CORRELATION OF HYPONATREMIA AS AN INDEPENDENT PREDICTOR OF SHORT TERM MORTALITY AND ADVERSE CARDIAC EVENTS AMONG HOSPITALIZED PATIENTS OF ACUTE STEMI

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CERTIFICATE

This is to certify that the Dissertation entitled **" *CORRELATION OF HYPONATREMIA AS AN INDEPENDENT PREDICTOR OF SHORT TERM MORTALITY AND ADVERSE CARDIAC EVENTS AMONG HOSPITALIZED PATIENTS OF ACUTE STEMI*",** submitted by **Dr. ARUN KAUSHIK . P.,** Post-Graduate in General Medicine, Coimbatore Medical College, to The Tamilnadu Dr. *M.G.R.* Medical University is a record of a bonafide research work carried out by him under my guidance and supervision from January 2007 to June 2009.

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I solemnly declare that the Dissertation titled **" *CORRELATION OF HYPONATREMIA AS AN INDEPENDENT PREDICTOR OF SHORT TERM MORTALITY AND ADVERSE CARDIAC EVENTS AMONG HOSPITALIZED PATIENTS OF ACUTE STEMI*",** was done by me at Coimbatore Medical College & Hospital during the period from Jan 2007 to Jun 2009 under the guidance and supervision of my unit chief Prof. Dr.M.Ramasamy.

This dissertation is submitted to The Tamilnadu Dr. *M.G.R.* Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch *I*) in General Medicine – March 2010

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INTRODUCTION

Myocardial Infarction is a serious complication of Atherosclerotic Coronary Heart Disease. Coronary Heart Disease was first described by William Herberden in 1768. In 1932 unipolar leads were discovered by Wilson and the establishment of coronary care units by Day and Brown has lead to the world wide proliferation of coronary care units. The current knowledge of pathophysiology of acute myocardial infarction started with the autopsy description of Dr. James Herrick from Chicago in 1912 who concluded that acute myocardial infarction results from thrombotic occlusion of coronary artery and prophesised that the hope of salvaging the muscle, lay in restoration of blood flow.

Despite impressive strides in diagnosis and management over the last three decades, acute myocardial infarction (AMI) continues to be a major public health problem even in the industrialized world. In the United States nearly 1.5 million patients annually suffer from AMI (about one patient every 20 seconds).[1] Myocardial Infarction[2] is an acute cardiac disability arising from reduction or arrest of blood supply to the myocardium due to atherosclerotic or non-atherosclerotic lesions of coronary arteries. Virtually all acute infarcts are caused by thrombosis developing in a culprit vessel with ruptured atherosclerotic plaque. Usually coronary artery occlusion is associated with infarction of

myocardium, though post-mortem examination of cases of sudden deaths reveals evidence in only 20% of cases, the remaining 80% do not show any change.

Accurate diagnosis is mandatory because mistaken diagnosis can be disastrous to the social, economical and family life of the patient. At one end of the spectrum is the danger of missing a potentially lethal illness, on the other hand mistaken diagnosis results in severe cardiac neurosis which is even more difficult to treat than the original disease itself.

The presenting symptoms may vary from severe pain in the chest to minimal symptoms, with the disease remaining unrecognized. In most patients there is a substernal heaviness[3] which radiates to the left shoulder or ulnar surface of forearm and hand. It can also radiate to back, interscapular region, root of neck, jaw and teeth. In others it presents as breathlessness, syncope, giddiness, fatigue, abdominal pain, nausea, vomiting and unexplained hypotension.

Coronary Heart Disease is more age dependant in women than in men. Women are usually 10 years older than men when any coronary manifestation first appears and Myocardial Infarction occurs as much as 20 years later [4]. Coronary Heart Disease is the leading cause of death in women and the lifetime risk of death is 31% in postmenopausal women.

The median age of menopause is 51.4 years[5] and age distribution ranges from 40-58 years.

Data from Framingham study says that the incidence of cardiovascular disease is 3 times more in men than women(before menopause) and approximately equal in men and women aged 75-79 years. The incidence in women rises after menopause due to hormonal changes

Overall mortality and morbidity in coronary heart disease depends on age, sex, site and extent of infarction, presence of good collateral circulation and associated co-morbid conditions.

Reperfusion strategies no doubt have resulted in nearly 50% reduction in in-hospital mortality of patients with AMI[(1)]. Still the early mortality (30 days mortality) rate from AMI remains 30% and 1 in 25 patients who survive initial hospitalization die in the first year following AMI [(1)]. Several factors that affect the early mortality after AMI like age, left ventricular dysfunction previous CAD, diabetes mellitus, hypertension, fibrinolysis, anterior wall infarction were extensively studied worldwide so far.

"Hyponatremia is the most commonly identified electrolyte abnormality in hospitalized patients" as per **J.A. Clayton** et al.[(2)].

Gill G. et al.[3] in there study found that severe hyponatremia in hospitalized patients was associated with increased mortality.

Lee WH et al.[4] states that hyponatremia is an independent risk factor for increased mortality among CCF patients.[33,34]

Goldberg et al.[5] and **Svanegaard** et al.[6] predicted that neuro - humoral activation similar to that of CCF occurs in AMI patients due to pain, stress, nausea and acute LV dysfunction.

Hence, it sounds worthy for me to take up a study to correlate the presence or development of hyponatremia among hospitalized patients of acute ST elevation myocardial infarction (Acute STEMI) with the short term (30 days) mortality of patients so that the prediction of hyponatremia as the independent risk factor for 30 days mortality among acute STEMI patients can be made possible.

AIM OF THE STUDY

1. To correlate hyponatremia on admission or developed during the first 72 hours with cardiac events, like rhythm disturbances, LV dysfunction among the hospitalized patients of acute STEMI.

2. To correlate hyponatremia on admission or developed during the first 72 hours among the hospitalized patients of acute STEMI with short-term (30 days) mortality.

REVIEW OF LITERATURE

A. ANATOMY OF CORONARY CIRCULATION

The epicardial coronary arteries take origin from the right and left coronary sinuses. In 85% of patient the right coronary artery which gives rise to posterior descending artery supplies the entire right ventricle and large a part of the posterior wall of the left ventricle. This is referred to as right dominant circulation.

In 8% of patients the left coronary artery supplies entire left ventricle, interventricular septum and portion of right ventricle. This is referred to as left dominant circulation.

In 7% of patients referred to as co-dominant circulation, the right coronary artery supplies right ventricle and posterior wall of interventricular septum while left coronary supplies the left ventricle and anterior portion of interventricular septum.

Table 1: RISK FACTORS FOR CORONARY HEART DISEASE

A. FIXED
1. Age 2. Male sex 3. Family History
B. MODIFIABLE
1. Smoking 2. Hypertension 3. Lipid Disorders 4. Diabetes Mellitus 5.Haemostatic variables 6. Sedentary Life Style 7. Obesity 8. Mental Stress 9. Personality 10. Oral Contraceptive Pills 11. Hyperhomocysteinemia 12. Inflammation

E.INVESTIGATIONS

1. LABORATORY FINDINGS:

Myoglobin levels are the earliest to rise. Creatine Kinase starts to rise at 4 hours, peaks at about 12 hours falls to normal levels within 48-72 hours [45]. The most sensitive markers of myocardial cell damage are the Cardiac Troponins T and I which are released within 4-6 hours and remain elevated for upto 2 weeks. Myoglobin levels peak at 6 hours and returns to normal at 24 hours. Aspartate transaminase starts to rise about 12 hours after infarction and reaches peak on the first or second day returning to normal within 3 or 4 days. Lactate dehydrogenase peaks at 3-4 days remains elevated for upto 10 days.

Lipid profile (cholesterol – total, LDL & triglycerides) may be raised. Leukocytosis is usual, reaching a peak on the first day. The ESR becomes raised.

2. CHEST RADIOGRAPHY(Fig 1):

Chest X-ray is important since it may show the consequences of ischaemic heart disease i.e. cardiac enlargement, ventricular aneurysm, signs of heart failure and pericardial effusion. These signs can support

the diagnosis of ischaemic heart disease and are important in assessing the degree of cardiac damage.

3. ELECTROCARDIOGRAPHY:(PH 2 – 7)

The ECG is usually a sensitive and specific way of confirming the diagnosis; however it may be difficult to interpret if there is bundle branch block or evidence of previous myocardial infarction. Occasionally the initial ECG is normal and the diagnostic changes appear a few hours later. The earliest ECG change is tall and widened T waves followed by ST elevation. Later on there is diminution in the size of R wave and in full thickness infarction a Q wave begins to develop. Subsequently T wave becomes inverted.

When there has been anteroseptal infarction abnormalities are found in one or more leads from V1 to V4, while Anterolateral Infarction produces abnormalities in V4-V6, aVL and in lead I. Inferior Wall Infarction is best shown in lead II, III and aVF, while at the same time leads I, aVL and the anterior chest leads may show reciprocal changes of ST depression. Infarction of the posterior wall of the left ventricle is not recorded in the standard leads by ST elevation or Q waves, but the reciprocal changes of ST depression and a tall R wave may be seen in leads V1-V3. Right ventricular infarction should be strongly suspected if, in the clinical setting of acute inferior wall

myocardial infarction, there is ST elevation of 1mm or more in lead V1,V4R or any of the extra right precordial leads V4R-V6R.

4. ECHOCARDIOGRAPHY(PH 2):

Two dimensional echocardiography can be done to assess the cardiac chamber size, regional wall motion abnormalities, left ventricular hypertrophy, valve leaflet thickness and mobility, valve calcification, appearance of subvalvular and supravalvular structures, pericardial effusion, intracardiac masses and great vessels.

Doppler echocardiography is done to assess valve regurgitation, valve stenosis, valve area, valve gradients, intracardiac pressures, intracardiac shunts and ventricular diastolic filling.

Transesophageal echocardiography is used to assess aortic disease, infective endocarditis, to find out source of embolism, abnormalities of mitral prostheses etc.

Stress echocardiography is done to find out new regional wall motion abnormalities, declining ejection fraction and increase in end systolic volume which are indicators of myocardial ischemia.

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F. COMPLICATIONS OF MYOCARDIAL INFARCTION [37]

1. ARRHYTHMIAS:

A. TACHYARRYTHMIAS:

a. Premature ventricular complexes:

The commonest arrhythmia is premature ventricular complexes. This can be suppressed with IV lignocaine 100mg given as bolus. To prevent recurrence lignocaine infusion of 500-1000mg in 500ml of 5% dextrose is administered at a rate of 1-2mg/min. premature ventricular complexes can be forerunners of life threatening ventricular tachycardia or ventricular fibrillation.

b. Ventricular Tachycardia:(PH 6)

It needs immediate attention and should be treated by IV lignocaine. In case the drug is ineffective, DC shock of 150-200 joules will be effective in majority of the cases. Repeated attacks of ventricular tachycardia can be prevented by IV infusion of lignocaine, amiodarone or mexilitene. Ventricular pacing may also be effective.

c. Ventricular Fibrillation:(PH7)

The patient is pulseless and will have features of cardiac arrest. Immediate thump on the chest and an external cardiac massage is required. Defibrillation should be one by DC shock of 200-400 joules. Patients with repeated episodes may benefit from intravenous bretylium, amiodarone, mexilitene or lignocaine.

d. Supraventricular Arrhythmias:

Atrial premature beats do not need specific treatment. However supraventricular arrhythmia, atrial flutter and atrial fibrillation require treatment with digoxin or verapamil.

e. Accelerated Ventricular or Junctional Rhythm:

Normally pace maker cells in the AV junctional and ventricular myocardium have a rate of 40-60/min. however in the settings of myocardial infarction, especially in acute inferior wall myocardial infarction, the rate of these pacemakers increases to about 80-120/min. such a rhythm do not require specific treatment and is normally self limiting. If hemodynamic compromise occurs IV atropine (1.2mg) suppresses it by increasing the sinus rate.

B. BRADYARRHYTHMIAS AND CONDUCTION DISTURBANCES:

a. Sinus Node Dysfunction:

It may present as sinus bradycardia, sinus arrest or sinoatrial block usually due to vagal stimulation or in the settings of inferior wall infarction due to sinus node ischaemia. Symptoms of profound hypotension and shock may occur and occasionally asystole and cardiac arrest. Immediate treatment consists of IV atropine (1.2mg). If atropine is ineffective or this problem is persistent or recurring temporary pace making is necessary.

b. AV Nodal Block:

It usually occurs with inferior wall myocardial infarction as first degree AV block, Wenkebach's block or complete AV block. These blocks are usually transient and respond to IV atropine. If giddiness, hypotension or other evidence of hemodynamic compromise occurs or if the ventricular rate is less than 50/min temporary pacing may be required.

c. Distal Conduction Disturbances:

The distal conduction system consists of the right bundle and the anterior and posterior fascicles of the left bundle. Since the major blood

supply to this part of the conduction system comes from the left coronary artery, conduction defects in the bundle branches are common in anterior wall infarction. Block of one of the fascicles of the left bundle does not have an ominous prognosis. However acute right or left bundle branch block or bifascicular block carries an ominous prognosis. Block in the three fascicles results in complete heart block with an unstable ventricular escape rhythm at a rate of 20-40 beats per minute. Clinical manifestations consists of syncopal attacks, hypotension and may lead to cardiac arrest. Temporary pacemaker insertion is necessary. Temporary pacing is also indicated in patients who develop bifascicular blocks since this can be a precursor of trifascicular block. Patients with bifascicular block who develop trifascicular block may need permanent pacemaker implantation.

2. ISCHAEMIA:

Post infarction angina occurs in upto 50% of patients. This is due to residual stenosis in infarct related vessel despite successful thrombolysis.

3. ACUTE CIRCULATORY FAILURE:

Hemodynamic evidence of left ventricular dysfunction appears when contraction is seriously impaired in 20-25% of the left ventricle.

Infarction of more than 40% of left ventricle results in Cardiogenic Shock which carries a bad prognosis.

4. PERICARDITIS:(PH 1)

This may occur at any stage but is particularly common on the second and third day. The patient may recognize a different pain that is positional and worsens on inspiration. Dressler's Syndrome may occur between 2 weeks and 3 months after acute myocardial infarction [46] and has an autoimmune basis often accompanied by pleural and pericardial effusions, fever and raised ESR. Treatment requires the use of steroids.

