluated, it will be of great value to

assess whether uric acid levels change in response to Heart failure therapy in a manner that predicts clinical outcome.

Whether or not uric acid levels are ready for clinical use, the observation that uric acid levels possess prognostic information adds an extremely intriguing finding to mounting evidence that xanthine oxidase and uric acid play pathophysiological roles in Heart failure and its precursor, hypertension. Indeed, the amassing data have led to the planning of a clinical trial entitled A phase II – III prospective, Randomized, Double – Blind, Placebo – Controlled Efficacy and safety study of Oxypurinol Added to Standard theraphy in patients with NYHA class III- IV Congestive Heart Failure (OPT-CHF) initiated in 2003, which will test clinical outcomes using a composite endpoint comprising measures of heart failure morbidity,exercise capacity, and mortality. The findings of Anker and colleagues, therefore, not only bring to light a potentially new diagnostic test but also provide a novel line of evidence that the xanthine oxidase pathway and / or uric acid itself may be of pathophysiological importance in heart failure progression.

MATERIALS AND METHODS

STUDY POPULATION:

This study was conducted in the Department of medicine and Department of cardiology Thanjavur medical College, Thanjavur, Tamil Nadu during the period of August 2004 to August 2006. Total number of patients included in this study were 100. There were 78 males 22 females patients ranging from 23 years to 83 years.

STUDY DESIGN :

This study is a prospective study. This study is aimed to assess the prognostic role of serum Uric acid level following Acute Myocardial Infarction and correlating the levels with short term complications.

This study included 100 patients of Acute Myocardial Infarction of which patient who had a normal Uric acid level were taken as a control and the rest who had elevated Uric acid level were taken up as study population.

In both groups the complications and short term outcome were compared.

INCLUSION CRITERIA :

Patients with a diagnosis of Acute ST Elevation Myocardial Infarction were entered into the study. A definite diagnosis of Acute ST

Elevation Myocardial Infarction was made if the patients satisfied the following criteria:

1. *A History of typical retrosternal compressive chest pain lasting for more than 30 minutes, not relieved by rest or nitrates.*
2. *Typical ECG changes of Acute ST Elevation Myocardial Infarction (ST,T changes in two contiguous leads)*

EXCLUSION CRITERIA :

1. *Patients with elevated renal parameters.*
2. *Patients with Gout.*
3. *Patients with History of chronic alcoholism.*
4. *Patients with previous History of Ischemic Heart Disease and on Aspirin theraphy.*
5. *Patients with Diabetes mellitus.*
6. *Patients on Diuretic theraphy.*

Above patients were excluded because the coexisting disease or drug theraphy might itself produce a high Uric acid level.

Very late presentations of patients more than 72 hours also excluded since uric acid level tends to fall subsequently (Journal of the Indian Medical Association 1977 Sep1).

VARIABLES RECORDED DURING THE STUDY:

Routine History, physical examination, Routine laboratory investigations were performed in all subjects.

1. ***Presenting History :***
    - ***Duration of chest discomfort***
    - ***Associated symptoms like sweating, palpitations, dyspnoea.***
    - ***Time of onset of symptoms.***
2. ***Killip's classification on admission :***
3. ***Admission Electrocardiogram (ECG) :***
    a) ***Site of infarction : Anterior, Inferior, Lateral, Right ventricular, Global.***
    b) ***No of leads with Q waves or ST Elevation.***
4. ***Laboratory Investigations :***
    - ***Full Blood count***
    - ***Blood Sugar, Blood Urea, Serum creatinine, Serum Electrolytes.***
    - ***Serum Uric acid level on admission.***
    - ***Urine Albumin, Sugar, Deposits.***
    - ***Serum cholestrol.***

Qualifying patients received thrombolytic theraphy with 1.5 million units of Streptokinase followed by Heparin for 5 – 7 days.

Assessment of left ventricular ejection fraction by Echocardiography was performed either on day 4 or 5 of hospitalisation in most patients or earlier if clinically indicated.

URIC ACID ESTIMATION :

Immediately after admission blood sample of 3cc was drawn by venipuncture and transferred to dry plain bottle and taken to biochemistry laboratory. The method used for analysis is Enzymatic method (Uricase method) by using Auto analyser.

In our laboratory, values taken as normal range[62]

For Males : 3.4 - 7.0 mg/dl

For Females : 2.4 - 6.0 mg/dl

METHODOLOGY:

Methods using URICASE, the enzyme that catalyzes the oxidation of uric acid to allantoin are most specific.[63] *The simplest of these methods measures the differential absorption of uric acid and allantoin at 293 nm.* [64] *The difference in absorbance before and after incubation with URICASE is proportional to the uric acid concentration. This method has been proposed as candidate reference method.*[65] *This method was done in our study. This is the most specific method.*

FOLLOW UP :

All the patients were followed up for a period of 10 days . During follow up any changes in killip's classification, features of Cardiac failure, Arrhythmias and any Mortality were noted in both group of patients. Routine daily physical examination was done. ECG's were taken daily and additional investigations carried out if necessary. Patients were discharged at 11th day if they were stable otherwise their hospital stay was prolonged.

Framingham criteria for Heart failure like JVP elevation , Basal Rales, Acute pulmonary edema, S_3 gallop, Tachycardia (>120/mt), Lower extremity edema were used in this study for making a diagnosis of CCF. [66]

All patients were subjected to continuous cardiac monitoring with the aim of identifying various Arrhythmias . In this study the incidence of Arrhythmias like Atrial fibrillation, Atrial flutter, Paroxysmal Supra Ventricular Tachycardia, Sustained and illsustained Ventricular Tachycardia and Ventricular fibrillation were noted in both group of patients. Patients presented with beningn ventricular premature beats were not included into the Arrhythmias category.

RESULTS & OBSERVATIONS

The study population consisted of 100 patients with 78 males and 22 females. All patients belonged to places around Thanjavur District. All patients were admitted in I.C.C.U initially for 5 days then cared in adjoining intermediate cardiac care ward and discharged after an average period of 10 days provided there were no complications.

The various observations made in this study are depicted below

AGE INCIDENCE (Fig :1)

Table : 1

Age in years	***21-30***	***31-40***	***41-50***	***51-60***	***61-70***	***71-80***	***81-90***
No of cases	*2*	*10*	*20*	*37*	*22*	*7*	*2*

SEX INCIDENCE (Fig :2)

Table : 2

Sex	***No of cases***	***Percentage***
Males	*78*	*78*
Females	*22*	*22*

CONTROL AND STUDY POPULATION (Fig :3&4)

Table : 3

Sex	***Control Population (53)***	***Study population(47)***
Male	*43 (81%)*	*35 (74%)*
Female	*10 (19%)*	*12 (26%)*

DISTRIBUTION OF PATIENTS ACCORDING TO URIC ACID LEVEL & SEX – IN TOTAL POPULATION (Fig :5)

Table : 4

Uric acid (mg/dl)	***3.0-3.9***	***4.0-4.9***	***5.0-5.9***	***6.0-6.9***	***7.0-7.9***	***8.0-8.9***	***9.0-9.9***
Male	*4*	*5*	*10*	*23*	*21*	*10*	*5*
Female	*2*	*1*	*5*	*8*	*3*	*2*	*1*

KILLIP CLASS IN HIGH SERUM URIC ACID POPULATION

(STUDY GROUP) (Fig :6)

Table : 5

Killip Class	***I & II***	***III & IV***
No of patients	*19*	*28*

Percentage of patients with
Killip I & II in high serum uric acid population $= \frac{19 \times 100}{47}$
$= 40\ \%$

Percentage of patients with
High killip class III & IV in High serum uric acid population $= \frac{28 \times 100}{47}$
$= 60\ \%$

KILLIP CLASS IN NORMAL SERUM URIC ACID POPULATION

(CONTROL GROUP) (Fig :7)

Table : 6

Killip Class	***I & II***	***III & IV***
No of Patients	*40*	*13*

Percentage of patients with
Killip I & II in normal uric acid population $= \frac{40 \times 100}{53}$
$= 75\%$

Percentage of patients with
Killip III & IV in normal uric acid population $= \frac{13 \times 100}{53}$
$= 25\ \%$

TYPE OF INFARCTION

Table : 7

TYPE	***IN HIGH SERUM URIC ACID POPULATION***	***IN NORMAL SERUM URIC ACID POPULATION***
AWMI	*19*	*18*
ASMI	*5*	*11*
IWMI	*5*	*12*
Infero posterior MI	*6*	*7*
IWMI + RVMI	*4*	*3*
Lateral wall MI	*6*	*1*
Global MI	*2*	*1*

INCIDENCE OF HEART FAILURE IN TOTAL POPULATION (Fig :8)

Table : 8

Total no of patients studied	***No of patients who developed Heart failure***
100	*41*

ie. 41 % of patients in the study developed Heart failure .

HEART FAILURE ACCORDING TO SEX (Fig :9)

Table : 9

Total no of Heart failure patients	*Male (%)*	*Female (%)*
41	*33 (80%)*	*8 (20 %)*

PROPORTION OF HEART FAILURE CONTRIBUTED BY PATIENTS WITH NORMAL & HIGH SERUM URIC ACID LEVEL (Fig :10)

Table : 10

Total no of patients with Heart failure	*No of patients with high serum uric acid*	*No of patients with normal serum uric acid*
41	*30*	*11*

$$\text{Contribution of patients with High Serum uric acid level to Heart failure} = \frac{30 \times 100}{41} = 73\ \%$$

$$\text{Contribution of patients with Normal serum uric acid level to Heart failure} = \frac{11 \times 100}{41} = 27\ \%$$

It is observed that patients with high uric acid level contributes 73% to the total incidence of Heart failure.

INCIDENCE OF HEART FAILURE IN PATIENTS WITH HIGH SERUM URIC ACID LEVEL (STUDY GROUP) (Fig :11)

Table : 11

No of patients with high serum uric acid level	*No of patients with Heart failure*
47	*30*

$$\textit{Incidence} = \frac{30 \times 100}{47}$$

$$= 64\ \%$$

ie. 64 % of patients with high uric acid level developed Heart failure.

ie. 36 % of patients with high uric acid level didn't develop Heart failure.