5. MECHANICAL COMPLICATIONS:

a. Mitral regurgitation:(PH 2)

It is due to ischaemia or rupture of papillary muscle and is recognized by the presence of systolic murmur at the apex. If trivial, it is of no hemodynamic significance. However severe mitral regurgitation can induce life threatening left ventricular failure and cardiogenic shock and may warrant urgent coronary angiography followed by coronary bypass surgery and mitral valve replacement.

b. Ventricular septal defect:

It is a defect due to rupture of infarcted interventricular septum and is recognized by the presence of pansystolic murmur at the left sternal border. Diagnosis is possible by Echo-Doppler studies. It produces severe left heart failure and needs immediate surgical intervention.

c. Cardiac Rupture:

It is a serious complication which results in cardiogenic shock and almost 100% mortality. Emergency treatment by pericardial tapping may prove life saving. Rare cases have been saved by emergency surgery.

6. OTHER COMPLICATIONS:

a. Left Ventricular Aneurysm:

The infarcted segments are dilated and show paradoxical movement and compromised left ventricular hemodynamics. It is recognized by persistent ST elevation in ECG and dyskinesia seen in echocardiography and radionuclide or contrast ventriculography. It may result in persistent left ventricular failure, arrhythmias and systemic embolism. Treatment consists of aneurysmectomy and associated coronary artery bypass surgery if so indicated.

b. Thromboembolism:

Formation of a thrombus within the left ventricle followed by systemic arterial embolism leading to occlusion of a peripheral artery requires immediate surgical embolectomy in accessible vessels.

Pulmonary embolism originates in the leg veins due to prolonged immobilization. These are prevented by anticoagulation. Massive embolism may result in shock and sudden death. Thrombolytic therapy and embolectomy are occasionally required. The condition can be prevented by low molecular weight heparin.

HYPONATREMIA IN MYOCARDIAL INFARCTION:

Hyponatremia is defined as a decrease is serum sodium concentration to a level below 135 mEq/L.

Serum sodium concentration and serum osmolarity are normally maintained by haemostatic mechanisms involving thirst, antidiuretic hormone (ADH) Renin angiotensin aldosterone system (RAAS) and renal handling of sodium and water.

Increase in serum osmalarity above the normal (> 290 mosm/kg) stimulate hypothalamic osmoreceptors which in turn causes an increase in thirst and release of ADH.

Hyponatremia is a common electrolyte disorder among hospitalized patients **J.A. clayton** et al.[2, 13] It also carries an increased mortality rate among the hospitalized patients (**G.Gill** et al.)[3]. The prevalence of hyponatremia in hospitalized patients is 2% (**CMDT 2006**, p 866). It occurs equally in males and females[13].

Congestive cardiac failure causes hypotonic, hypervolemic hyponatremia. Hyperglycemia is the most common cause of trans locational hyponatremia. An increase in 100 mg/dl in serum glucose concentration decreases serum sodium by 1.6 mEq/L with the end result of rise of serum osmolality of approximately 2 mosm/Kg of water. Retention of mannitol also has the same effect.

After taking careful thorough history, including medication and clinical examination to look for volume status, patients may be subjected to biochemical investigations as follows :

1) The initial laboratory measurement needed in the evaluation of hyponatremia is serum osmolality. The common cause of hyperosmolar hyponatremia (serum osmolality >290 mosm/kg) are hyperglycemia hypertonic solutions like mannitol. Iso-osmolar hyponatremia is caused by hyperlipidemia and hyperproteinemia. Hypoosmolar hyponatremia can be again divided into three groups depending on volume status.

2) Urine osmolality is the next measurement which can very well delineate many causes of hyposmolar hyponatremia.

   This index indicates whether water excretion is impaired or not. Normally when the body is faced with water load, serum osmolality is decreased, ADH is suppressed and excess free water is excreted in very dilute urine (osmolality as low as <50 moml/kg). Patients with hyponatremia and urine osmomality of less than 100 mosm/kg are appropriately excreting very dilute urine as occurs in primary polydipsia and reseting of osmostat (i.e., a form of SIADH). However most patients with hyponatremia have urine osmolality or more than 200 mosm/kg reflecting impairment of water excretion.

3) The final step in evaluation of hyponatremia is to measure the urine sodium concentration and using this in conjunction with volume status to determine the cause of hyponatremia. This can help to guide therapy. In general, a spot test showing urine sodium concentration of <30 mEq/L differentiates patients with hypovolemic hyponatremia from patients with euvolemic hyponatremia.

Mechanism of hyponatremia in acute MI :

It is not clear whether the mechanisms that contribute to the development of hyponatremia in heart failure are involved in acute myocardial infarction. Increased hypothalamic expression of vasopressin and up-regulation of water channels in the collecting duct require several weeks of heart failure to develop[4]. However many patients developed acute hyponatremia during AMI either at admission or later during the hospital stay.

Flear CT et al. [7] found that hyponatremia developed in patients with AMI and it adversely affected the outcome of patients. Also he stated that mortality increases when the level of serum sodium fell below 130 mEq/L.

Similar study by **Wan LF** et al. from China classified AMI patients who had developed hyponatremia during their hospital stay into two groups depending on the degree of hyponatremia, and ultimately found that mortality increased with the degree of hyponatremia.

Goldberg et al.[4] from Israel in his study with large patients number found that hyponatremia was found in 12.5% of patients with AMI and developed in 19.9% during first 72 hours of hospital stay.

According to **Satish** et al., for South India hyponatremia developed in 18.5% patients with AMI on admission and 0.8% patients developed hyponatremia during initial 72 hours.

According to **Schaler MD** et al.[12], plasma arginine vasopressin level increases after acute myocardial infarction. The probable reasons put forth by Goldberg et al.[4] for elevated arginine vasopressin level was pain, nausea, major stress, acute development of LV dysfunction and in response to administration of NSAIDs and diuretics.

Rowe JW et al.[26] and **Madias** et al.[14] also related vasopressin release with emetic reflex and also following diuretic intake respectively. However level of vasopressin didn't correlate with plasma osmolality[12] in patients of AMI. Hence it was proposed that, the non osmotic release of vasopressin due to carotid baroreceptors stimulation may cause hyponatremia in patients with acute STEMI[4].

Along with vasopressin release, neurohumoral activation occurs following AMI involving renin angiotensin – Aldosterone system and nor epinephrine release contribute to hyponatremia following AMI [26,27].

Hence acute hyponatremia following acute STEMI can be explained on the basis of **non osmotic release of vasopressin**, further aggravated by, concomitant activation of the renin angiotensin

aldosterone system (RAAS) and increased norepinephrine production. These factors decrease the glomerular filtration rate, and subsequent delivery of tubular fluid to the diluting segment of the nephron, further contributing to decreased renal water excretion[10].

As already mentioned, limited number of studies were executed worldwide to find out the prevalence of hyponatremia in acute STEMI and also its correlation with 30 day (short term) mortality.

Goldberg et al.[4] in his largest series of 1067 patients admitted with acute STEMI had considered all the possible factors that could affect short term mortality among AMI patients like diabetes mellitus, female sex, smoking, hypertension, previous CAD/LVD, anterior infarction, killip scorings, reperfusion therapy etc. along with acute hyponatremia that developed after acute STEMI and concluded that hyponatremia is an independent risk factor for 30 days (short term) mortality among acute STEMI patients.

A retrospective study from China, **Wang LF** et al., in 2006 analysed acute hyponatremia along with enzymes level, infarct size, cardiac function and found that as the degree of hyponatremia increases, the short term mortality (30 days mortality) increases. He concluded that hyponatremia may be considered as one of the important markers that predict a worst prognosis in AMI.

Similar study by **Flear CT, Hilton P**[7] in 1979 in the series of 235 patients admitted for AMI found that day to day variability of serum sodium was often increased and also concluded finally that short term mortality increases with degree of hyponatremia (<130 mEq/L). However in this study he didn't consider LV dysfunction as one of the factors for short term mortality among AMI patients.

A limited study from **Satish** et al. from South India of about 54 patients, concluded that hyponatremia can be considered as an independent risk factor following acute STEMI.

Laurie Barday and **Charles Vega**[28] analyzed a parallel study by Goldberg et al.[29] correlating hyponatremia in early phase of STEMI with long term mortality and post discharge admission for cardiac failure. In this series of 978 patients with acute STEMI, without a history of heart failure. 11% had hyponatremia (<72 hrs of admission). Patients were followed up from 9-61 months (mean 31 months). It was found that overall mortality for hyponatremic patients was 24.1% as against (0.9%) for normonatremic patients. 11.7% of hyponatremic patients developed heart failure during their follow up period. Laurie Barday and Charles Vegas on the basis of Goldberg et al., study concluded that hyponatremia within 72 hours of acute STEMI was an independent factor for long term mortality and hospitalization for heart failure following AMI. However

and its risk increased with the degree of hyponatremia. However, it was not a significant risk factor for promoting recurrent myocardial infarction.

The correlation of possible factors like age, LVD, female sex, anterior infarction etc, that can affect the short term mortality of acute STEMI have been studied exhaustively worldwide and are proved beyond doubt[32].

MATERIAL AND METHODS

The study is designed to evaluate the correlation of serum sodium level with 30 days mortality, and with cardiac events that occur during hospital stay among acute STEMI patients.

During the period from 1st Jan 2008 to 30th Jun 2009, 100 patients admitted with acute myocardial infarction in coronary care unit, CMC Hospital, Coimbatore ,within a period of three days who fulfilled the inclusion / exclusion criteria were analysed. The patients were divided into two equal groups.

100 patients admitted in ICCU, Department of Cardiology, Coimbatore Medical College, Coimbatore, who fulfilled the inclusion / exclusion criteria were enrolled. The patients were divided into two equal groups.

1. Group A : Patients with hyponatremia on admission or developed during first 72 hours of acute STEMI.
2. Group B : Patients with normal serum sodium level during the first 72 hours of acute STEMI.

INCLUSION CRITERIA :

Patients having acute STEMI defined by ST segment elevation of >2 mm in precordial leads, (or) >1 mm in frontal leads in 2 or more consequtive leads with or without Q waves in standard electrocardiogram (ECG) with any one of the following.

(a) Typical chest pain suggestive of angina lasting for more than 20 minutes, (or) anginal equivalents like breathlessness, chest discomfort or sweating.

(b) Raised cardiac enzymes (CPK-MB, Troponin I or T).

(c) Fresh regional wall motion abnormalities in Echocardiogram (ECHO).

EXCLUSION CRITERIA :

1. Patients with co-morbid conditions like previously detected CCF, LV dysfunction, renal disease, decompensated liver disease, fresh cerebrovascular accidents, malignancies, acute gastroenteritis
2. Patients on any medications that alter serum sodium level like diuretics, steroids, antacids ACE inhibitors, amiodarone, clofibrate etc.
3. Patients with very late presentation of acute STEMI.
4. Patient with acute onset LBBB.

Patients fulfilling inclusion criteria were subjected to thorough history, clinical examination biochemical investigations, ECG, Chest X-ray and ECHO Biochemical investigations.

1. Complete blood count.
2. **Blood sugar by glucose oxidase method.**
3. Blood urea.
4. Serum creatinine.
5. **Serum sodium by ion specific electrode method**
6. Cardiac Enzymes (CPK MB, Troponin I or T) if required.
7. Lipid profile.
8. X-ray chest.(fig 1)
9. **ECG.(fig 2-7)**

Types of Myocardial infarction on the basis of ECG are as follows :

(a) Q or ST elevation in V1-V6 – Anterior wall MI.

(b) Q or ST elevation in V1-V4 – Anteroseptal MI.

(c) Q or ST elevation in II, III, avf – Inferior wall MI.(fig 5)

(d) Q or ST elevation in I, AVL, V5-V6 – Lateral wall MI.(fig 3)

(e) R>S, ST Depression and upright T in V1-V2– Posterior wall MI

(f) ST elevation >1 mm in V1 and RV4 – Right ventricular MI.

(g) Q (or) ST elevation in I, AVL and V1-V6 – Extensive anterior wall MI.(fig 4)

10. **Echocardiogram (ECHO):** Patients were subjected to ECHO on day 3.

Venous samples for serum sodium were obtained on admission, 24 hours, 48 and 72 hours. Thereafter blood sugar levels were determined simultaneously and serum sodium levels were corrected by adding 1.6 mEq/L for every 100 mg/dl increase in blood sugar above 100 mg/dl.

Hyponatremia is defined as serum sodium level below 135 mEq/L.

Patients were then followed up after 30 days, either personally or through telephone and cardiac events were recorded.

RESULTS AND ANALYSIS

HYPONATREMIA FOLLOWING ACUTE MYOCARDIAL INFARCTION

According to the level of serum sodium patients were classified into the following groups(TABLE)

TABLE 1

SEX DISTRIBUTION AMONG PATIENTS WITH NORMAL AND LOW SODIUM LEVELS

Gender	Normonatremia	Hyponatremia	Total
Male	55 (80.9%)	27 (84.4%)	82 (82.0%)
Female	13 (19.1%)	5 (15.6%)	18 (18.0%)
Total	68 (100.0%)	32 (100.0%)	100

Out of all 100 MI patients, 32(32.0%) had hyponatremia in any of 3 days values. And 68 (68.0%) had completely normal sodium levels in all 3 days. Out of those 32 hyponatremics, 27(84.4%) were males and 5(15.6%) were females. And out of those 68, 55(80.9%) were males and 13(19.1%) were females.