INCIDENCE OF HEART FAILURE IN PATIENTS WITH NORMAL SERUM URIC ACID LEVEL (CONTROL GROUP) (Fig :12)

Table : 12

No of patients with normal serum uric acid level	*No of patients with Heart failure*
53	*11*

$$\textit{Incidence} = \frac{11 \times 100}{53}$$

$$= 21\ \%$$

ie. 21 % of patients with normal uric acid level developed Heart failure.

Ie. 79 % of patients with normal uric acid level didn't develop Heart failure.

ECHOCARDIOGRAM ANALYSIS (Fig :13)

Table : 13

Echo findings	*In high uric acid patients*	*In normal uric acid patients*
Normal LV systolic function	*6*	*36*
Mild LV dysfunction	*14*	*9*
Moderate LV dysfunction	*13*	*3*
Severe LV dysfunction	*3*	*2*
Total	*36*	*50*

INCIDENCE OF ARRHYTHMIAS (IN TOTAL POPULATION) (Fig :14)

Table : 14

Total no of patients studied	*No of patients who developed Arrhythmias*
100	*7*

ie. 7 % of patients in the study developed Arrhythmias.

ARRHYTHMIAS ACCORDING TO SEX (Fig :15)

Table : 15

Total no of Arrythmia patients	***Male (%)***	***Female (%)***
7	*6 (86%)*	*1 (14 %)*

PROPORTION OF ARRHYTHMIAS CONTRIBUTED BY PATIENTS WITH NORMAL & HIGH SERUM URIC ACID LEVEL (Fig :16)

Table : 16

Total no of patients with Arrhythmias	***No of patients with high serum uric acid***	***No of patients with normal serum uric acid***
7	*5*	*2*

Contribution of patients with High serum uric acid level to Arrhythmias = $\frac{5 \times 100}{7}$ = ***71%***

Contribution of patients with Normal serum uric acid level to Arrhythmias = $\frac{2 \times 100}{7}$ = ***29 %***

It is observed that patients with high uric acid level contributes 71% to the total incidence of Arrhythmias.

INCIDENCE OF ARRHYTHMIAS IN PATIENTS WITH HIGH SERUM URIC ACID LEVEL (STUDY GROUP) (Fig :17)

Table : 17

No of patients with high serum uric acid level	*No of patients with Arrhythmias*
47	*5*

Incidence = 5 x 100 / 47

= 11%

ie. 11 % of patients with high uric acid level developed Arrhythmias.

INCIDENCE OF ARRHYTHMIAS IN PATIENTS WITH NORMAL URIC ACID LEVEL (CONTROL GROUP) (Fig :18)

Table : 18

No of patients with normal uric acid level	*No of patients with Arrhythmias*
53	*2*

Incidence = 2 x 100 / 53

= 4 %

ie. 4% of patients with normal uric acid level developed Arrhythmias.

INCIDENCE OF MORTALITY (IN TOTAL POPULATION) (Fig :19)

Table : 19

Total no of patients studied	***No of patients died***
100	*15*

ie 15 % of patients in the study died.

`MORTALITY ACCORDING TO SEX (Fig :20)

Table : 20

Total no of deaths	***Male (%)***	***Female (%)***
15	*14 (93%)*	*1 (7%)*

PROPORTION OF MORTALITY CONTRIBUTED BY PATIENTS WITH NORMAL & HIGH SERUM URIC ACID LEVEL (Fig :21)

Table : 21

Total no of deaths	*No of patients with high uric acid level*	*No of patients with normal uric acid level*
15	*12*	*3*

Contribution of patients with

High serum uric acid level to Mortality $= \frac{12 \times 100}{15}$

$= 80\ \%$

Contribution of patients with

Normal serum uric acid level to Mortality $= \frac{3 \times 100}{15}$

$= 20\%$

It is observed that patients with high uric acid level contributes 80% to the total incidence of mortality.

INCIDENCE OF MORTALITY IN PATIENTS WITH HIGH SERUM URIC ACID LEVEL (STUDY GROUP) (Fig :22)

Table : 22

No of patients with high serum uric acid level	*No of deaths*
47	*12*

Incidence $= \frac{12 \times 100}{47}$

$= 26\ \%$

ie. 26 % of patients with high uric acid level died in the study.

INCIDENCE OF MORTALITY IN PATIENTS WITH NORMAL SERUM URIC ACID LEVEL (CONTROL GROUP) (Fig :23)

Table : 23

No of patients with normal uric acid level	*No of deaths*
53	*3*

$$\textit{Incidence} = \frac{3 \times 100}{53}$$

$$= 6\ \%$$

ie. 6 % patients with normal uric acid level died in the study.

MORTALITY IN AGE GROUP (Fig :24)

Table : 24

Age	*Total no of patients*
41-50	*3*
51-60	*6*
61-70	*4*
71-80	*1*
81-90	*1*

DISCUSSION

Total number of patients included in this study was100, out of which 47 patients had elevated level of uric acid above normal range following Acute Myocardial Infarction.

AGE :

Of the 100 patients 2 patients were in the age group of 21-30 years, 10 patients were in the age group of 31-40 years, 20 patients were in the age group of 41 –50 years, 37 patients were in the age group of 51-60 years, 22 patients were in the age group of 61 –70 years, 7 patients were in the age group of 71-80 years and 2 patients were in the age group of 81 –90 years (Table1 & Fig 1).

SEX :

In this study number of male patients were 78, while number of female patients were 22. (Table 2 & Fig 2)

CONTROL & STUDY POPULATION:

Out of 100 patients studied 53 patients had Normal uric acid level and they were taken up as control. Of which 43 (81%) were males and 10 (19%) were females. The rest 47 patients had elevated uric acid level and they were taken up as study group. Of which 35(74%) were males and 12 (26%) were females. (Table 3, Fig : 3 & 4). Both were compared with various out comes.

CLINICAL STATUS- KILLIP CLASS & URIC ACID:

In this study 43 patients presented with Killip class I, 16 patients presented with Killip class II, 18 patients presented with Killip class III, 23 patients presented with Killip class IV. Killip class III & IV were taken as high risk category in this study and evaluated whether high uric acid concentration after myocardial infarction correlated with this high risk Killip class.

When clinical status of patients based on killip class I to IV and uric acid were analysed, the following observations were made.

In the control group who had normal serum uric acid level, 75 % belonged to I & II Killip class and only 25% belonged to Killip class III & IV as against the study 40 % Killip class I & II and 60% Killip class III & IV which parallely correlates with the elevated uric acid level and the clinical status (Table 5 & 6. Fig 6 & 7)

Our study correlates with kojima S, Sakamoto et al., (American journal of cardiology, 2005 Aug 15) who also showed patients who had high uric acid level belonged to higher Killip class. Hence uric acid can also be used as an predictor of prognosis, but also a predictor of severity.

TYPE OF INFARCTION & URIC ACID :

In this study 37 patients presented with Anterior Wall Myocardial Infarction (AWMI) of which 19 patients had high uric acid level, 16

patients presented with Antero Septal Myocardial Infarction (ASMI), of which 5 patients had high uric acid level, 17 patients presented with Inferior Wall Myocardial Infarction (IWMI), of which 5 patients had high uric acid level, 13 patients presented with Infero posterior wall Myocardial Infarction, of which 6 patients had high uric acid level , 7 patients presented with inferior and Right Ventricular Myocardial Infarction (RVMI), of which 4 patients had high uric acid level, 7 patients presented with Lateral Wall Myocardial Infarction , of which 6 patients had high uric acid level, 3 patients presented with Global Myocardial Infarction ,of which 2 patients had high uric acid level.

When areas of infarction and uric acid levels were observed, an increased level of uric acid in Anterior wall Myocardial Infarction was noted. This cannot be taken into statistical account, because the overall incidence of Anterior Wall Myocardial Infarction itself was high (Table 7).

HEART FAILURE :

41 out of 100 patients in this study had Heart failure in the post Myocardial Infarction period. So the incidence of heart failure was 41 %. Of which 33(80%) were males, 8 (20%) were females.(Table 8&9, Fig 8&9)

It was observed that among 41 Heart failure patients, 30 patients had high uric acid level and 11 patients had normal uric acid level. So

patients who had high uric acid level and normal uric acid level contributed to 73% and 27 % respectively to Heart failure. (Table 10, Fig. 10)

It was also found that 30 patients out of 47 patients with high uric acid level had Heart failure amounting to an incidence of 64 % Heart failure in this group. While only 11 out of 53 patients with normal uric acid level had Heart failure. ie. Only 21% of patients with normal uric acid level had Heart failure. (Table 11&12, Fig 11 &12)

The above figures suggest that the occurrence of Heart failure is high in patients with high uric acid level. Our studies comparable with other studies who showed similar findings and elevated serum uric acid level is an early predictor of short term outcome.

Kojima S. Sakamoto et al, (American journal of cardiology 2005 Aug 15) Anker SD, Doehner W et.al., (Circulation 2003, Apr 22; circulation 2003 Nov 25) Sakai H, Tsutamoto T et. al.,(J cardiol.2006 May), Joshua M, Hare MD et.al., (circulation 2003, American Heart association), Virendra singh, RK Goyal et.al., (Journal of the Indian Medical association 1977 Sep 1) studies support this study. Their studies revealed that serum uric acid level reflects circulatory xanthine oxidase activity and oxidative stress production. Increased serum uric acid level has been identified in patients who have congestive cardiac failure and is a marker of poor prognosis in such patients.

ECHOCARDIOGRAM:

In high uric acid population, 6 patients had normal LV function, 14 patients had mild LV dysfunction, 13 patients had moderate LV dysfunction, 3 patients had severe LV dysfunction.

In normal uric acid level population, 36 patients had normal LV function, 9 patients had mild LV dysfunction, 3 patients had moderate LV dysfunction, 2 patients had severe LV dysfunction. (Table 13, Fig 13).

Patients who had elevated serum uric acid level in the study group showed moderate to severe LV dysfunction (34%) This has correlated with an initial observation of cardiac failure which was 27% in this population.

So serum uric acid level can also be correlated with Echocardiographic cardiac dysfunction later, retrospectively with clinical findings earlier.

So uric acid level can be used as a definite predictor of cardiac failure.

ARRHYTHMIAS :

7 out of 100 patients developed Arrhythmias in this study. So the incidence of Arrhythmias was 7% of which 6 (86%) were males, 1 (14%) was female. 3 patients had ventricular tachycardia and 4 patients had supra ventricular tachycardia (Table 14 & 15, Fig 14&15).

It was observed that among 7 Arrhythmias 5 patients had high uric level and 2 patients had normal uric acid level. So patients who had high uric acid level and normal uric acid level contributed to 71% and 29% respectively to Arrhythmias (Table 16 , Fig 16) .

It was also found that 5 patients out of 47 patients with high uric acid level had Arrhythmias amounting to an incidence of 11% Arrhythmias in this group. While only 2 out of 53 patients with normal uric acid level had Arrhythmias. ie.only 4 % of patients with normal uric acid level had Arrhythmias. (Table 17&18, Fig 17&18).

The above findings suggest that the occurrence of Arrhythmias is also high in patients with high uric acid level.

This observation can be matched with the outcome of a large randomized double blind placebo control clinical trial "Oxypurinol theraphy for CHF" conducted in 2003, which could establish a beneficial effect for oxypurinol in reducing the incidence of Arrhythmias and other adverse cardiac events by lowering serum uric acid level.

The above trial & our trial tells there is a high incidence of Arrhythmias when there is an elevated serum uric acid level and it is hypothetical an increased uric acid level may be arrhythmogenic. Further studies are needed to conclude.

MORTALITY :

15 out of 100 patients died due to their cardiac ailments in this study. This amounts to mortality rate of 15% of which 14 (93%) were males, 1 (7%) was female. (Table 19&20, Fig 19&20).

To find out the prognostic significance of elevated uric acid level following Acute Myocardial Infarction, mortality rate in patients with normal and high uric acid level were separately calculated.

It was observed that among 15 deaths 12 deaths were contributed by patients with high uric acid levels and 3 deaths by those who had normal uric acid levels. Thus 80% of death in post infarction period occurred in those who had a high uric acid level and only 20% in those who had a normal uric acid level. (Table 21, Fig 21)

It was also found that 12 out of 47 patients with high uric acid level died. This implies a mortality rate of 26%.Like wise a mortality rate of 6 % was observed for patients with normal uric acid level following Myocardial Infarction (Table 22&23, Fig 22&23).

This striking difference in the mortality figures for both group of patients implies uric acid level can be used as a predictor of mortality following Myocardial Infarction.

It this study ,4 patients died on the day of admission, 6 patients died on 2nd day, 4 patients died on 3rd day, 1 patient died on 7th day.

Out of 15 deaths, 3 patients (20%) were in the age group of 41-50 years, 6 patients (40%) were in the age group of 51-60 years, 4 patients (26%) were in the age group of 61-70 years, 1 patient (7%) was in the age group of 71-80 years and 1 patient (7%) was in the age group of 81-90 years. (Table 14, Fig 24)

Kojima S, Sakamoto et. al.,(American journal of cardiology 2005 Aug 15) Fang J, Alderman M H et. al., (Serum uric acid and cardiovascular mortality, JAMA 2000) Bengtsson C, Lapidus L et.al., (Acta Med Scand 1998) Freedman DS, Williamson DF et.al., (Relation of serum uric acid to mortality and Ischemic Heart disease Am. J. Epidemiol 1995) Culleton BF, Lassonmia et.al ., (Serum uric acid and risk of cardiovascular disease and death Ann. Intern. Med July 6. 1999) studies supports this study. This study revealed that patients who developed short term adverse events like mortality following Myocardial Infarction had high uric acid concentrations.

Our study also parallels with previous authors and uric acid can be used as a good predictor of mortality.

CONCLUSION

1. ***Measuring serum Uric acid level is one of the predictable prognostic indicator in Acute Myocardial Infarction and one of the early and short term predictor.***
2. ***A high serum Uric acid level correlated with short term mortality in Acute Myocardial Infarction.***
3. ***Elevated serum Uric acid is strongly associated with cardiac Arrhythmias as against controls and can be used as an immediate prognostic indicator in Acute Myocardial Infarction.***
4. ***Elevated serum Uric acid level may be Arrhythmogenic. Further studies require to confirm and to treat.***
5. ***There is a strong correlation of elevated serum Uric acid and cardiac failure***
6. ***Patients with high Uric acid level belonged to higher Killip class status(III & IV) .***
7. ***Elevated Uric acid level had a objective correlation with Echo cardiographic evaluation of LV dysfunction.***
8. ***Our study is compatible with other studies done with Uric acid as a predictor.***

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BIBLIOGRAPHY

1. ***Roger's WJ, Canto JG et.al., Temporal trends in the treatment of over 1.5 million patients with Myocardial Infarction in the US from 1990 through 1999. The national registry of Myocardial Infarction 1,2&3. J.Am.Coll Cardiol 36 ; 2056;2000.***

2. ***Kesteloot H, Sans S et.al., Evolution of all causes and Cardio vascular mortality in the age group of the 75 to 84 years in Europe during the period 1970-1996: A comparison with world wide changes. Eur. Heart J 23:384,2002.***

3. ***Carmeliet E Cardiac inonic currents and acute ischemia: from channels to arrhythmias Physiol.Rev. 79 ; 917;1999.***

4. ***Thompson CA, Goldberg RT et.al., Changes over time in the incidence & case fatality rates of primary VF complicating Acute Myocardial Infarction Am.Heart J 139;1014;2000.***

5. ***Hochman et al., Cardiogenic shock complicating Acute Myocardial Infarction. Circulation 107;2998;2003.***

6. ***Bertrand M, Mc Fadden E , Cardiogenic shock : Is there light at the end of tunnel ? J.Am College cardiology 42;1387;2003.***

7. ***Lewis EF, Moye LA et.al., Predictors of late development of heart failure in stable survivors of Myocardial Infarction: The CARE study. J.Am. College cardiology 42 ;1446;2003.***

8. ***Milionis HJ, Alexandrides GE et.al., Hypomagnesemia and concurrent acid base and electrolyte abnormalities in patients with CCF. Eur. J Heart failure. 4 : 167,2002.***

9. *Ridker PM, Morrow DA et.al., C- Reactive Protein, inflammation and coronary risk. Cardiol clin 21:315,2003.*

10. *Polmerkuriusz Lek, Comparan Nunez A Domanski, L, et.al., Malonyldialdehyde, Uric acid and white cell count as markers of oxidative stress in acute Myocardial Infarction and acute coronary insufficiency. J Clin Pharm Ther. 1998 Feb ;23(1) : 25-9.*

11. *Robbins, Pathologic basis of disease, 7th edition. P.571.*

12. *Brown B.G. Coronary vasospasm. Archives of internal medicine 141; 716;1981.*

13. *William F. Ganang Review of Medical Physiology . 21st edition P.624.*

14. *Robbins, Pathologic basis of disease, 7th edition P.575.*

15. *Slone et.al ., Risk of Myocardial Infarction in relation to current and discontinued use of oral contraceptives. New England Journal of medicine. 305;420;1981.*

16. *Brain C et.al.,Cigarette consumption and deaths from coronary Heart disease . Lancet 1 ; 1087;1978.*

17,18,19,20. Robbins Pathologic basis of disease, 7th edition P.576.

21.Desmond G. Julian, cardiology 8th edition P.79

22.Robbins, Pathologic basis of disease, 7th edition P.577.

23.Alpart JS. Antman E et.al., Myocardial Infarction redefined – A concensus document of the joint European society of

cardiology. Journal of American college of Cardiology .36;959;2000.

24.Paster nak RC, E. Braunwald & BE.Sobel; " Acute Myocardial Infarction", in Heart disease : A text book of cardiovascular medicine.

25.Bean WB: Masquerade of Myocardial Infarction. Lancet : 1; 1044;1977.

26.Uretsky et.al., Symptomatic Acute Myocardial Infarction without chest pain; Prevalence & clinical course. Am.J. Coll. Cardiol 40; 498;1947.

27,28,29,30. Harrison's principles of Internal Medicine. 16th edition II vol P.1450-51.

31.Killip T & Kimball J T; Treatment of Myocardial Infarction in a coronary care unit – A 2 year experience with 250 patients. Am.J.cardiol 20;457;1967.

32.Forrester J et.al., N.Engl.J.Med. 295;1356;1976.

33.Davidson's principles & practice of Medicine 20th edition P.542.

34.Hurst's The Heart. 11th edition Vol.I. P. 704.

35.Micheal H Crawford, John P. Dimarco Cardiology.

36.Reitt. et.al., Relationship between symptom, duration & final infarct size. Circulation 93(1) : 48-53;1996.

37.Julian JC. Time as a factor in Thrombolytic Theraphy . Ind. J. of cardiology 49(5); 517-19.

38.Yusuf et.al., Intra venous & Intra coronary fibrinolytic theaphy in Myocardial Infarction . Overview of results from 33 trials . Eur. Heart J. 6 ; 556-85; 1985.

39.Rowlands DJ. Can coronary reperfusion be detected by the ECG? Recent advances in cardiology Vol 12, P.27-41;1996.

40. Rapaport E : ISIS-3; A critical analysis of the preliminary results. J.Myocardial Ischemia 3: 25-32; 1991.

41.Demirovic J. et.al., Sex differences in early Mortality after Myocardial Infarction (the Minnesota Heart survey) Am. J. Cardiol. 75(16) : 1096-101; 1995.

42.Pamela S Dauglas." Coronary arterial disease in women" – A text book of cardiovascular Medicine. Braunwald E. ed.

43.Kodama K . et.al., Prognostic significance of diabetes mellitus in patients with Myocardial Infarction after recanalisation. Diabetes Res clin; Pract 30 (suppl) 71-5;1996.

44.Fresco C et.al., Prognostic value of hypertension in 11,483 patients with acute Myocardial Infarction treated with thirombolysis GISSI-2 investigators. J. Hypertension 14 (6) : 743-50;1996.