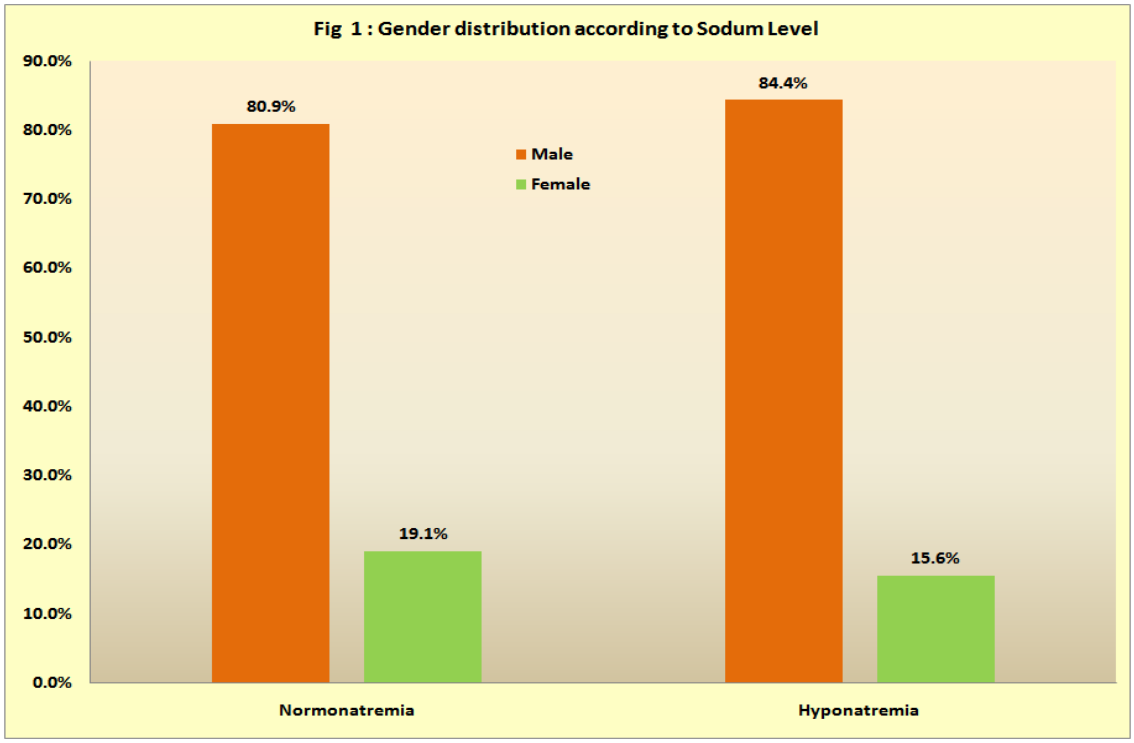


Table 2

Types of Myocardial Infarction among Male and Females

Territory of MI	Male	%	Female	%	Total	%
ASMI	18	22.0	6	33.3	24	24.0
AWMI	39	47.6	8	44.4	47	47.0
ALMI	4	4.9	1	5.6	5	5.0
IWMI	19	23.2	2	11.1	21	21.0
PWMI	2	2.4	1	5.6	3	3.0
Total	82	100.0	18	100.0	100	100.0

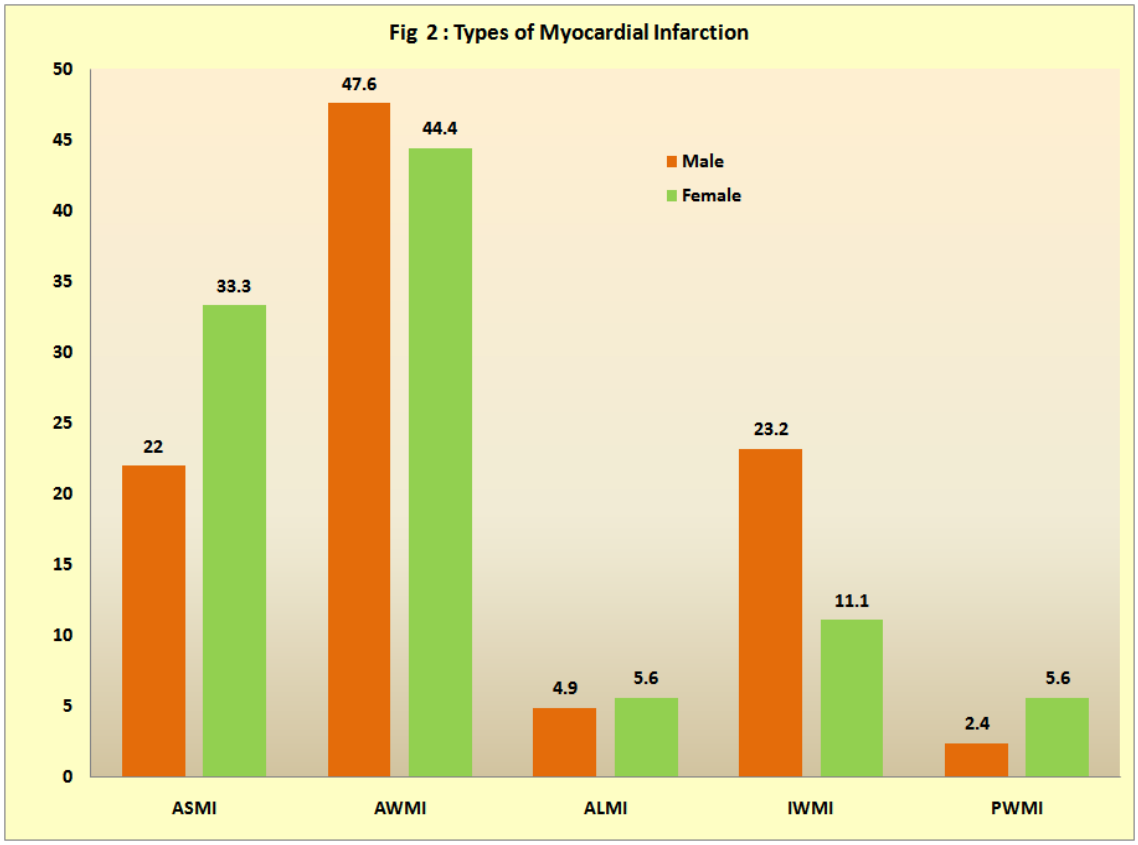
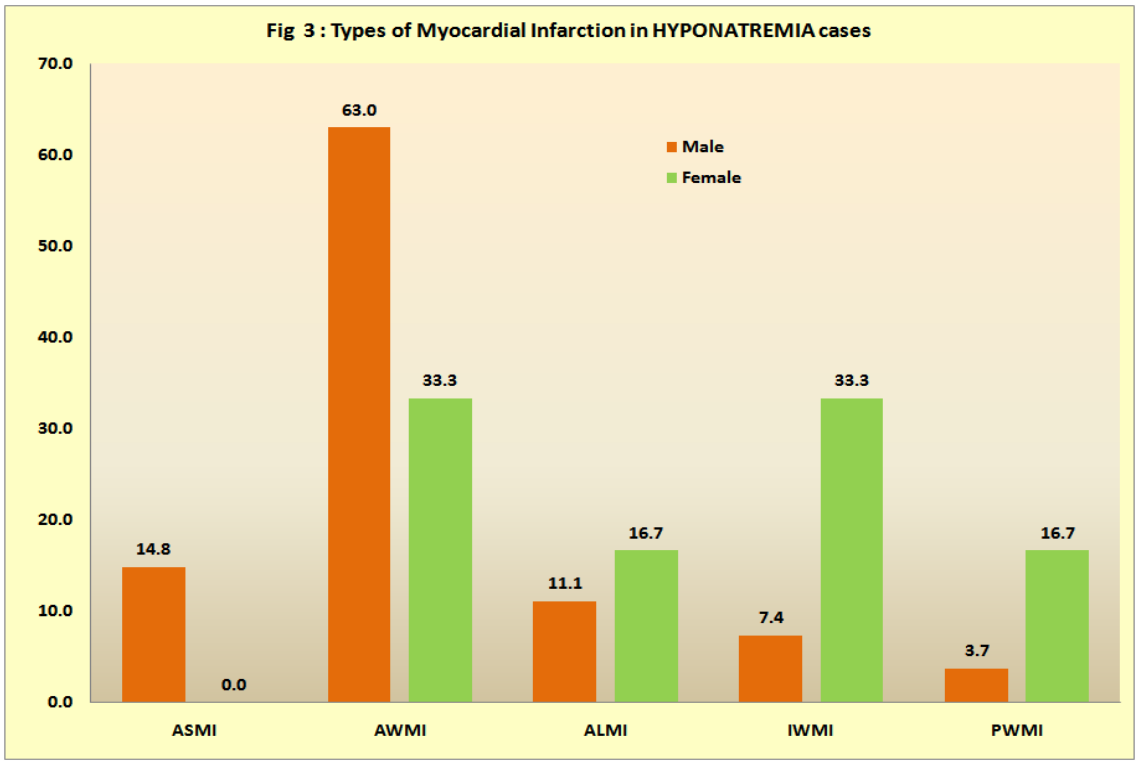


Table 3

Type of MI in hyponatremics among Males and Females

Territory of MI	Male	%	Female	%	Total	%
ASMI	4	14.8	0	0.0	4	12.1
AWMI	17	63.0	2	33.3	19	57.6
ALMI	3	11.1	1	16.7	4	12.1
IWMI	2	7.4	2	33.3	4	12.1
PWMI	1	3.7	1	16.7	2	6.1
TOTAL	27	100.0	6	100.0	33 (32 pts)	100.0

Within the MI s male female ratio were studied. One patient had combined high lateral MI and ASMI. The patients who had hyponatremia were 32 and MIs were 33.in that AWMI were the highest.



(ONE PATIENT HAD A COMBINED ASMI WITH HIGH LATERAL WALL MI.)

TABLE 4

SHORT TERM MORTALITY IN NORMO AND HYPONATREMIC PATIENTS

Mortality	Hyponatremia	%	Normonatremia	%	Total	%
Alive	24	75.0	48	70.6	72	72.0
Death	8	25.0	20	29.4	28	28.0
Total	32	100.0	68	100.0	100	100.0

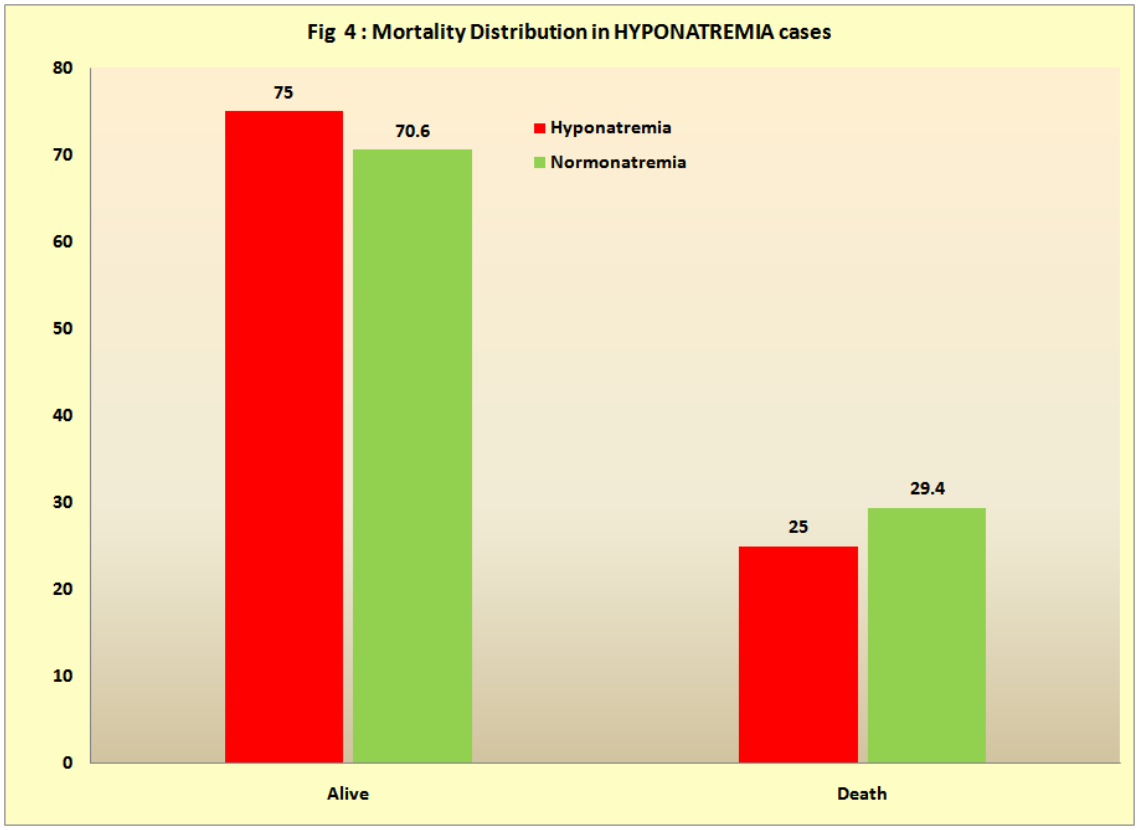


FIG. 5. SHORT TERM MORTALITY AMONG HYPONATREMIC PATIENTS

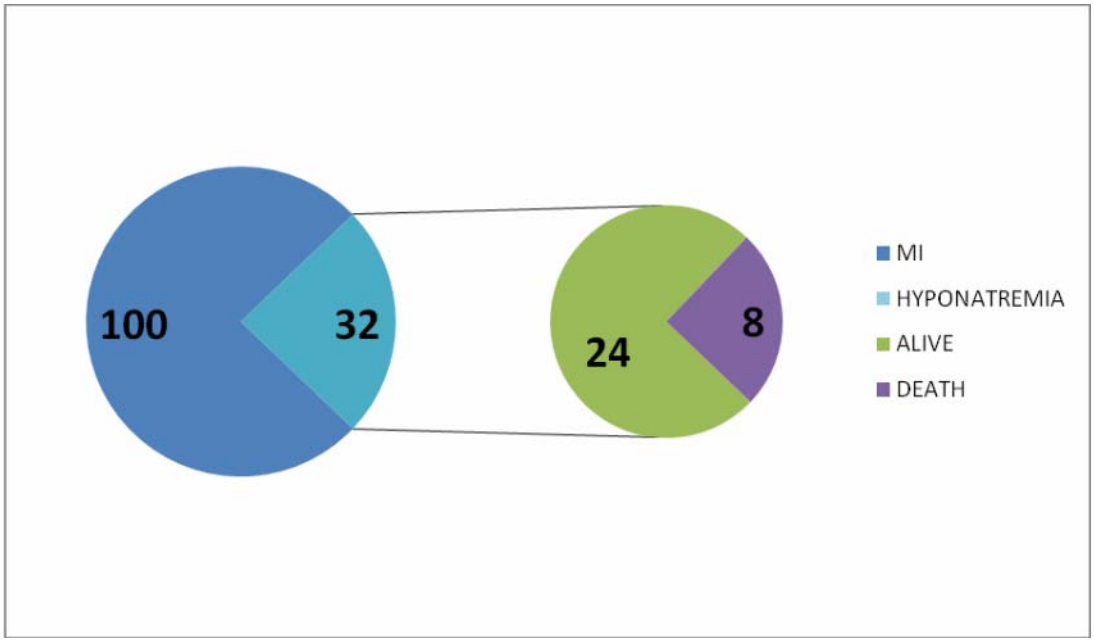


TABLE 5

TYPE OF MI WITH HYPONATREMICS AND ITS CORRELATION WITH DAY OF HYPONATREMIA

.Territory of MI	TOTAL	Hyponatremia	Hyponatremia at		
			Day 1	Day 2	Day 3
ASMI	24	4	2 (50.0%)	1 (25.0%)	1 (25.0%)
AWMI	47	19	14 (73.7%)	1 (5.3%)	4 (21.1%)
ALMI	05	4	2 (50.0%)	0	1 (25.0%)
IWMI	21	4	3 (75.0%)	0	1 (25.0%)
PWMI	03	2	1 (50.0%)	0	1 (50.0%)
Total	100	33(32 patients)	22 (68.8%)	2 (6.3%)	8 (25.0%)

FIG 6.