45.Hands ME et.al., Incidence. Predictors & outcome after the in hospital development of cardiogenic shock after acute Myocardial Infarction. J.Am.Coll. Cardiol. 14 : 40-6;1989.

46.Micheal H Crawford, John P. Dimarco Cardiology.Sec : 2 (14.8)

47.Harper's biochemistry. 26th edition. P.297-300.

48. *Harrison's principles of internal Medicine Vol II. 16th edition.P.2309.*

49. *Oxford text book of Medicine Vol : II P.50-1.*

50. *Mallat Z, Philip I.et.al., Elevated levels of 8-iso PG F_2 α in pericardial fluid of patients with Heart failure : A potential role for in vivo oxidant stress in ventricular dilatation & progression to Heart failure. Circulation 97; 1536;1998.*

51. *Li JM, Gall NP et.al., Activation of NADPH oxidase during progression of cardiac hypertrophy to failure. Hypertension 40 ; 477;2002.*

52. *Hare JM. Oxidative stress and apoptosis in Heart failure progression Circ. Res . 89; 198;2001.*

53. *Dhalla AK, Hill MF: Role of oxidative stress in transition of Hypertrophy to Heart failure J.Am.Coll. Cardiol 28;506;1996.*

54. *Anker S, Doehner W, et.al., Uric acid and survival in chronic Heart failure : Validation and application in metabolic, functional and Hemodynamic staging. Circulation 2003 ; 107;1991-1997.*

55. *Perez NG, Gaowd, Marban E, Novel myo filament calcium sensitizing property of xanthine oxidase inhibitors. Circ Res. 1998 ; 83;423-430.*

56. *Roch-Ramel F, Guisan B. Effects of uricosuric and antiuricosuric agents on urate transport in human brush border membrane vesicles. J. Pharmacol Exp Ther : 1997;280;839-845.*

57.Mc cord JM. Oxygen derived free radicals in post ischemic tissue injury. N. Eng. J. Med. 1985; 312; 159-163.

58.Dejong JW. Xanthine oxido reductase activity in perfused hearts of various species , including humans. Circ. Res . 1990; 67; 770-773.

59.Waring WS, Webb DJ. Et.al., Systemic uric acid administration increases serum antioxidant capacity in healthy volunteers. J. Cardio Vasc. Pharmacol. 2001 ;38;365-371.

60.Kang DH, Feng . L. et.al., A role for uric acid in the progression of renal disease J. Am. Soc. Nephrol – 2002;13;2888-2897.

61.Maisel AS, Nowak RM. et.al., Rapid measurement of – Brain natriuretic peptide in the emergency diagnosis of Heart failure. N. Eng. J.Med. 2002;347;161-167.

62.Trivedi R.C , Robar L, Berka E ., Strong; clinical chemistry. 24 (1978), 1908.

63.Clinical chemistry principles, procedures, correlation and Analytic methods. Michael L. Bishop 5th edition.P.229.

64.Feichtmeier TV, Wrenn HT. Direct determination of uric acid using uricase. Am J clinic pathol 1955; 25:833.

65. Duncan PH, Cooper et.al., A candidate reference method for uric acid in serum.Optimization & evaluation clin.chem. 1982,28;384.

66. KKL Ho et.al., Circulation 88;107, 1993.

PROFORMA

NAME : ***AGE :*** ***SEX:***

OCCUPATION : ***I.P.NO:***

ADDRESS : ***D.O.A :***

D.O.D :

SYMPTOMS AT THE TIME OF ADMISSION:

☐ ***CHEST PAIN*** ☐ ***DYSPNOEA*** ☐ ***SWEATING*** ☐ ***PALPITATIONS***

☐ ***OLIGURIA*** ☐ ***PAIN & SWELLING IN JOINTS***

PAST HISTORY :

☐ ***RENAL DISEASE*** ☐ ***GOUT*** ☐ ***CHRONIC ALCOHOLISM***

☐ ***IHD*** ☐ ***DIABETES*** ☐ ***ASPIRIN & DIURETIC THERAPHY***

ECG :

KILLIP'S CLASSIFICATION : ***I II III IV***

THROMBOLYSED : ***NOT THROMBOLYSED :***

CLINICAL EXAMINATION : ***a. PR :***

b. BP :

c. JVP elevation : Yes / No

d. Pedal edema : Yes / No

e. Basal Rales : Yes / No

INVESTIGATIONS :

a. Hb % : ***b. TC :*** ***c. DC :***

d. URINE : ALB : ***SUGAR :*** ***DEPOSITS :***

e. BLOOD SUGAR : ***f. BLOOD UREA:***

g. SERUM CREATININE :

h. SERUM ELECTROLYTES : ***Na+ :*** ***K+ :***

i. SERUM URIC ACID LEVEL ON ADMISSION :

j. SERUM CHOLESTEROL :

k. ECHOCARDIOGRAM :

ADVERSE CARDIAC EVENTS:

a. CARDIAC FAILURE :

b. ARRHYTHMIAS

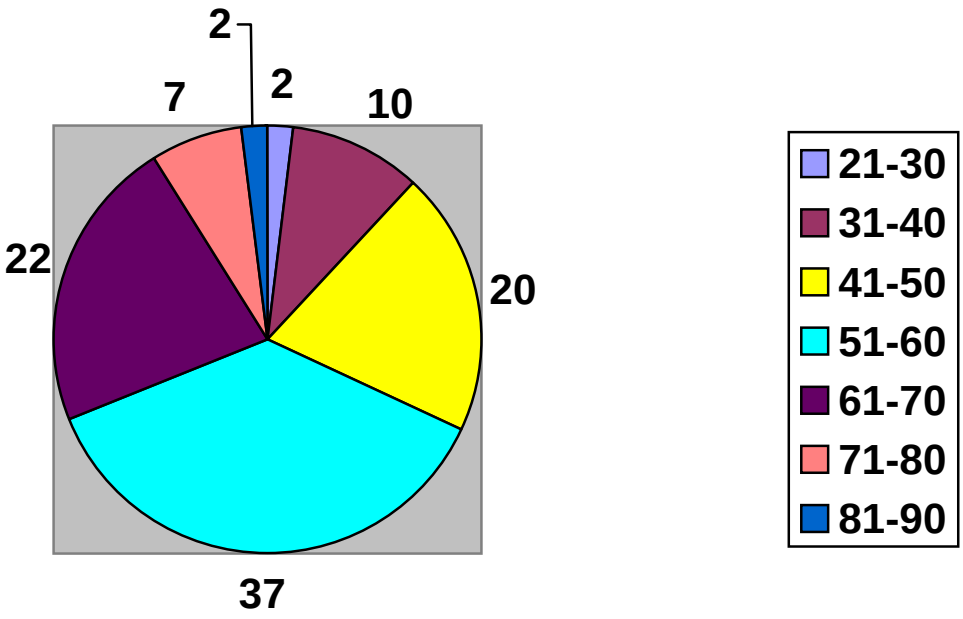
c. SHOCK

d. DEATH

HOSPITAL STAY :

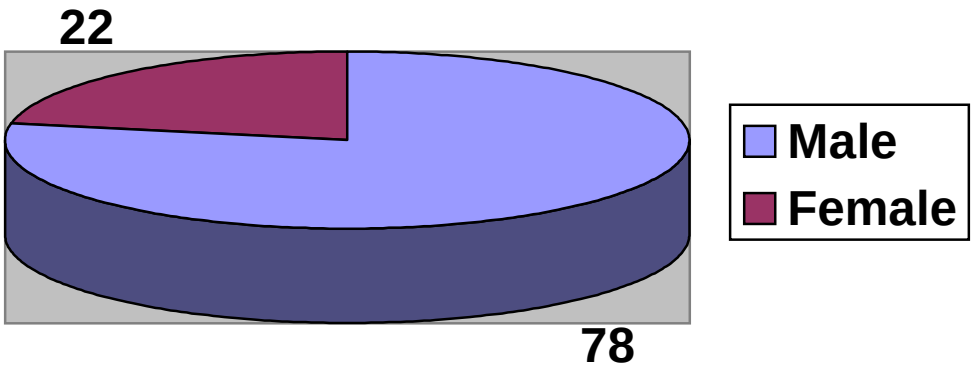
AGE INCIDENCE- TOTAL POPULATION

FIG : 1



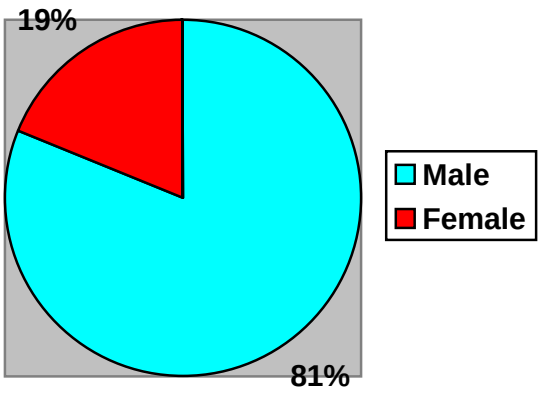
SEX INCIDENCE-TOTAL POPULATION

FIG : 2



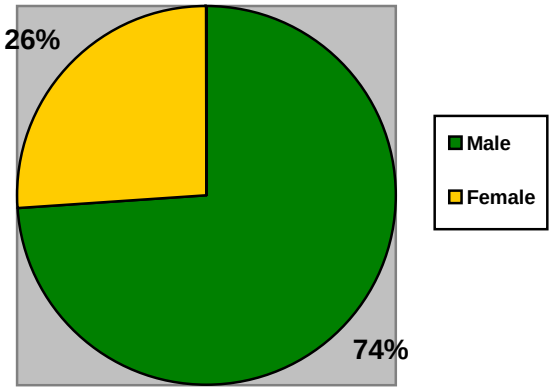
SEX INCIDENCE (CONTROL GROUP)

Fig : 3



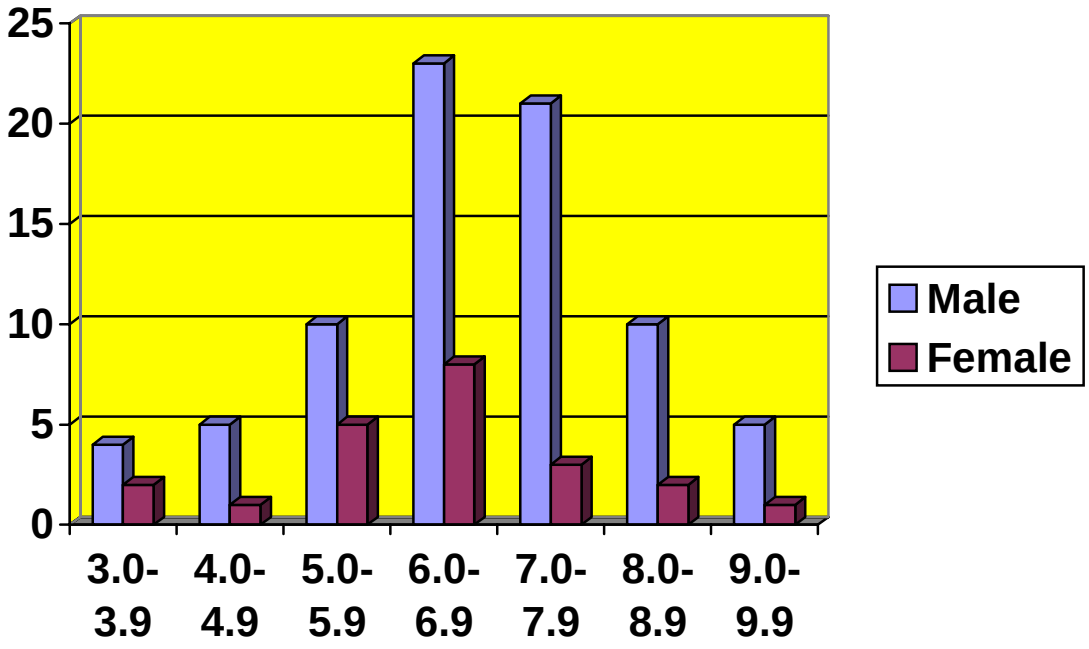
SEX INCIDENCE (STUDY GROUP)

Fig : 4



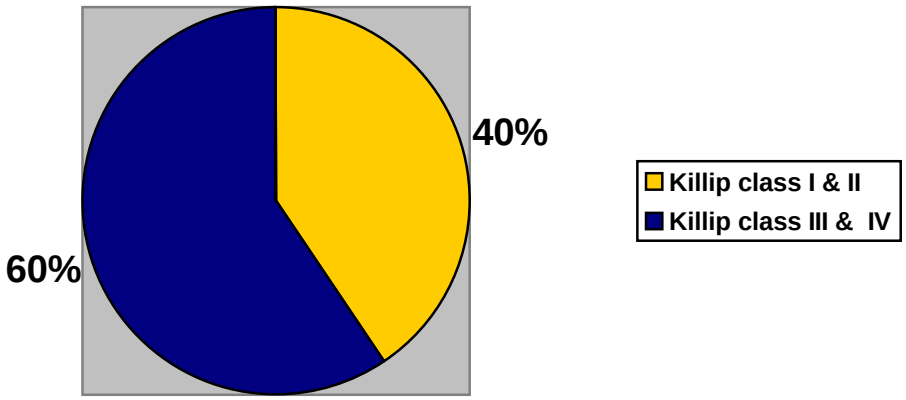
DISTRIBUTION ACCORDING TO URIC ACID LEVEL & SEX

Fig : 5



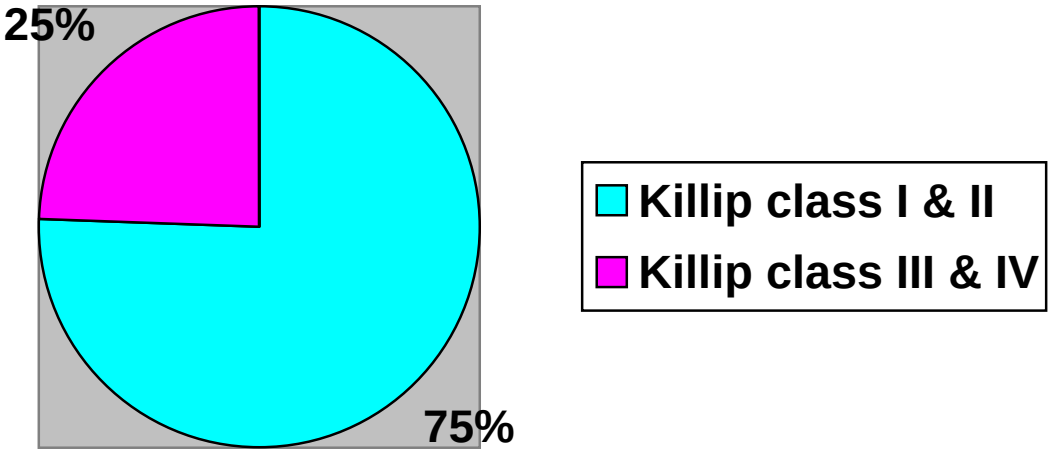
KILLIP CLASS – HIGH URIC ACID POPULATION (STUDY GROUP)

Fig : 6



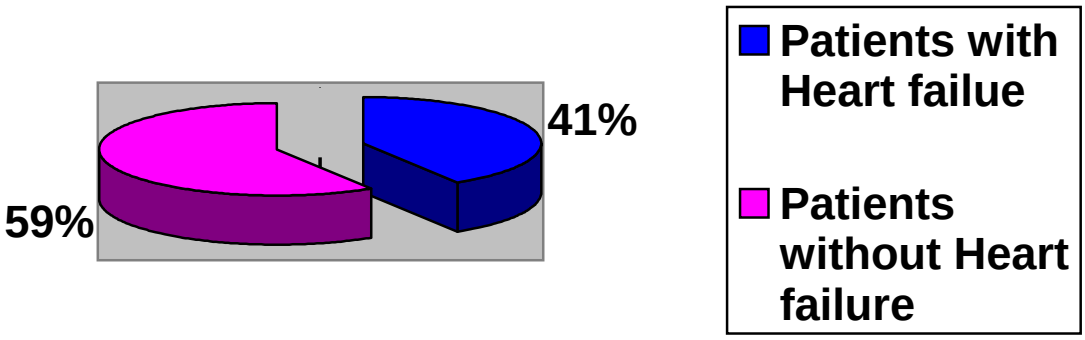
KILLIP CLASS – NORMAL URIC ACID POPULATION (CONTROL GROUP)

Fig : 7



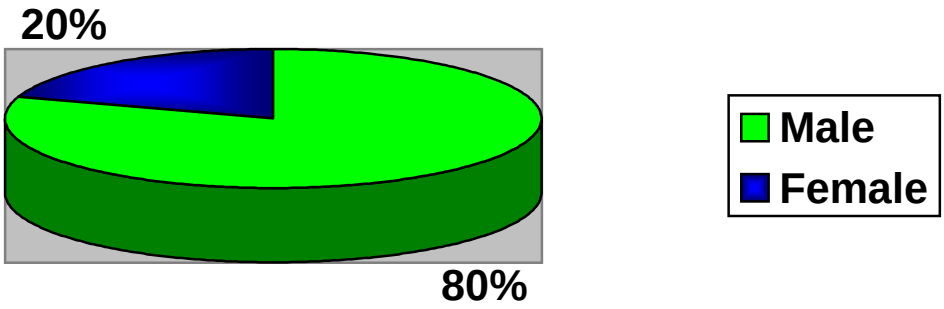
CARDIAC FAILURE IN TOTAL POPULAITON

Fig : 8



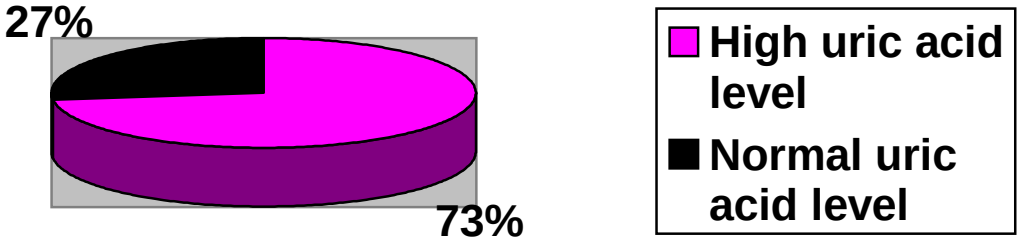
HEART FAILURE ACCORDING TO SEX

Fig : 9



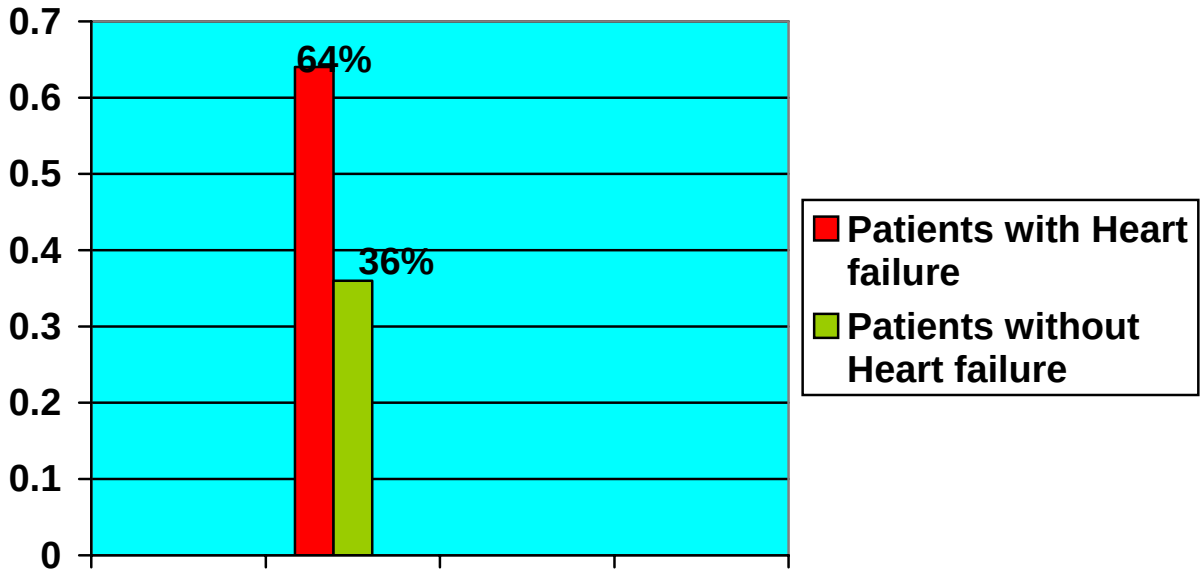
URIC ACID STATUS IN HEART FAILURE POPULATION