DAY OF HYPONATREMIA WITH TERRITORY OF MI

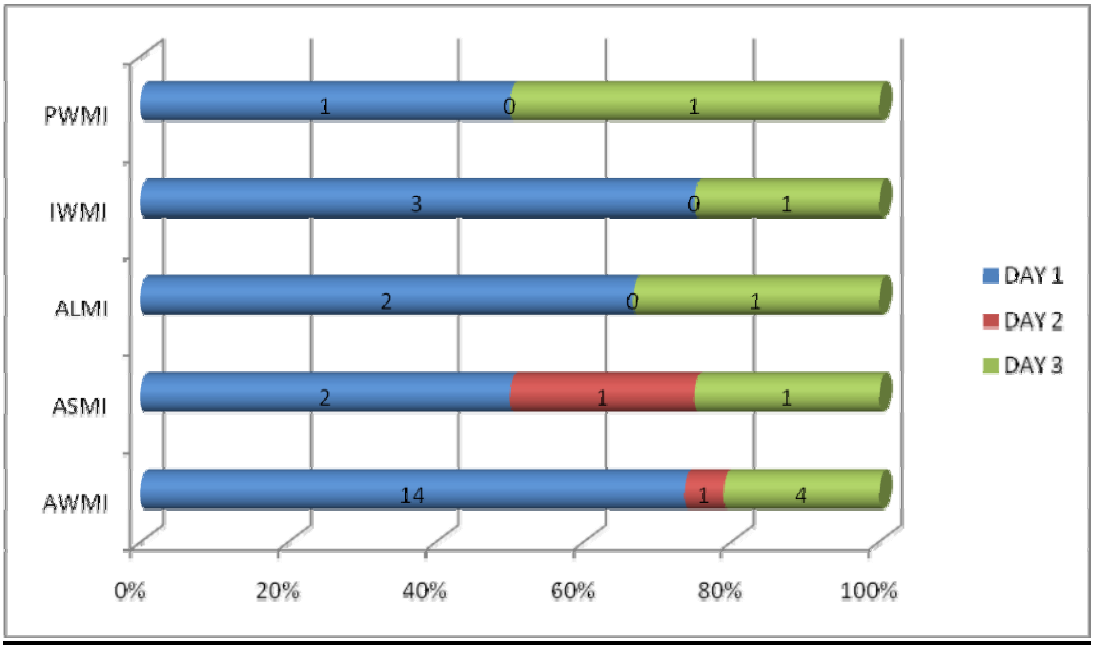


TABLE 6

DEGREE OF HYPONATREMIA WITH TERRITORY OF MI

Territory of MI	TOTAL	Hyponatremia	Severity of Hyponatermia	
			131 – 135	**125 – 130**
ASMI	24	4	1 (25.0%)	3 (75.0%)
AWMI	47	19	13 (68.4%)	5 (26.3%)
ALMI	05	4	3 (75.0%)	1 (25.0%)
IWMI	21	4	2 (50.0%)	2 (50.0%)
PWMI	03	2	0	2 (100.0%)
Total	100	33	19 (59.4%)	13 (40.6%)

FIG 6

DEGREE OF HYPONATREMIA WITH TERRITORY OF MI

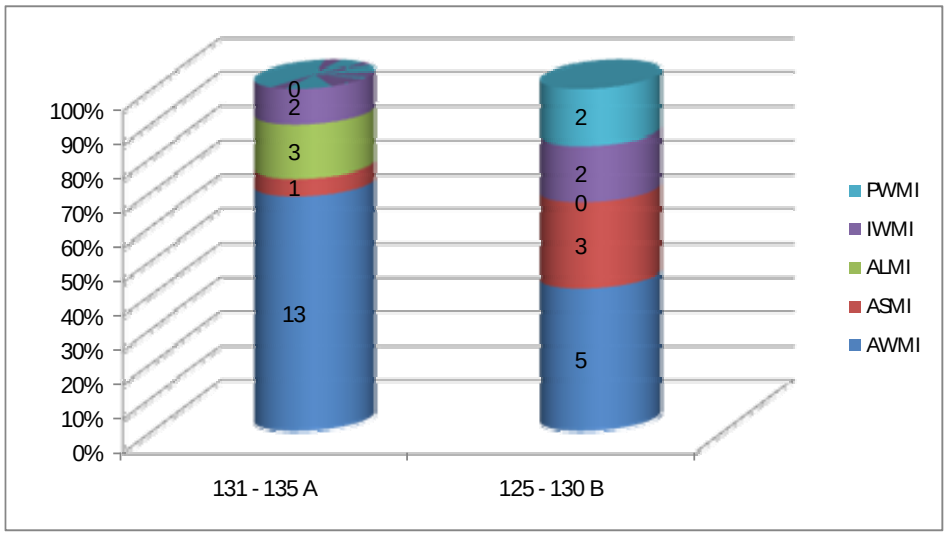


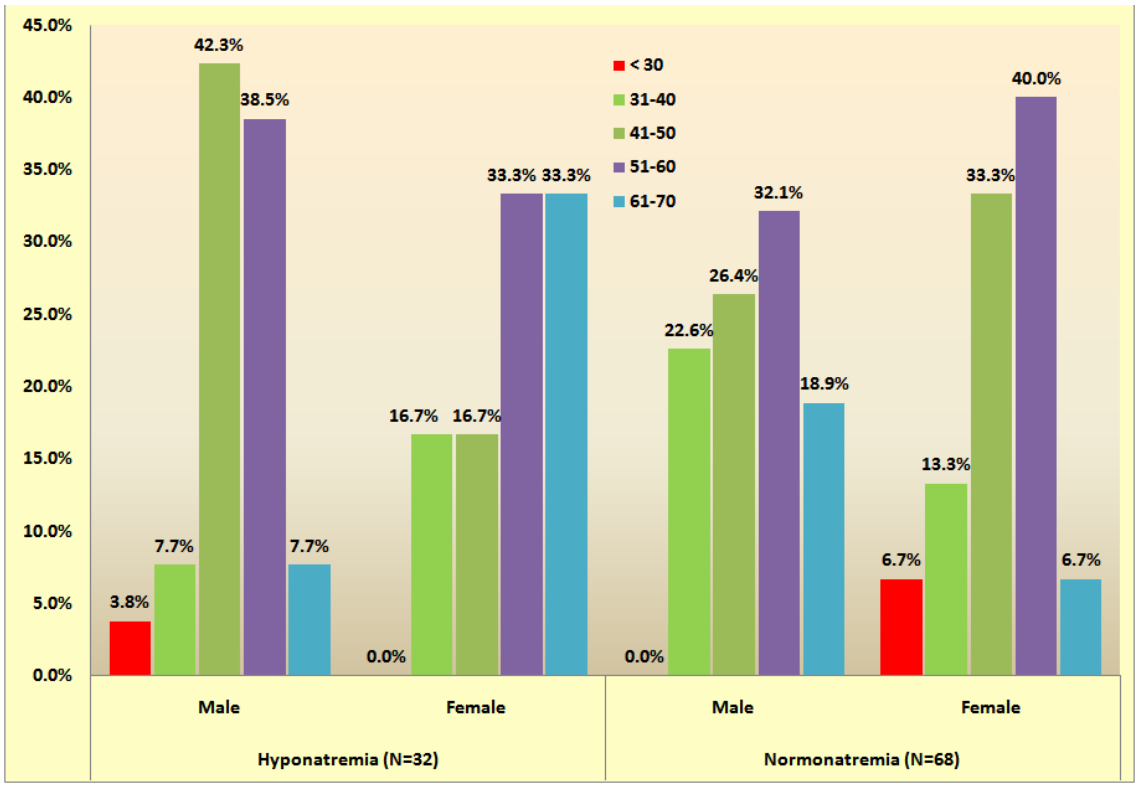
TABLE - 7

AGE, HYPONATREMIA AND MORTALITY

	Total	Hyponatremia (N=32)		Normonatremia (N=68)	
		Male	Female	Male	Female
< 30	2	1 (3.8%)	0	0	1 (6.7%)
31-40	17	2 (7.7%)	1 (16.7%)	12 (22.6%)	2 (13.3%)
41-50	31	11(42.3%)	1(16.7%)	14 (26.4%)	5 (33.3%)
51-60	35	10 (38.5%)	2 (33.3%)	17 (32.1%)	6 (40.0%)
61-70	15	2 (7.7%)	2 (33.3%)	10 (18.9%)	1 (6.7%)
TOTAL	100	26 (100.0%)	6 (100.0%)	53 (100.0%)	15 (100.0%)

One from less than 30 years was hyponatremic and one normonatremic.in 31-40 yrs group 3 out of 17 was hyponatremic. In 41-50 yrs 12 out of 31 was hyponatremic. In 51-60 yrs group 12 out of 35 was hyponatremic. 1n 61-70 yrs 4 out of 15 developed hyponatremia.

Fig. 8 AGE, HYPONATREMIA AND MORTALITY



The male female ratio was also studied. The proportion of the males was more in 41 – 60 yrs groups. In younger groups the female ratio was less.

Table 8

AGE, HYPONATREMIA AND MORTALITY

Age	Hyponatremia (N=32)	Alive	Death
< 30	1	1 (100.0%)	0
31-40	3	3 (100.0%)	0
41-50	12	7 (58.3%)	5 (41.7%)
51-60	12	7 (58.3%)	5 (41.7%)
61-70	2	1 (50.0%)	1 (50.0%)

Fig. 9 AGE, HYPONATREMIA AND MORTALITY

DIABETES

TABLE NO. 9

SEX DISTRIBUTION OF MI PATIENTS IN DIABETES

Gender	Number	percentage
Male	12	80.0
Female	3	20.0
Total	15	100.0

FIG.10 SEX DISTRIBUTION OF MI PATIENTS IN DIABETES

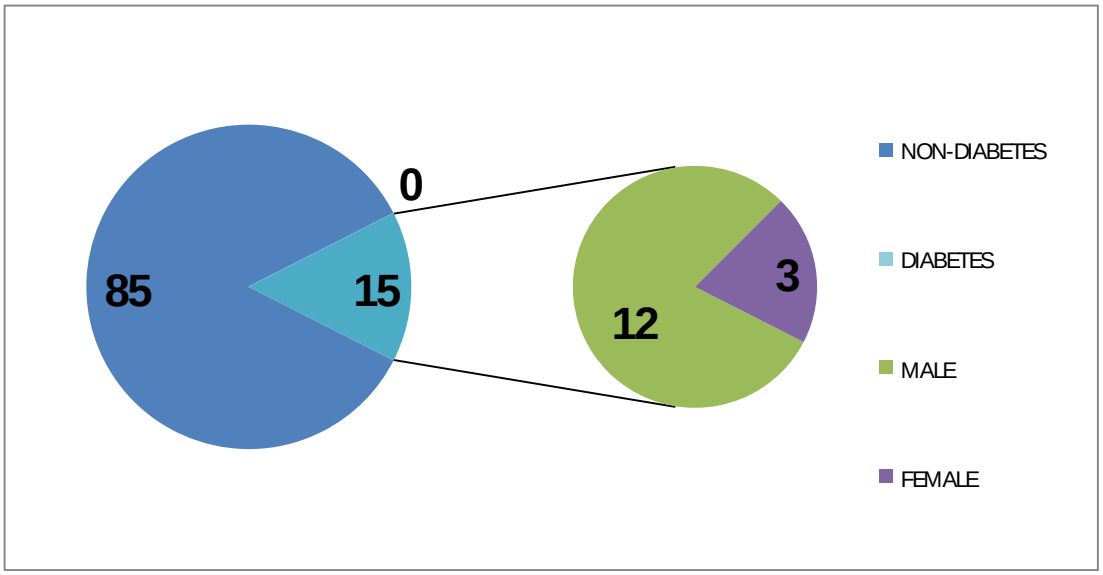


Fig. 11 HYPONATREMIA AMONG DIABETES

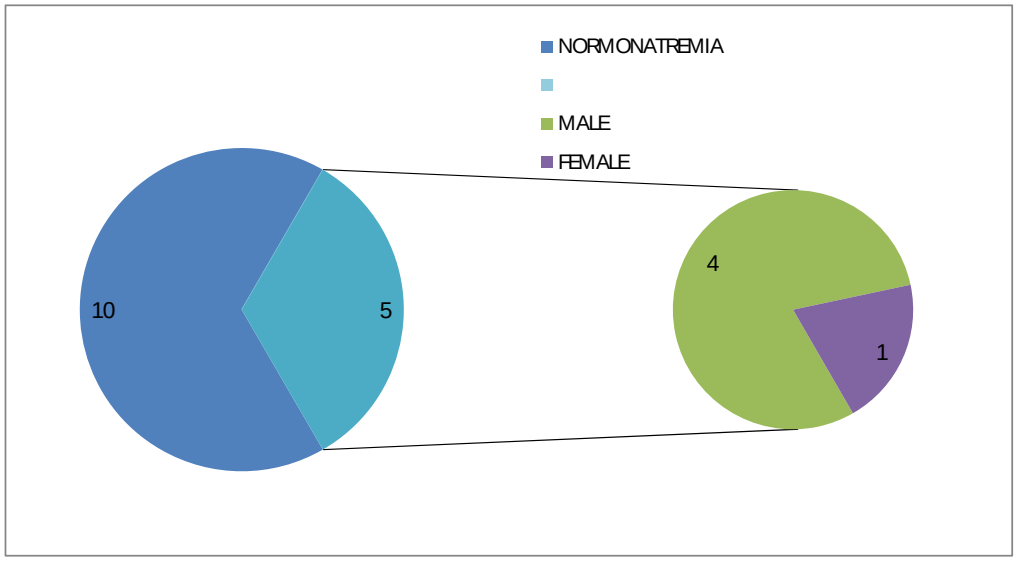


Table 10

HYPONATREMIC PATIENTS AMONG DIABETES VS DAY

Gender	Total	DAY 1	DAY 2	DAY 3
Male	4	2 (50.0%)	2 (50.0%)	4 (100.0%)
Female	1	1 (100.0%)	0	0
Total	5	3 (60.0%)	2 (40.0%)	4 (100.0%)