Fig : 10



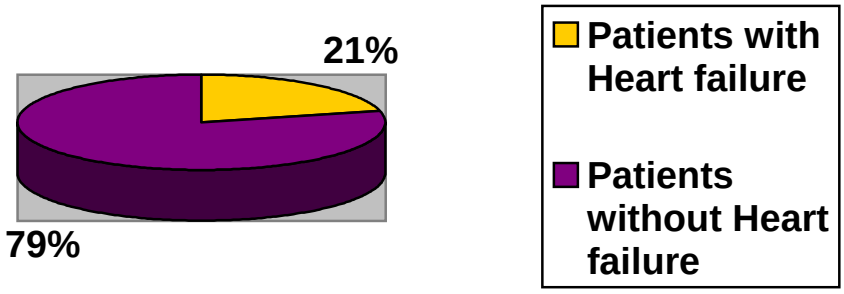
HEART FAILURE PATIENTS – HIGH URIC ACID POPULATION (STUDY GROUP)

Fig : 11



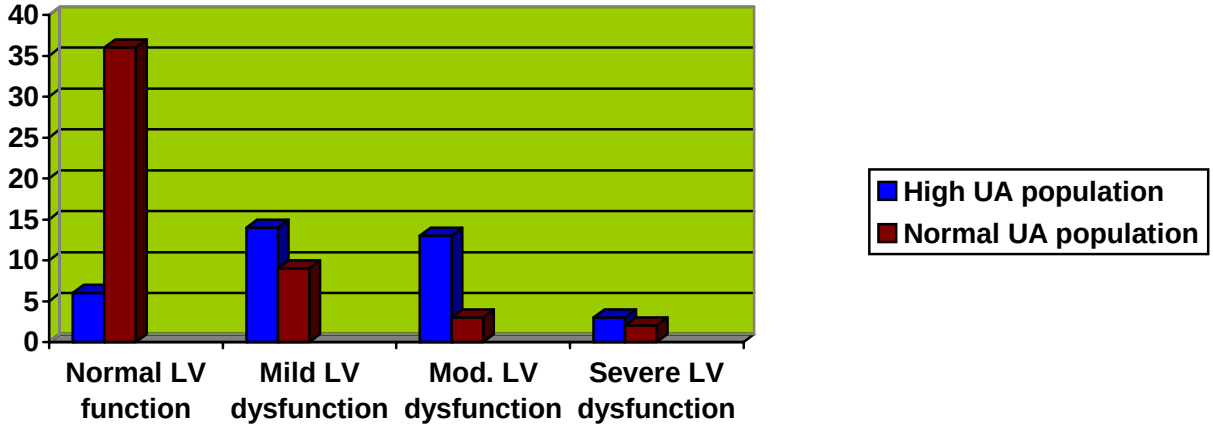
HEART FAILURE – NORMAL URIC ACID POPULATION (CONTROL GROUP)

Fig : 12



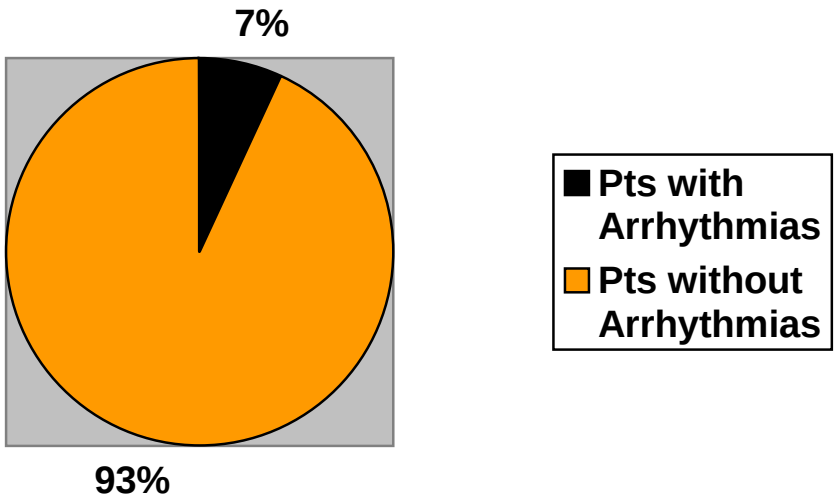
ECHOCARDIOGRAM ANALYSIS

Fig : 13



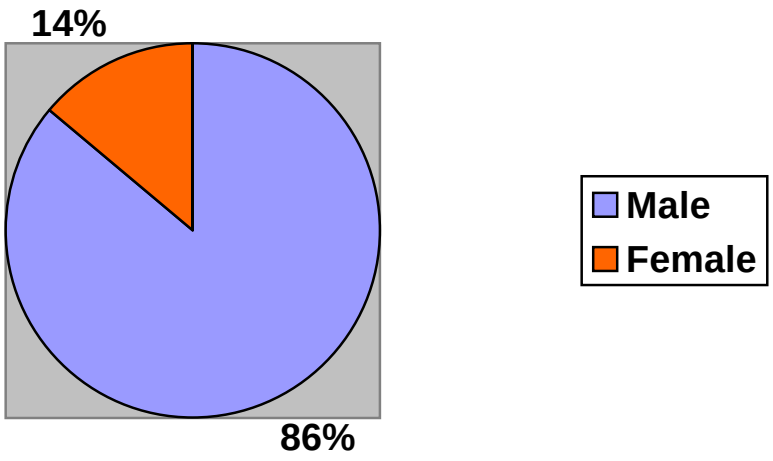
ARRHYTHMIAS IN TOTAL POPULATION

Fig : 14



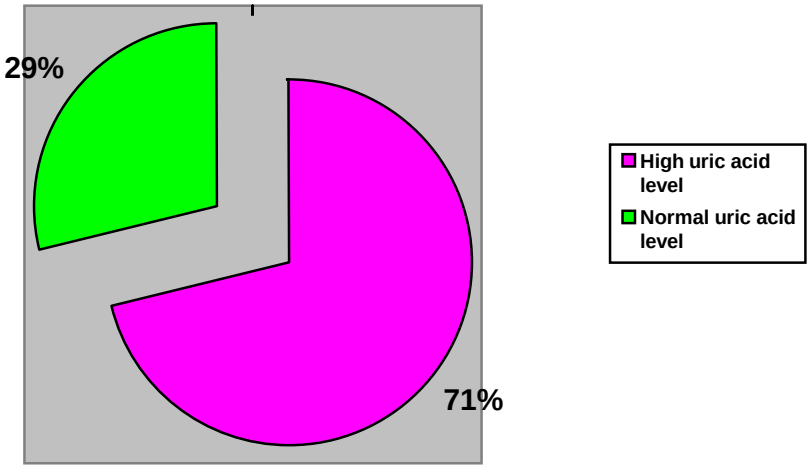
ARRHYTHMIAS ACCORDING TO SEX

Fig : 15



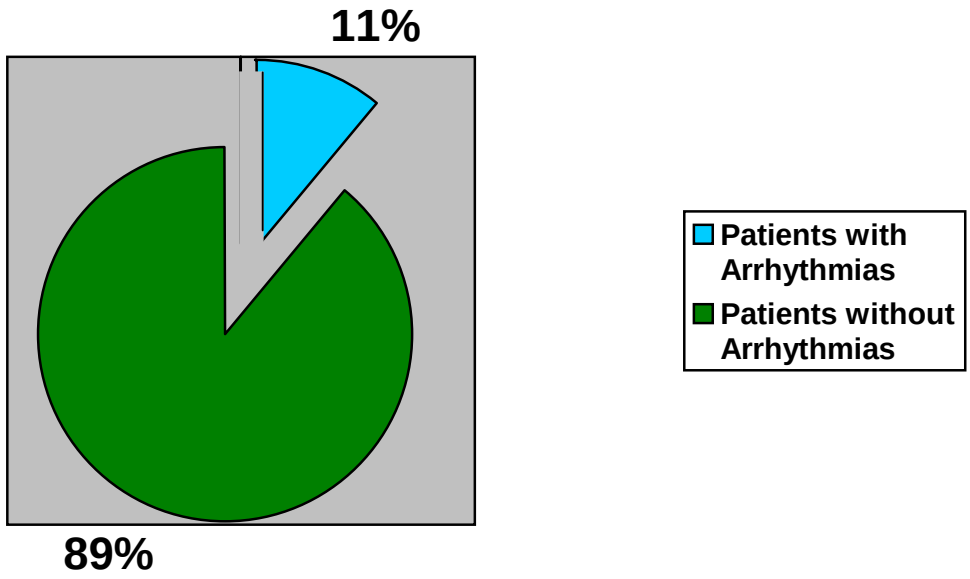
URIC ACID STATUS IN PATIENTS WITH ARRHYTHMIAS

Fig : 16



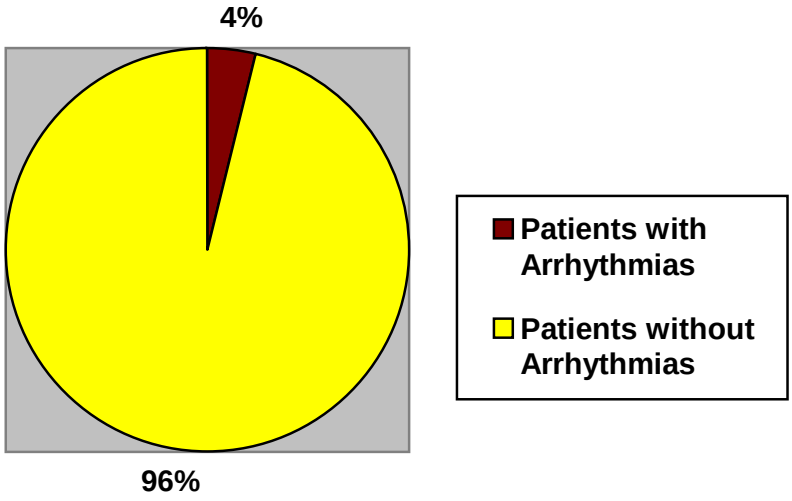
ARRHYTHMIAS – HIGH URIC ACID POPULATION (STUDY GROUP)

Fig : 17



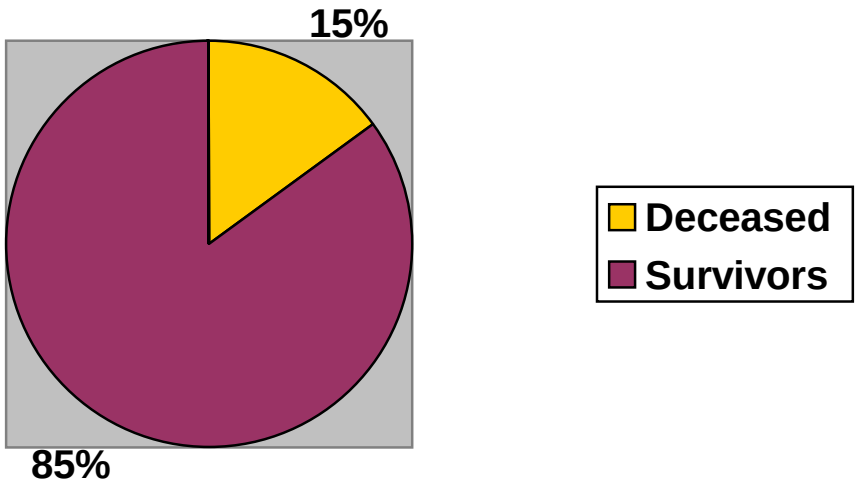
ARRHYTHMIAS – NORMAL URIC ACID POPULATION (CONTROL GROUP)

Fig : 18



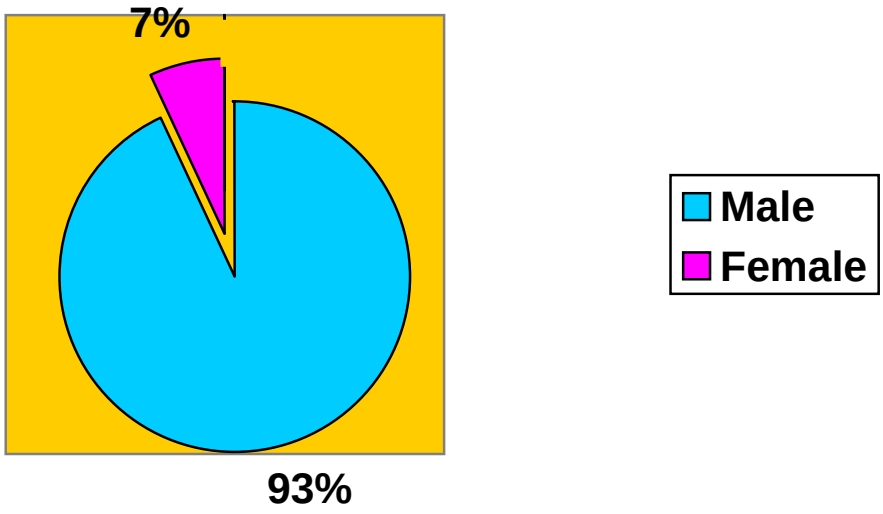
OUTCOME IN TERMS OF MORTALITY – TOTAL POPULATION

Fig : 19



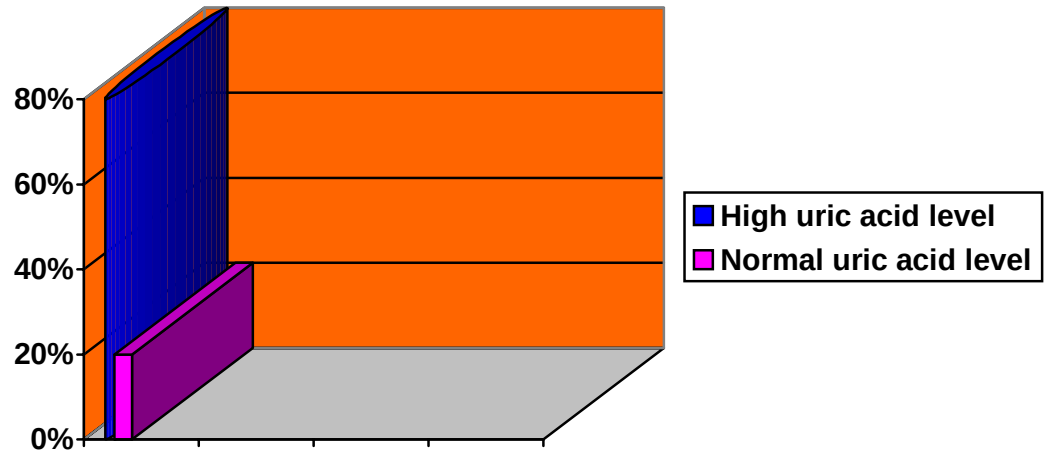
MORTALITY ACCORDING TO SEX

Fig 20



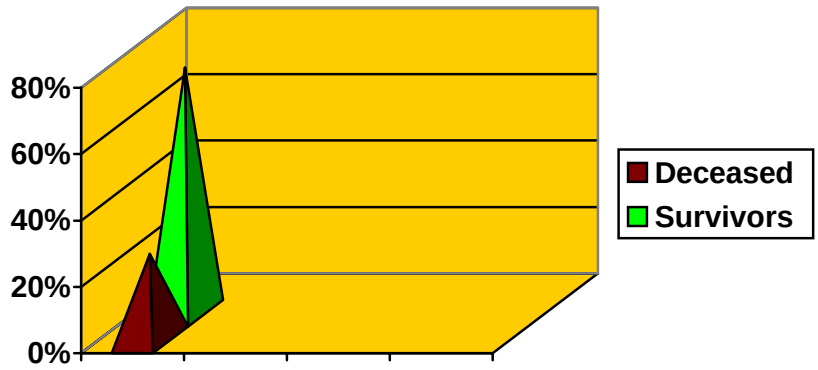
URIC ACID STATUS IN MORTALITY

Fig : 21



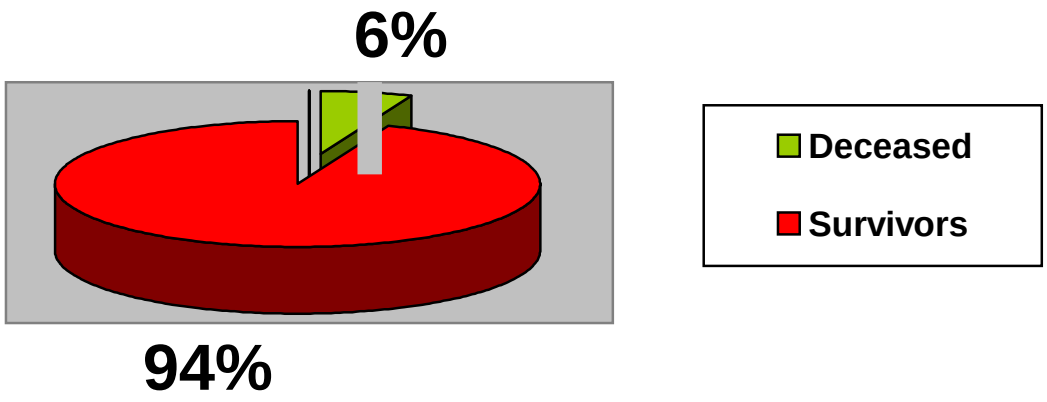
OUTCOMES IN TERMS OF MORTALITY – HIGH URIC ACID LEVEL (STUDY GROUP)

Fig : 22



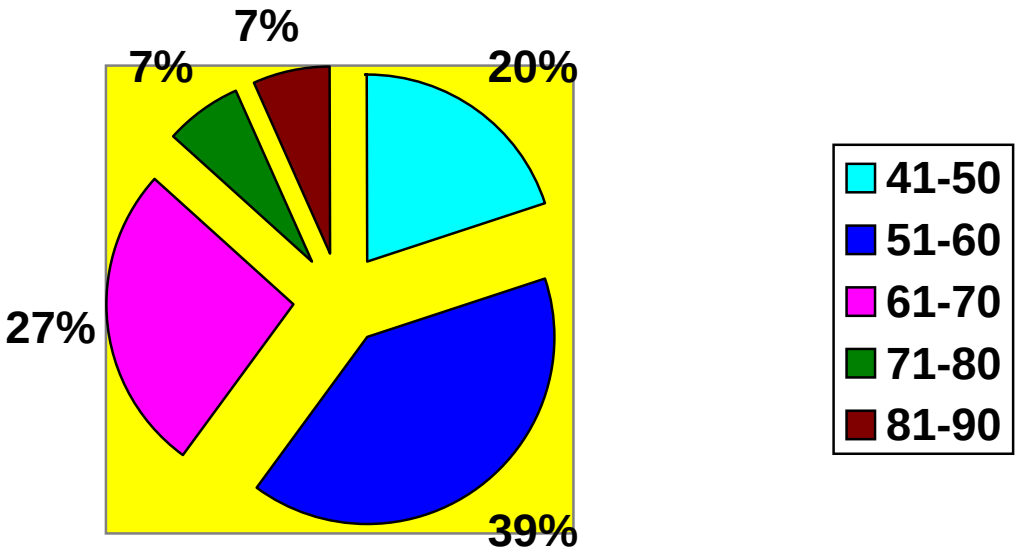
OUTCOMES IN TERMS OF MORTALITY – NORMAL URIC ACID LEVEL (CONTROL GROUP)