Fig. 12

HYPONATREMIC PATIENTS AMONG DIABETES VS DAY

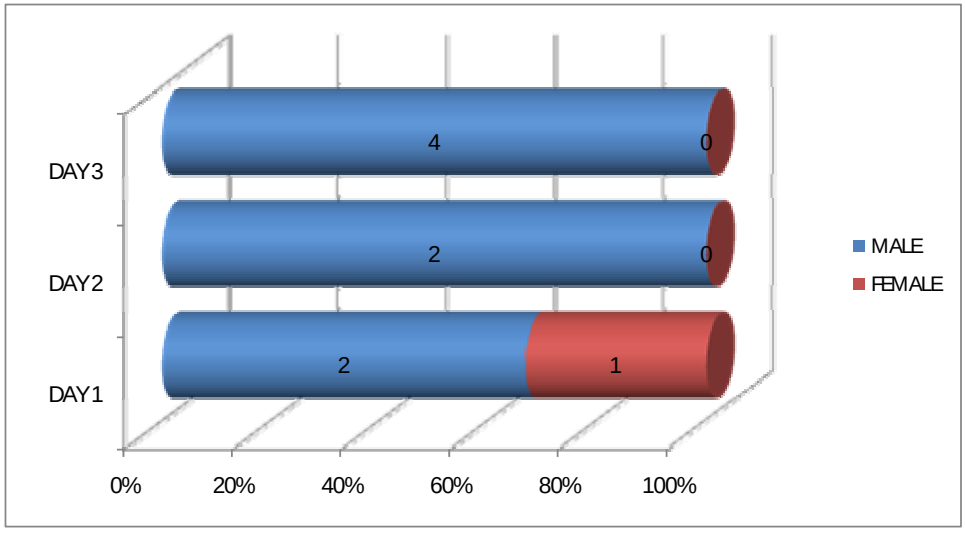


TABLE 11

HYPONATREMIA AMONG DIABETES VS SHORT TERM MORTALITY:

Mortality	Hyponatremia	Normonatremia	Total
Alive	3 (60.0%)	7 (70.0%)	10 (66.7%)
Death	2 (40.0%)	3 (30.0%)	5 (33.3%)
Total	5 (100.0%)	10 (100.0%)	15 (100.0%)

FIG. 13

HYPONATREMIA AMONG DIABETES VS SHORT TERM MORTALITY:

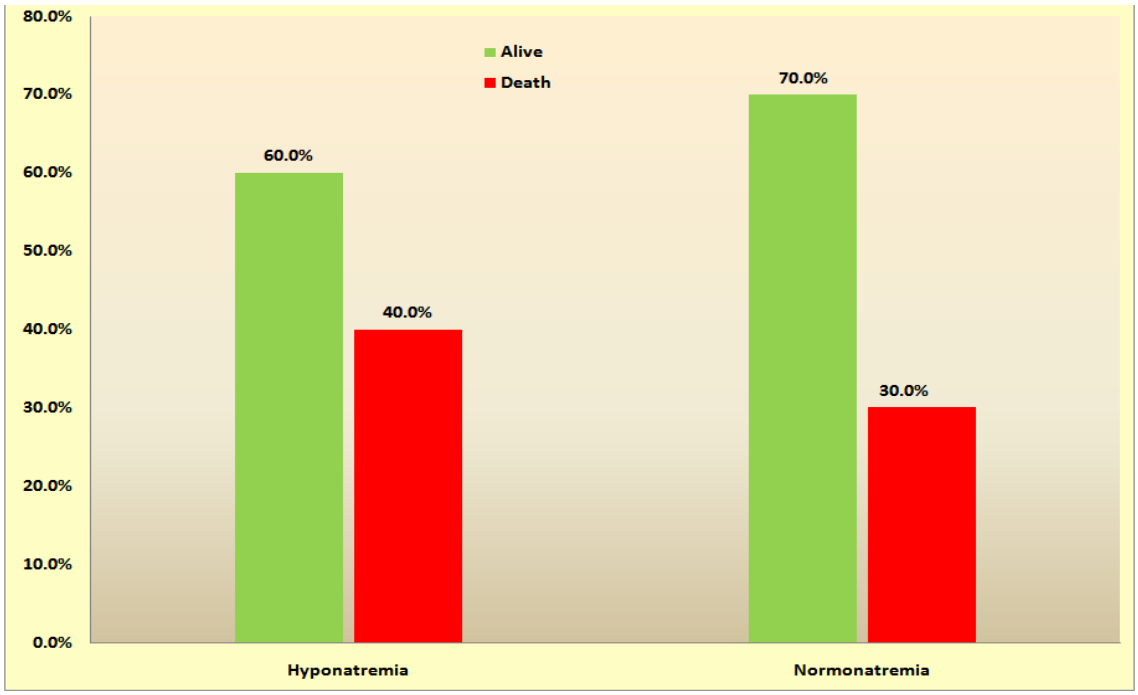
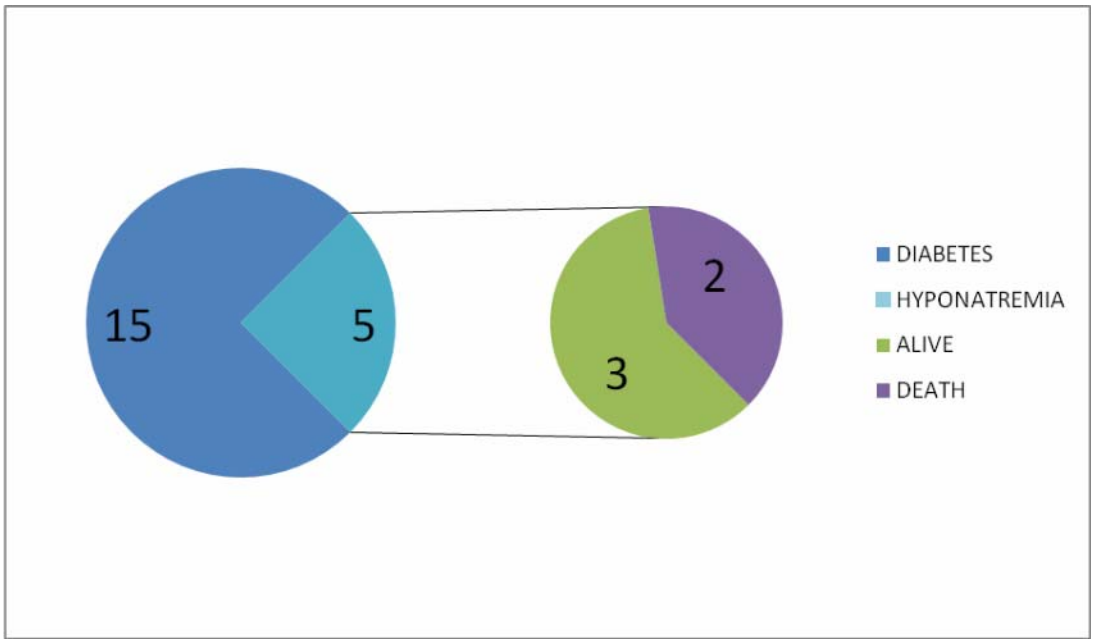


FIG. 14

HYPONATREMIA AMONG DIABETES VS SHORT TERM MORTALITY:



CORONARY ARTERY DISEASE:

TABLE 12

CAHD HISTORY VS SEX RATIO

Gender	Number	percentage
Male	4	80.0
Female	1	20.0
Total	5	100.0

FIG. 15

CAHD HISTORY VS SEX RATIO

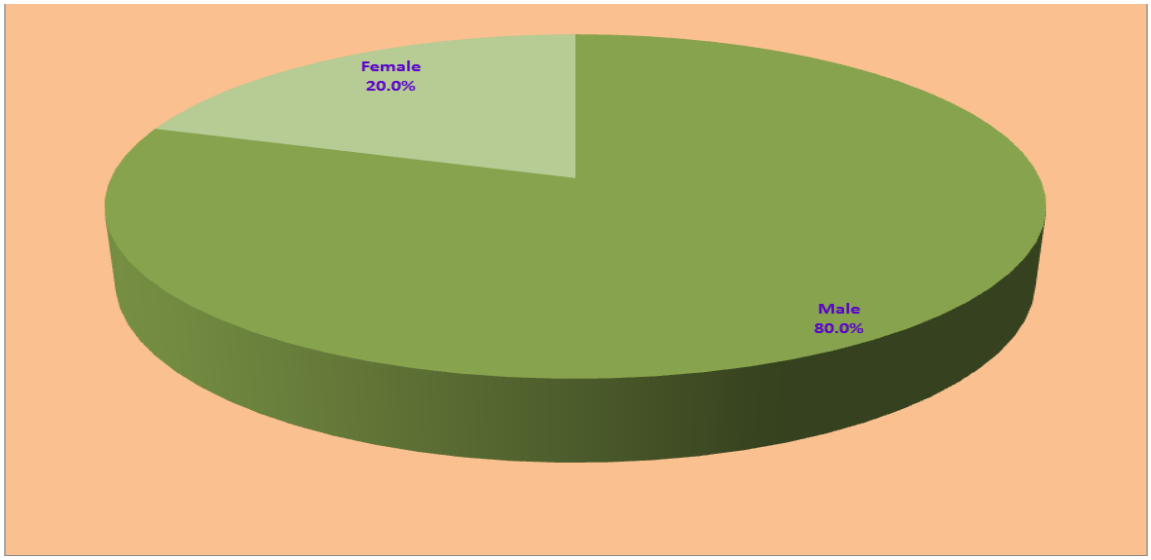


FIG. 17

CAHD HISTORY VS SEX RATIO

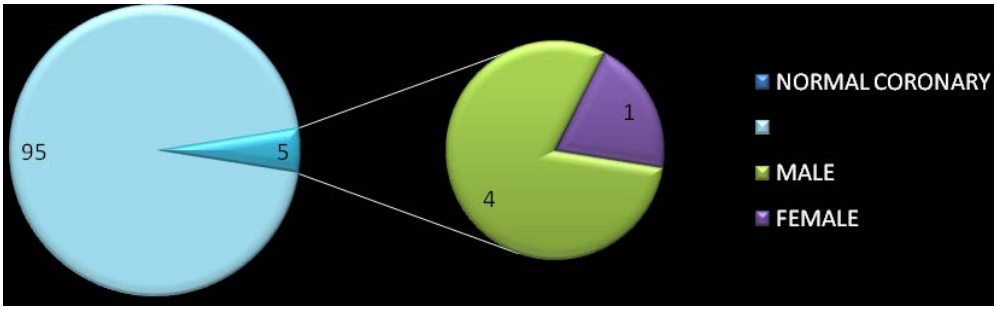


TABLE 13

HYPONATREMICS AMONG OLD CAHDS :

Gender	Total	Number	Percentage
Male	4	1	25.0
Female	1	1	100.0
Total	5	2	40.0

FIG. 17

CAHD HISTORY VS SEX RATIO

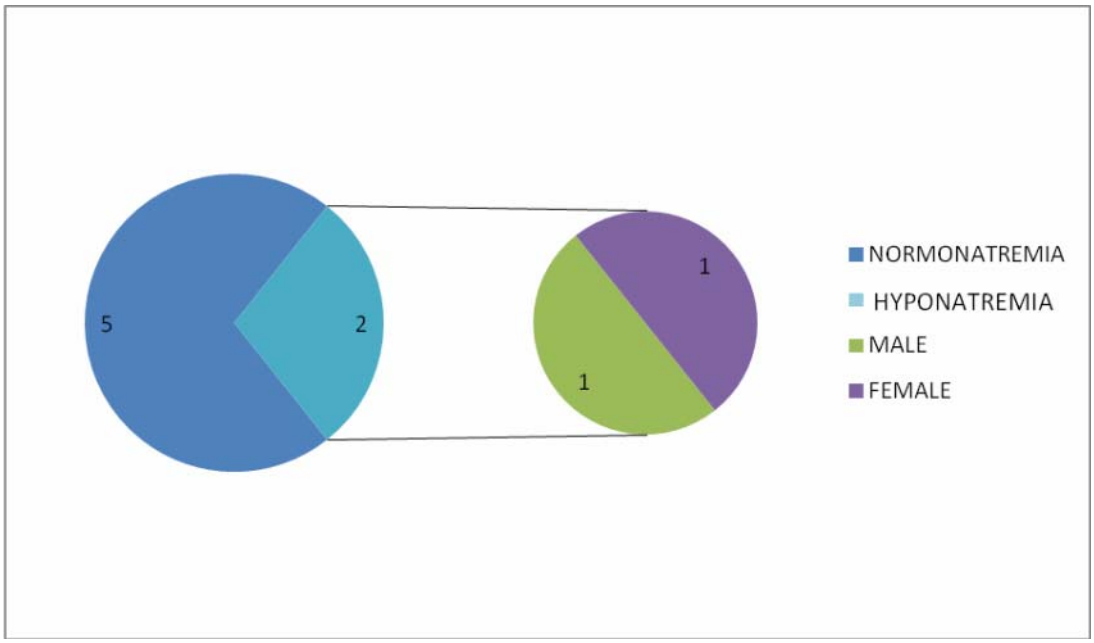


TABLE 14

HYPONATREMICS AMONG OLD CAHD VS DAY :