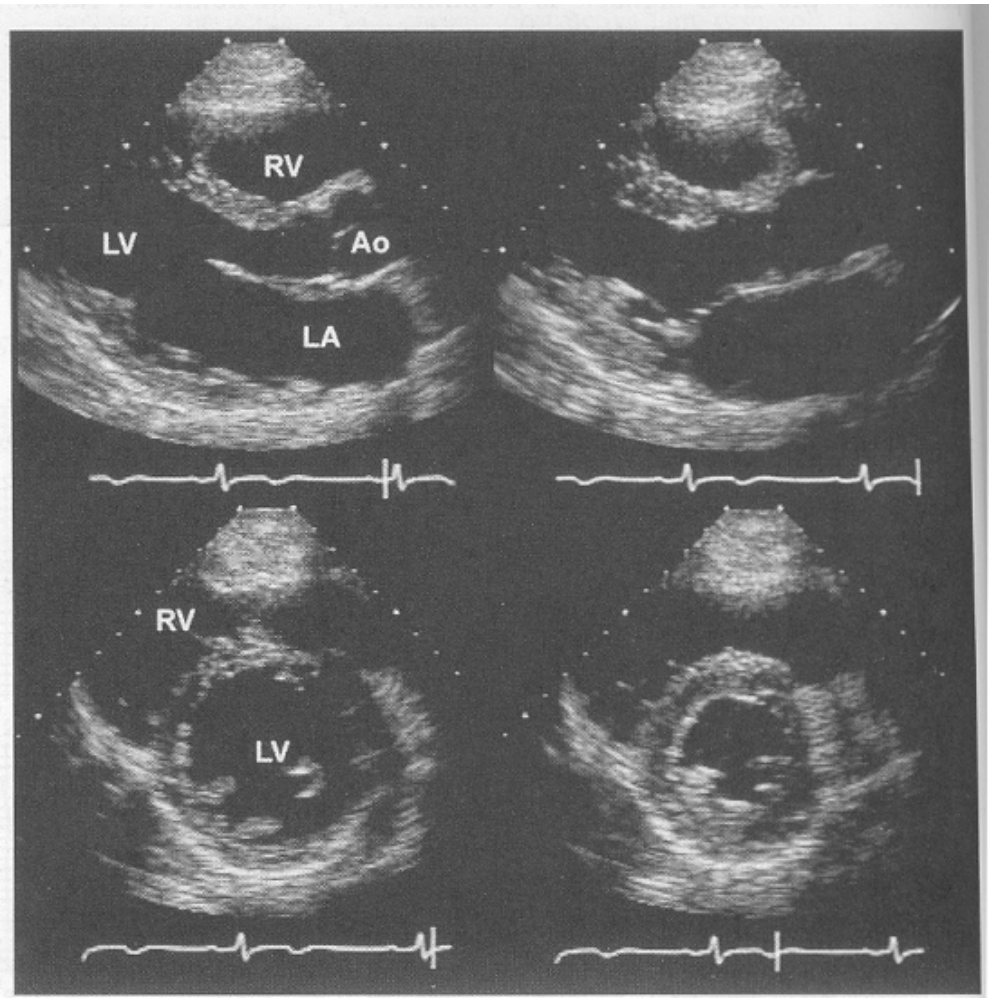
Fig : 23



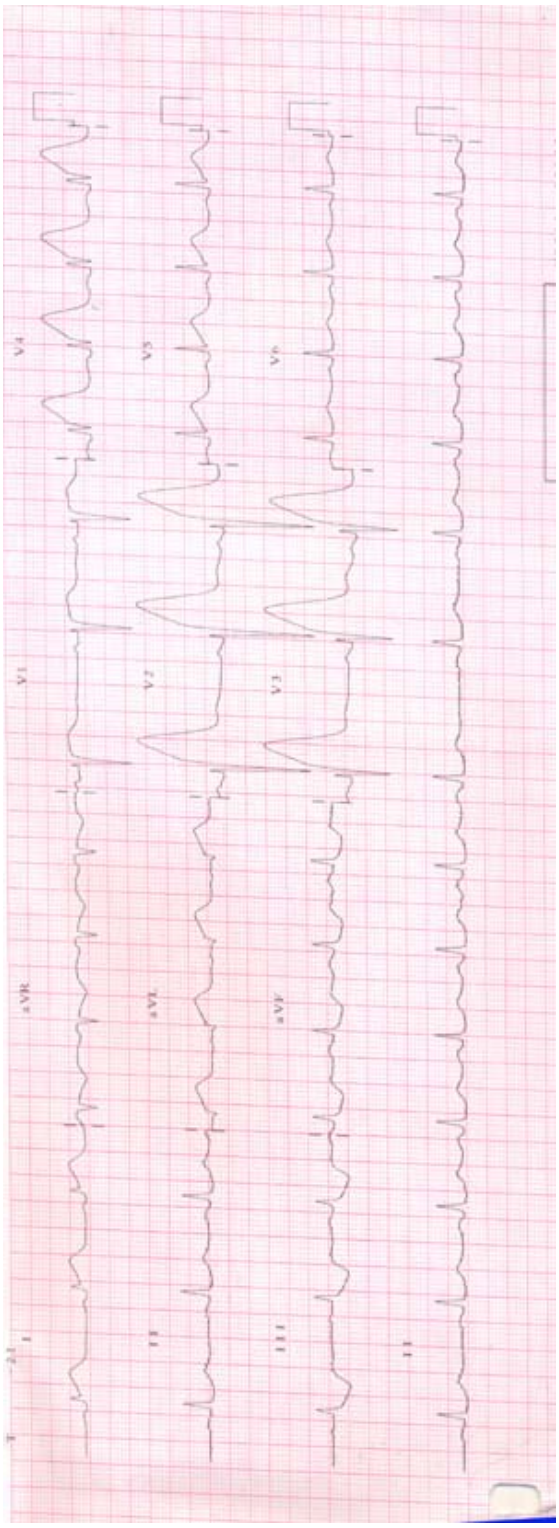
MORTALITY IN AGE GROUP

Fig : 24

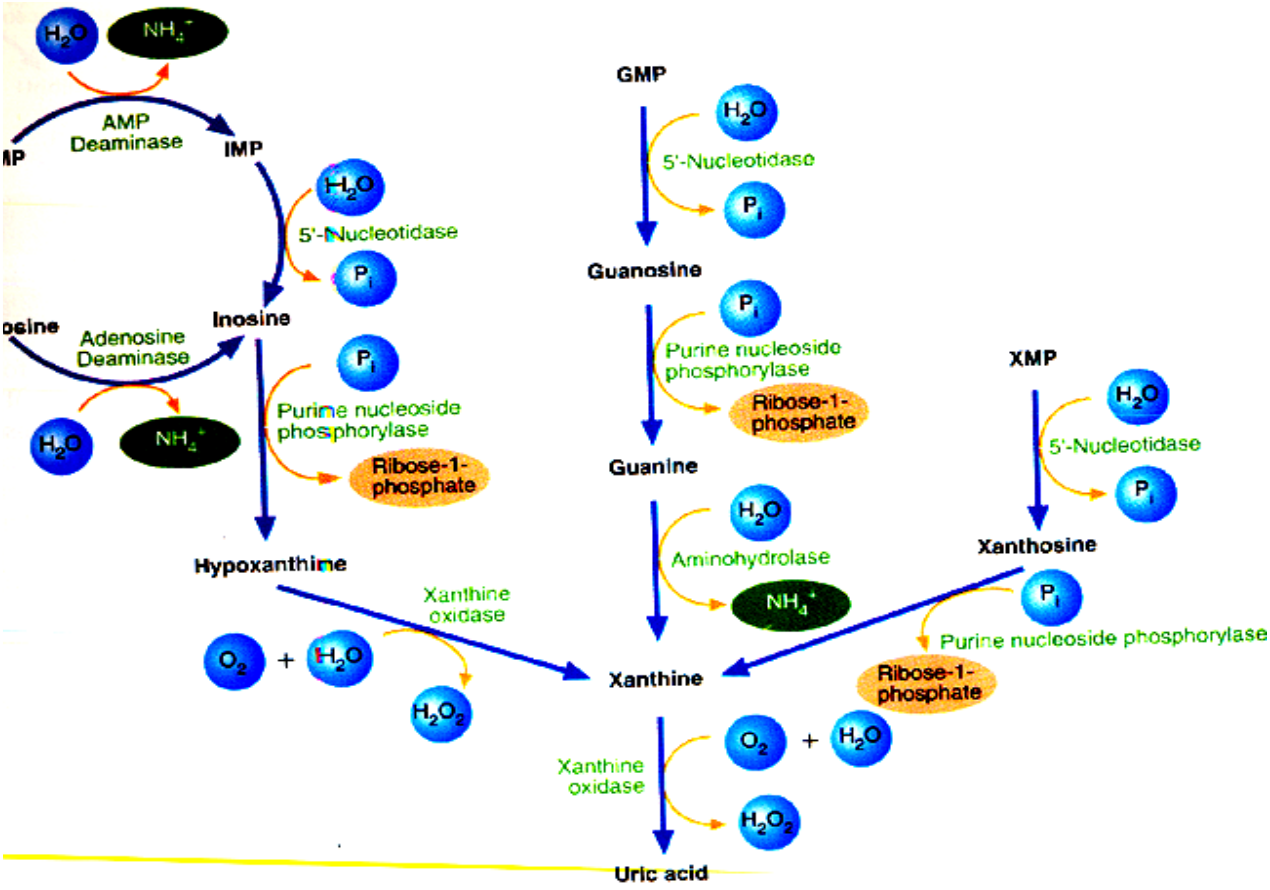




ECHO OF ONE OF THE STUDY PATIENT SHOWS NORMAL CHAMPERS OF HEART



ECG OF ONE OF THE STUDY PATIENT SHOWS EXTENSIVE ANTERIOR WALL MI



SCHEMATIC REPRESENTATION OF PURINE METABOLISM