Gender	Total	DAY 1	DAY 2	DAY 3
Male	1	1	1	1
Female	1	1	0	0
Total	2	2	1	1

FIG. 15

CAHD HISTORY VS SEX RATIO

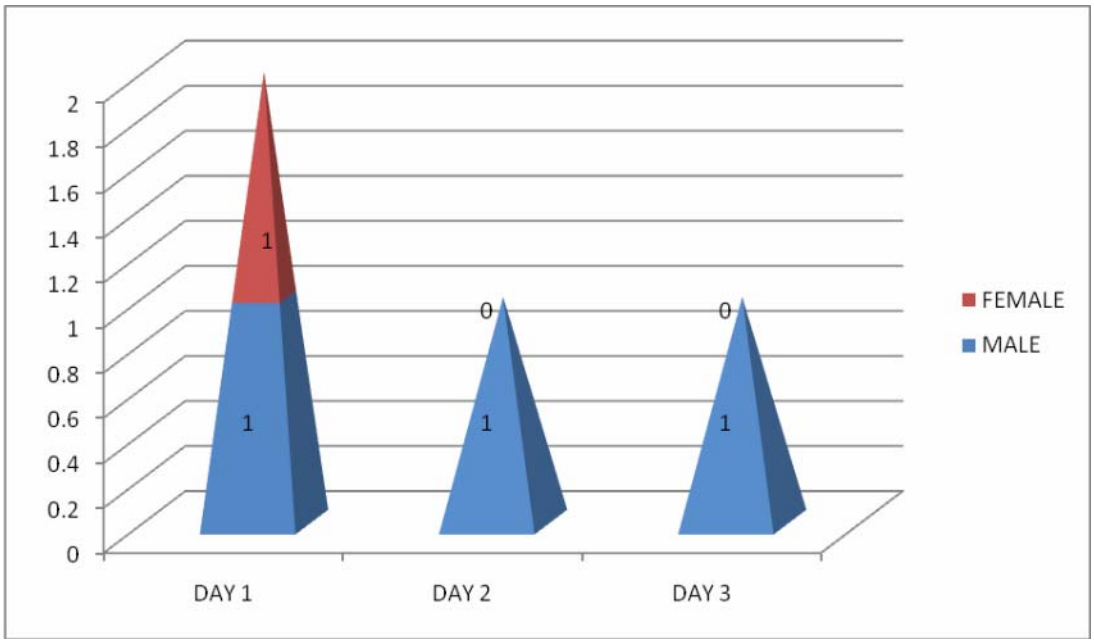


TABLE 15

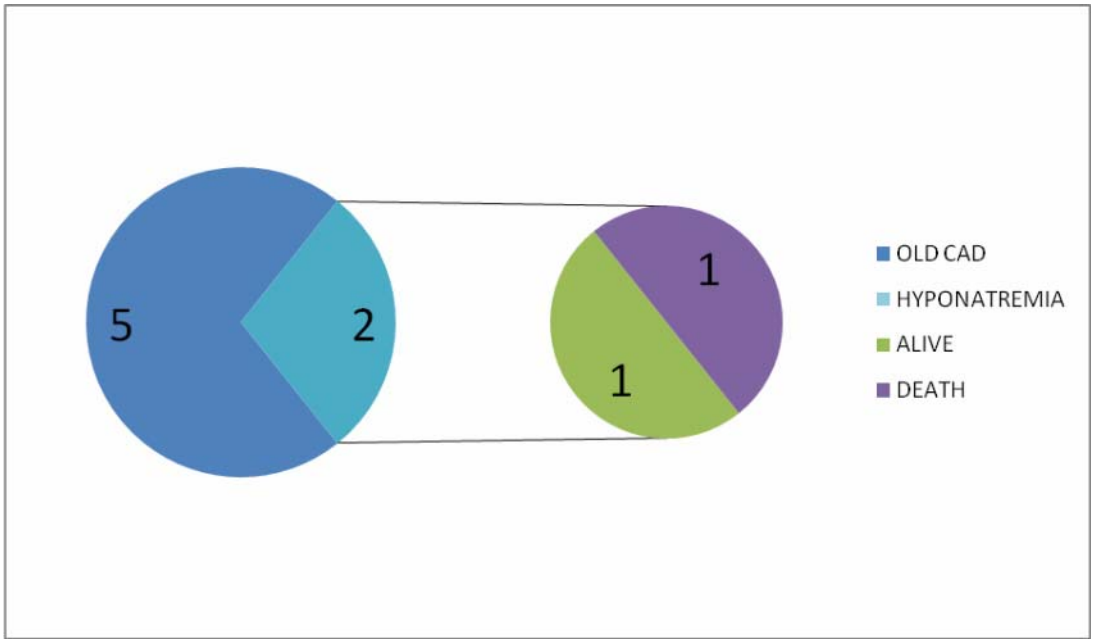
HYPONATREMICS AMONG OLD CAHDS VS SHORT TERM MORTALITY:

Mortality	Hyponatremia	Normonatremia	Total
Alive	1 (50.0%)	3 (100.0%)	4 (80.0%)
Death	1 (50.0%)	0	1 (20.0%)
Total	2 (100.0%)	3 (100.0%)	5 (100.0%)

$\chi 2=1.50$, $p=0.2206$

FIG. 19

HYPONATREMICS AMONG OLD CAHDS VS SHORT TERM MORTALITY:



Out of 2 hyponatremics one was alive and the other was dead.

THROMBOLYSIS:

Fig. 20

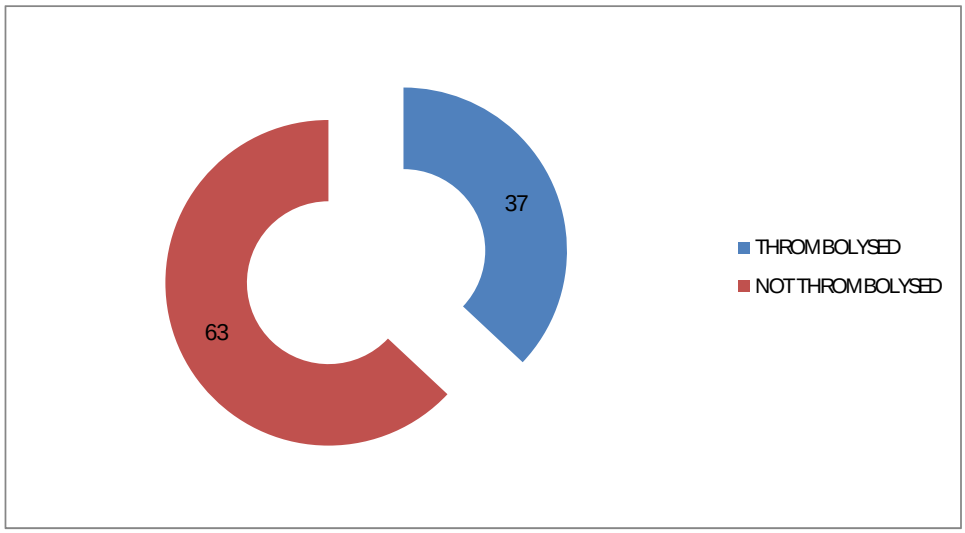


TABLE 16

THROMBOLYSIS VS SEX RATIO

Gender	Number	percentage
Male	33	89.2
Female	4	10.8
Total	37	100.0

Fig. 21

THROMBOLYSIS VS SEX RATIO

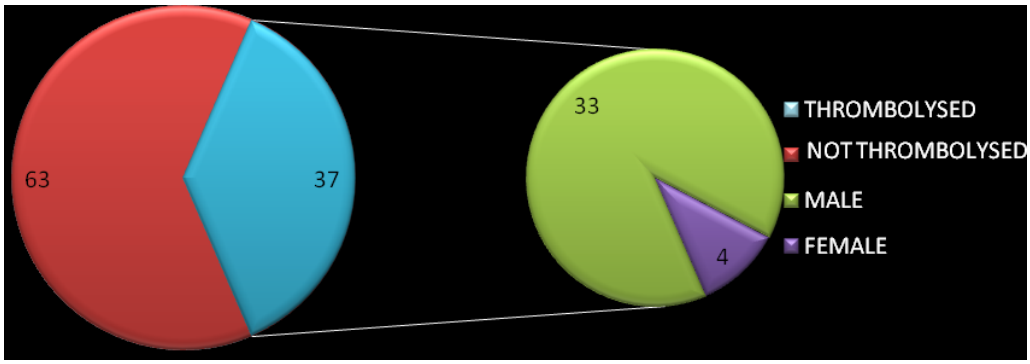


TABLE 17

HYPONATREMICS AMONG THROMBOLYSED :

Gender	Total	Hyponatremia	Percentage
Male	33	12	36.4
Female	4	02	50.0
Total	37	14	37.8

Fig. 22

HYPONATREMICS AMONG THROMBOLYSED :

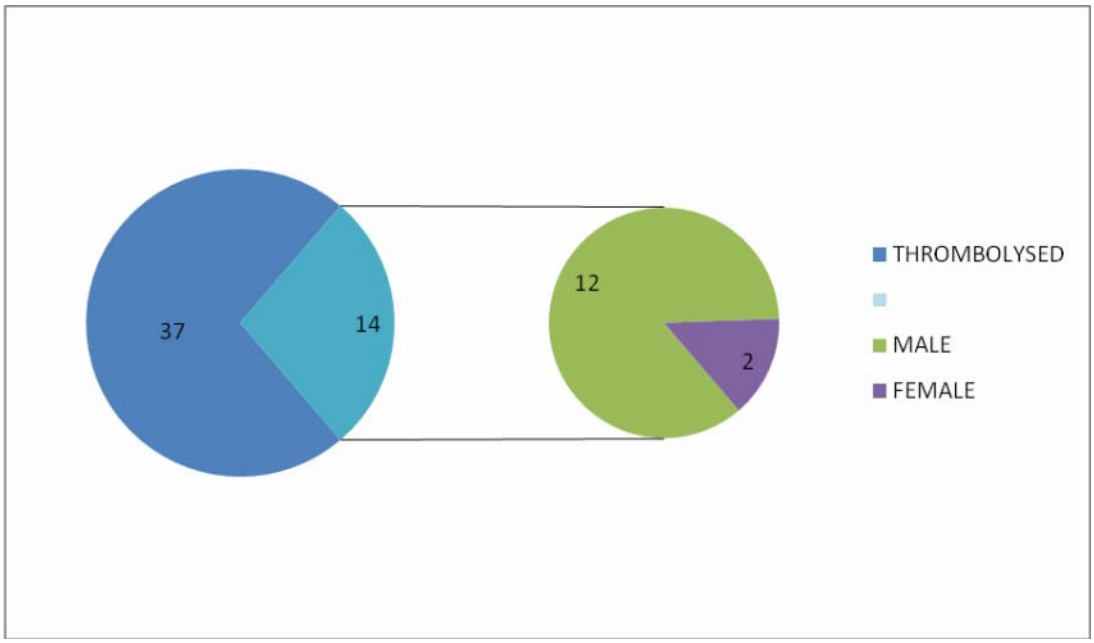


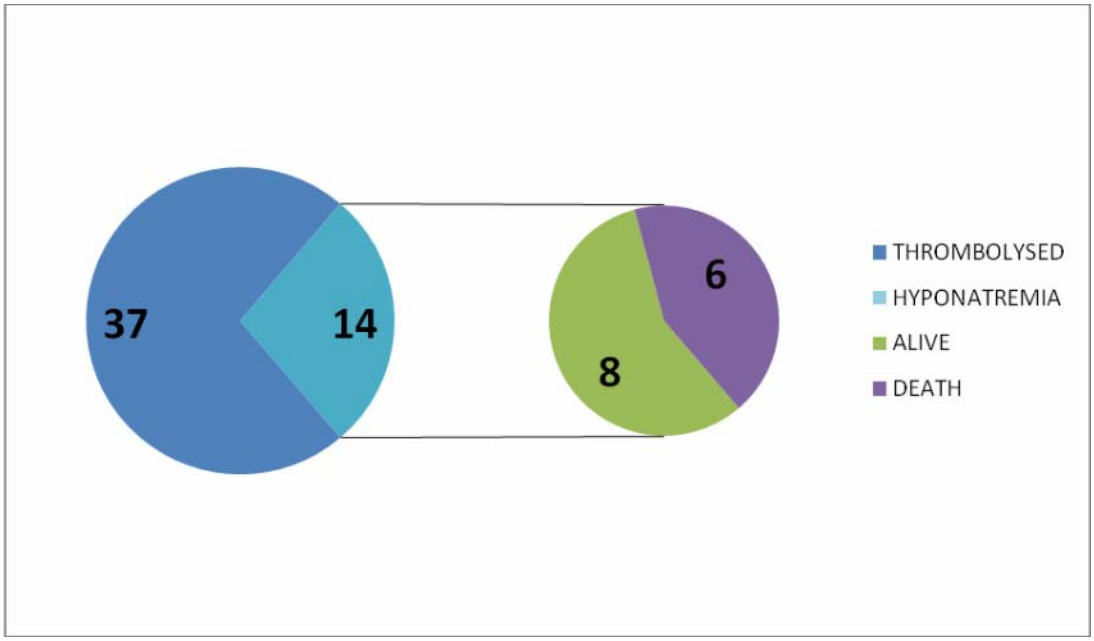
TABLE 18

HYPONATREMIA AMONG THROMBOLYSED VS SHORT TERM MORTALITY :

Mortality	Hyponatremia	Normonatremia	Total
Alive	8 (57.1%)	16 (69.6%)	24 (64.9%)
Death	6 (42.9%)	7 (30.4%)	13 (35.1%)
Total	14 (100.0%)	23 (100.0%)	37 (100.0%)

FIG. 23

HYPONATREMIA AMONG THROMBOLYSED VS SHORT TERM MORTALITY :



LV DYSFUNCTION

EJECTION FRACTION:

TABLE 19

AGEWISE DISTRIBUTION OF LVEF WITH SEX RATIO

EF IN %	MALE	FEMALE	TOTAL
< 30	4	1	05
30-35	3	0	03
36-40	9	4	13
41-45	5	2	07
46-50	10	1	11
51-55	8	3	11
56-60	27	4	31
61-65	13	1	14
66-70	3	2	05
TOTAL	82	18	100

Fig. 24

AGEWISE DISTRIBUTION OF LVEF WITH SEX RATIO

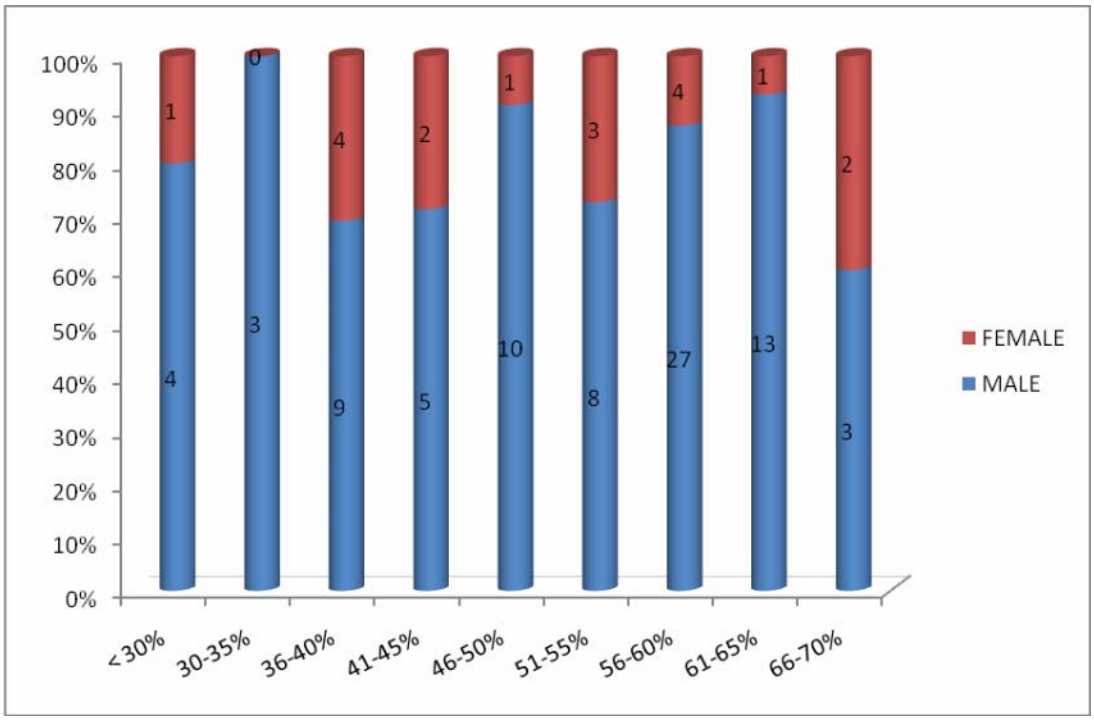


TABLE 20

EJECTION FRACTION < 50 %

Gender	Total	Number	Percentage
Male	82	27	32.9
Female	18	8	44.4
Total	100	35	35.0

Fig. 25

SEX RATIO AMONG LV DYSFUNCTION

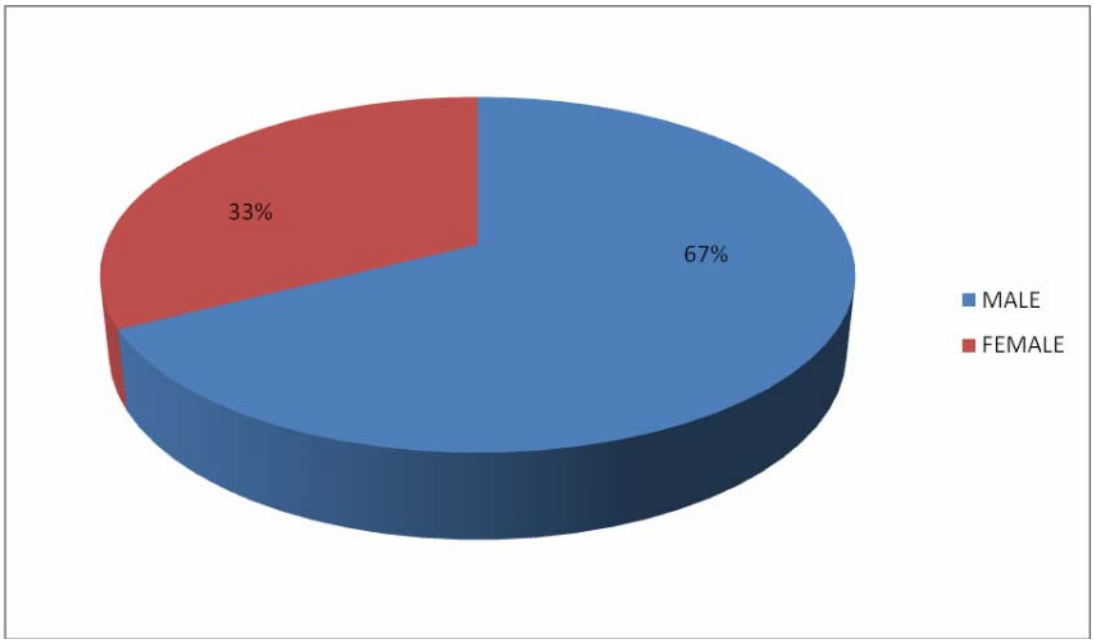


TABLE 21

HYPONATREMIC PATIENTS AMONG LVDS

Gender	Total	Hyponatremia	percentage
Male	27	13	48.1
Female	8	4	50.0
Total	35	17	48.6

FIG. 26

HYPONATREMIC PATIENTS AMONG LVDS

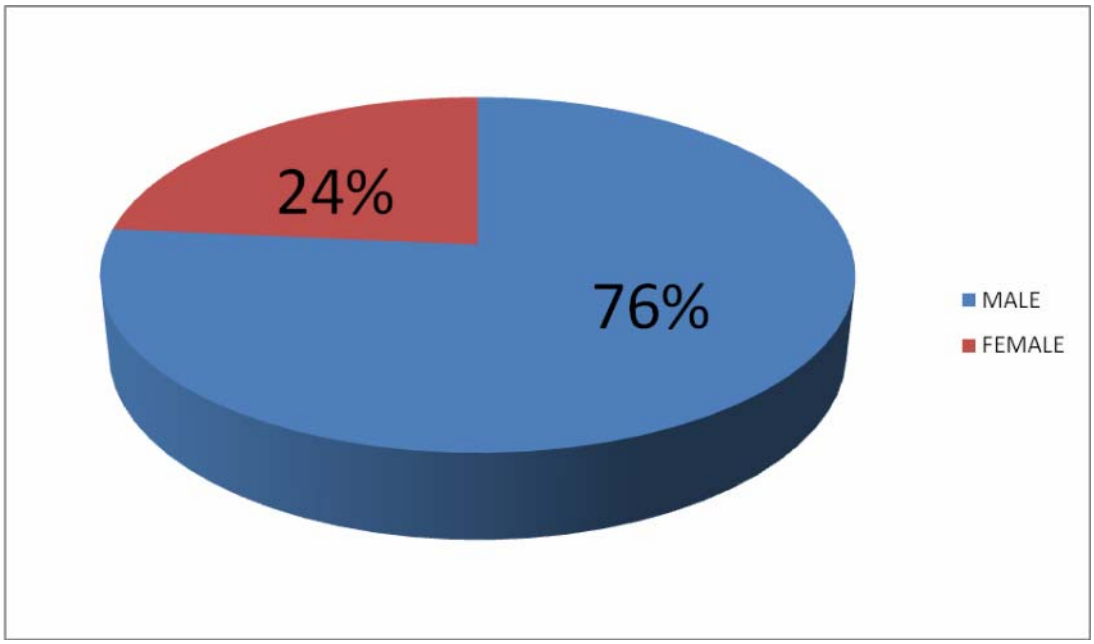


TABLE 22

HYPONATREMICS AMONG LVDS VS MORTALITY:

Mortality	Hyponatremia	Normonatremia	Total
Alive	6 (35.3%)	7 (38.9%)	13 (37.1%)
Death	11 (64.7%)	11 (61.1%)	22 (62.9%)
Total	17 (100.0%)	18 (100.0%)	35 (100.0%)

FIG. 27

HYPONATREMICS AMONG LVDS VS MORTALITY:

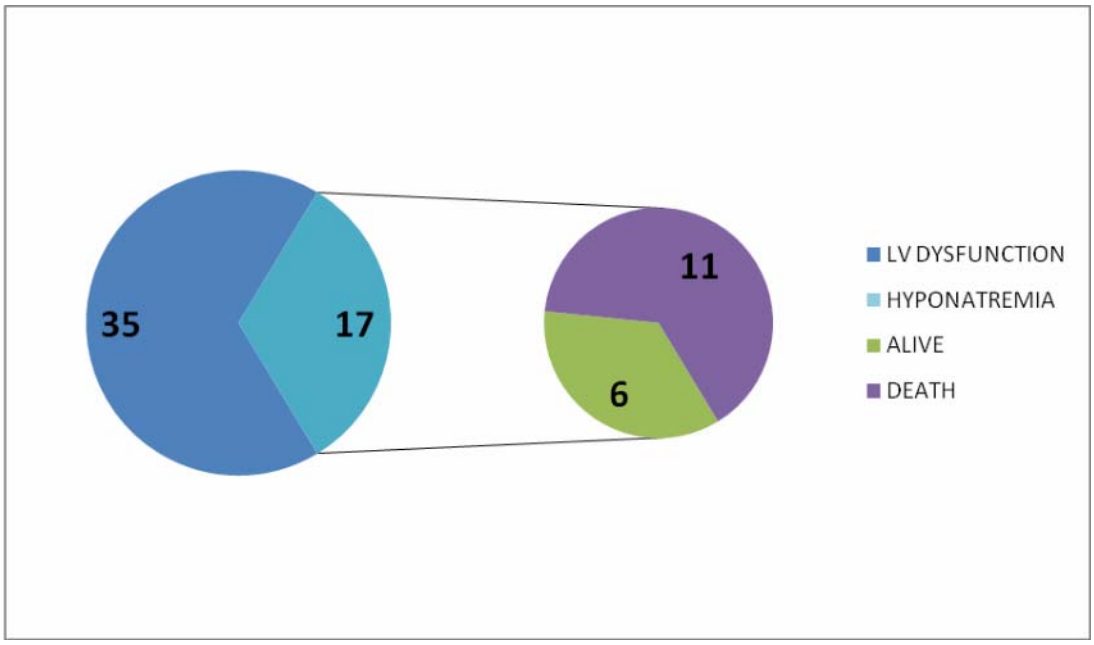


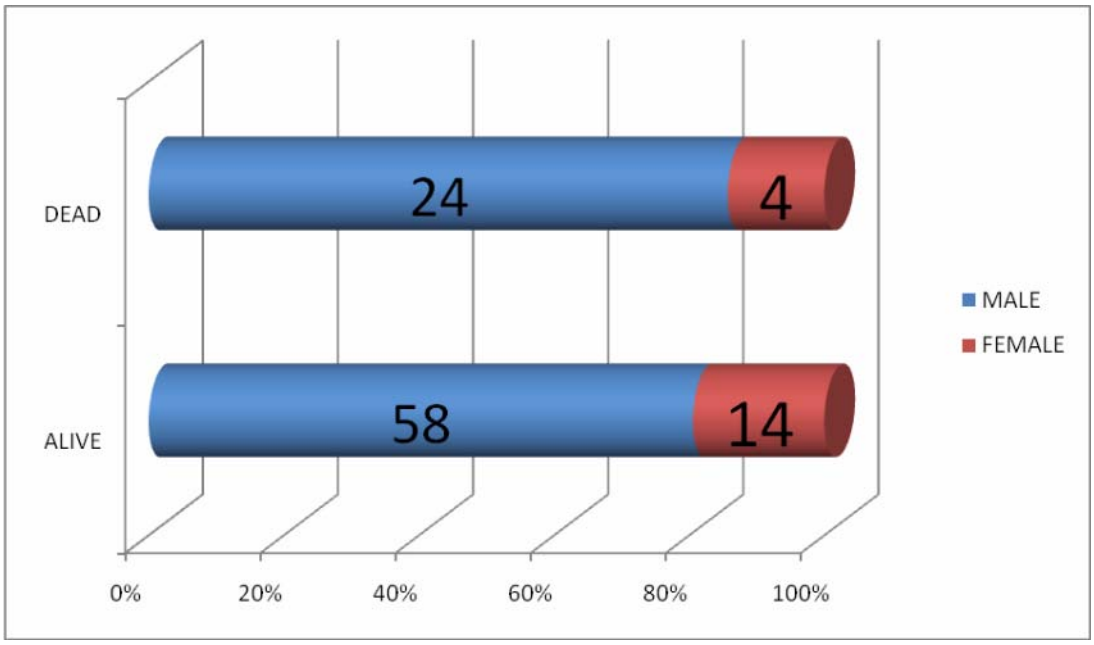
TABLE 23

SHORT TERM MORTALITY:

Mortality	**Male**	**Female**	**Total**
Alive	58 (70.7%)	14 (77.8%)	72 (72.0%)
Death	24 (29.3%)	4 (22.2%)	28 (28.0%)
Total	82 (100.0%)	18 (100.0%)	100 (100.0%)

FIG. 28

SHORT TERM MORTALITY:



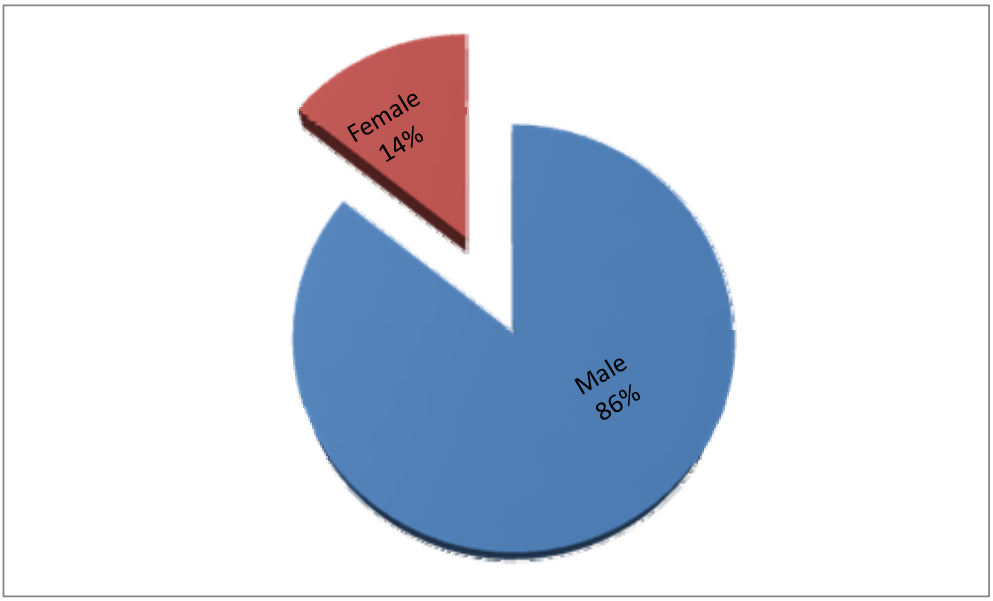
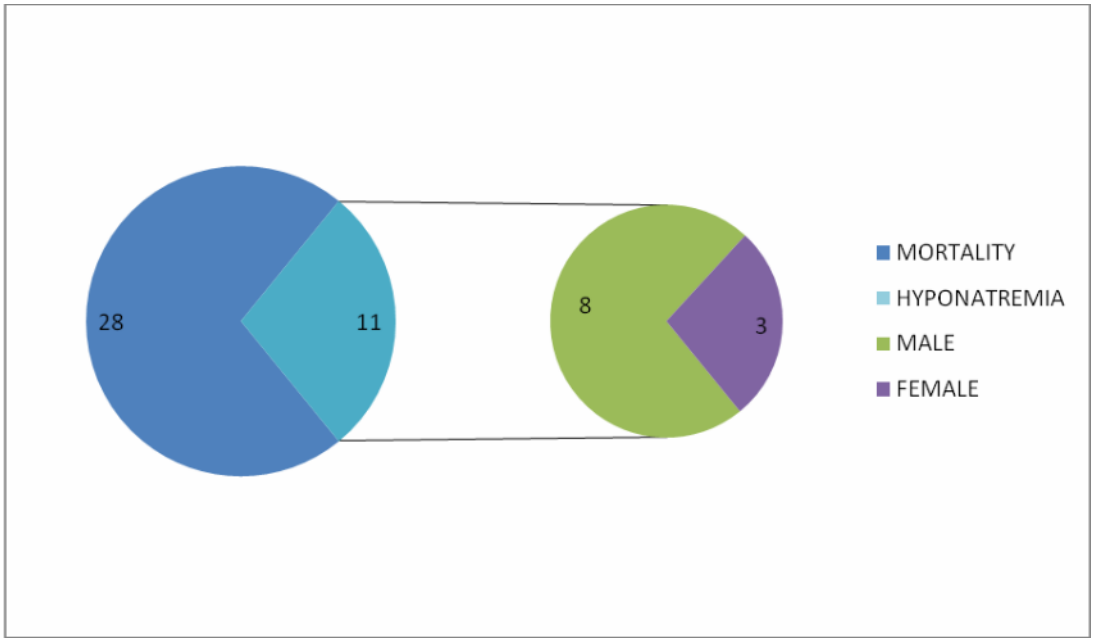


TABLE.24

HYPONATREMIA VS SHORT TERM MORTALITY

Mortality	Hyponatremia	Normonatremia	Total
Male	8 (72.7%)	16 (94.1%)	24 (85.7%)
Female	3 (27.3%)	1 (5.9%)	4 (14.3%)
Total	11 (100.0%)	17 (100.0%)	28 (100.0%)



ADVERSE CARDIAC EVENTS:

TABLE.25

SEX RATIO AMONG ADVERSE CARDIAC EVENTS

Gender	Total	Number of Cardiac Events	percentage
Male	82	17	20.7
Female	18	5	27.7
Total	100	22	22.0

FIG 31

SEX RATIO AMONG ADVERSE CARDIAC EVENTS

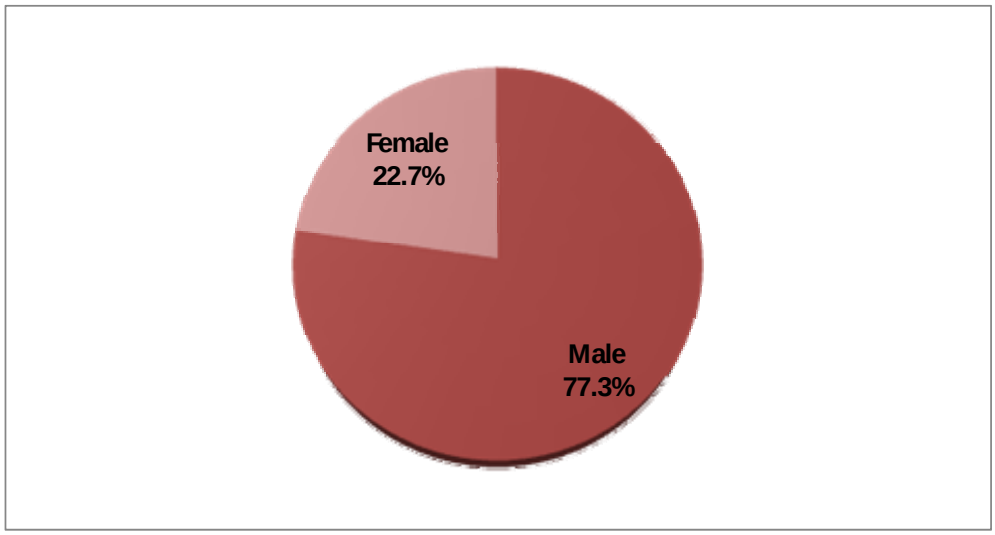


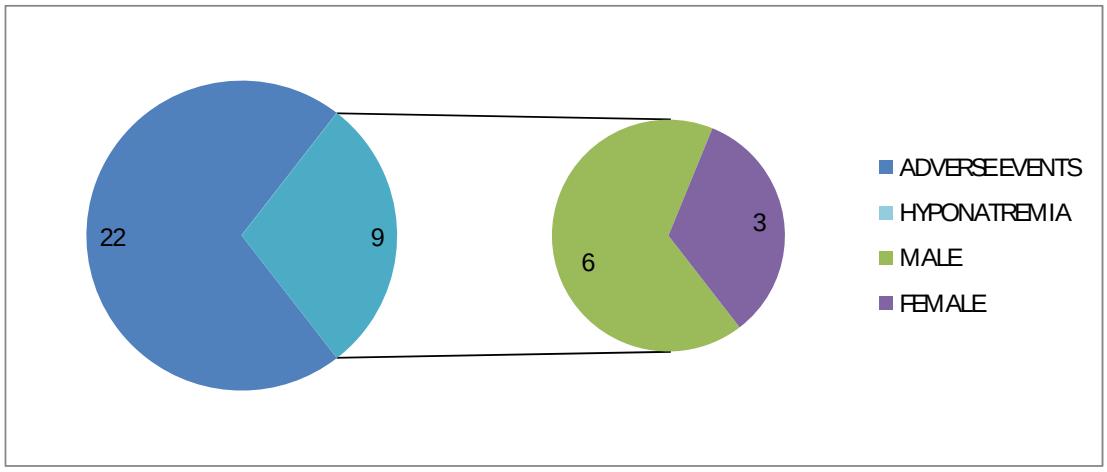
TABLE.26

HYPONATREMCS AMONG ADVERSE CARDIAC EVENTS

Gender	Total	Hyponatremia	Total
Male	17	6	35.3
Female	5	3	60.0
Total	22	9	40.9

FIG.32

HYPONATREMCS AMONG ADVERSE CARDIAC EVENTS



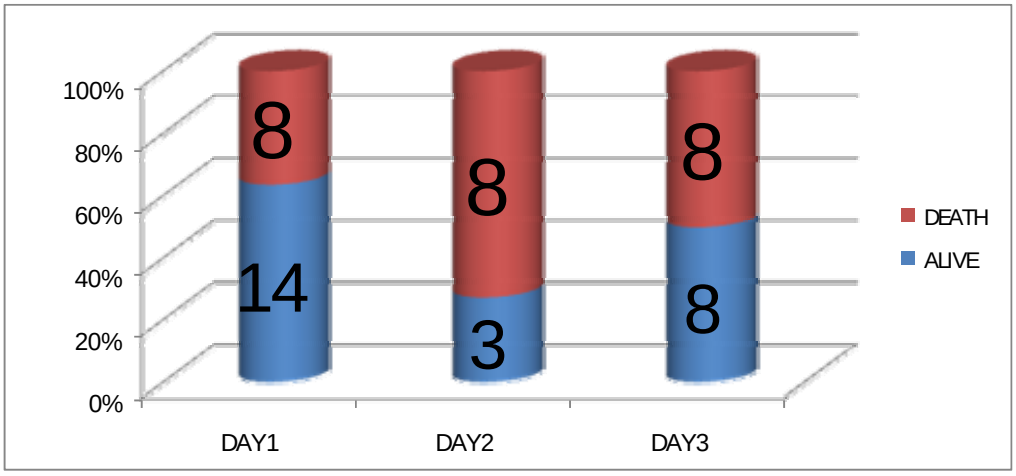
MORTALITY WITH DAY OF HYPONATREMIA:

TABLE.27

Gender	Total	DAY 1	DAY 2	DAY 3
Alive	14	14 (100.0%)	3 (21.4%)	8 (57.1%)
Death	8	8 (100.0%)	8 (100.0%)	8 (100.0%)
Total	22	22 (100.0%)	11 (50.0%)	16 (72.7%)

FIG 33

MORTALITY WITH DAY OF HYPONATREMIA:



RHYTHM ABNORMALITIES (N=100) :

Incidence of hyponatremia and normonatremia in cases of rhythm abnormalities

TABLE 28

RHYTHM ABNORMALITIES AMONG HYPONATREMIC PATIENTS

	Hyponatremia	Normonatremia	Total
Bradyarrythmias			
Fascicular Block	1 (14.3%)	6 (85.7%)	7 (100.0%
Av Block	3 (50.0%)	3 (50.0%)	6 (100.0%)
Tachyarrythmias			
SVT/AF	0	3 (100.0%)	3 (100.0%)
VT/VF	4 (80.0%)	1 (20.0%)	5 (100.0%)

DISCUSSION

Out of all 100 MI patients, 32(32.0%) had hyponatremia in any of 3 days values. And 68 (68.0%) had completely normal sodium levels in all 3 days. Out of those 32 hyponatremics, 27(84.4%) were males and 5(15.6%) were females. And out of those 68, 55(80.9%) were males and 13(19.1%) were females.

TYPES OF MI IN THE STUDY GROUP (TABLE 2,3)(FIG 2,3)

Out of all MI patients 82 were males and 18 were females. Out of all MIs anteroseptal MI were around 24 , AWMI 47 , ALMI 5 , IWMI 21 , AND PWMI 3

Within the MI s male female ratio were studied. One patient had combined high lateral MI and ASMI. The patients who had hyponatremia were 32 and MIs were 33.in that AWMI were the highest in the male group (63 %) and AWMI & IWMI were the same in the female group (33.3 %)

SHORT TERM MORTALITY IN NORMO AND HYPONATREMICS (TABLE 4)(FIG 4,5)

Among hyponatremics 75 % were alive and among normonatremics 70 % were alive. The short term mortality rate for hyponatremics and normonatremics were 25 % and 28 % respectively.

TYPE OF MI WITH HYPONATREMICS AND ITS CORRELATION WITH DAY OF HYPONATREMIA(TABLE 5,6)(FIG 6)

The territory of MIs were studied with days of hyponatremia. Certain patients had hyponatremia in all 3 or 2 days among 3 days of hyponatremia. The first day of hyponatremia is taken into account. In this regard , out of all 48 AWMI s , 19 had hyponatremia. This is divided within 3 days as 14,1,4 respectively.

Out of all 4 ASMIs with hyponatremia , the distribution within days were 2,1,1 respectively Out of all 3 anterolateral MIs with hyponatremia , the distribution were 2,0,1 respectively Among 4 IWMIs with hyponatremia , the distribution were 3,0,1 respectively Among PWMIs with hyponatremia , the distribution were 1,0,1respectivel Among 100 MIs , 32 had hyponatremia.

Out of all 32 hyponatremia , 22 (68.8 %) had on the first day, 6.3 % on the second day , 8 % on the third day. PWMI had hyponatremia equally on first and the third day.

DEGREE OF HYPONATREMIA WITH TERRITORY OF MI

(FIG 7)

The hyponatremia was classified into A (131 – 135) and B (125 – 130) to compare with the MI with severity.

ASMI had the highest incidence (75%) of severe hyponatremia and ALMI had the least incidence (25%) of severe hyponatremia.

AGE , HYPONATREMIA AND MORTALITY(TABLE 7,8)

(FIG 8,9)

Maximum cases of hyponatremia were in 41 – 50 yrs group in males and 51 – 70 yrs in females.

Coming to mortality in hyponatremics among age groups 41 – 60 yrs which had the highest incidence of hypos among both sexes the mortality was 58.3 % and 100 % in less than 40 yrs group.

DIABETES , HYPONATREMIA AND MORTALITY(TABLE 9,10,11)(FIG 10-14)

Out of 100 patients studied 15 were diabetics. Out of which 12 were males and 3 were females. Out of 15 diabetics 5 were hyponatremic.

Out of those 5 , 4 were males and 1 was a female. Out of 5 hyponatremics among diabetics 3 were Alive and 2 died.

CAHD HISTORY AND HYPONATREMIA , MORTALITY(TABLE 12-15)(FIG 15-19)

Out of 100 in the study population 5 had old history of coronary heart disease. Out of those 4 were males and one was a female Out of 5 old CAD patients 2 developed hyponatremia. Out of which 1 was a male and the other a female Out of 5 old CAD patients 1 male developed hyponatremia and 1 female developed hyponatremia. The male hyponatremia persisted for all three days and the female hyponatremia persisted for only a single day. Out of 2 hyponatremics one was alive and the other was dead.

THROBOLYSIS AND HYPONATREMIA, MORTALITY(TABLE 16-18) (FIG 20-23)

Out of all MI patients 37 were thrombolysed based upon the inclusion and exclusion criteria . Out of those 37 , 33 were males and 4 were

females. Out of 37 who were thrombolysed 14 developed hyponatremia . out of those 14 8 were alive and 6 expired.

LV DYSFUNCTION (TABLE 19-22)(FIG 24-27)

LV Dysfuction is defined in our study as LVEF less than 50% as routine ECHO was done for all patients with MI Out of all 100 MIs patients , 35 patients had LVEF less than 50%. The male female ratio was 27 : 8 The incidence of hyponatremia was studied among those had LVEF less than 50%. Total hyponatremias were 17 where male female ratio was 13 :4

Then the incidence of mortality was studied among those who had hyponatremia among low LVEF. Out of all 35 low LVEF , 17 had hyponatremia. Out of this 17 , 11(64.7 %) expired and 6 (35.3 %) are alive.

ADVERSE CARDIAC EVENTS(TABLE 25,26)(FIG 31,32)

Out of all MIs 22 patients developed adverse cardiac events such as arrhythmias , new onset failures during hospital stay. Out of those 22 , 17 were males and 5 were females.

Out of those 22 who developed adverse cardiac events 9 developed hyponatremia during hospital stay. The male female ratio was 2 : 1.

HYPONATREMICS AMONG MORTALITY (TABLE 23,24)(FIG 28-30)

Out of all MI s 72 were alive at 30 days follow up and 24 expired at 30 days follow up. Out of 72 , 58 were male and 14 were females. Out of 28 , 24 were males and 4 were females.

Out of all 28 who expired within 30 days 11 developed hyponatremia during hospital stay. Out of those 11 (39%), 8 (72 %) were males and 3 (27 %) were females.

RHYTHM ABNORMALITIES(TABLE 28)

Incidence of hyponatremias in patients developed rhythm abnormalities were studied. Out of those rhythm abnormalities fascicular blocks were 7 where one had hyponatremia. In patients with AV blocks totally 6 , 3 had hyponatremia. With patients with SVT/AF , no one had hyponatremia. From 5 patients with VT/VF , 4 had hyponatremia

CONCLUSION

1. The short term mortality among patients who had hyponatremia who had LV dysfunction was higher when compared to patients who had normal sodium levels who had LV dysfunction.

2. The incidence of adverse cardiac events within first 72 hours was the same between patients who had hyponatremia and patients who had normal sodium levels among STEMI patients

3. Short term mortality among MI patients who had hyponatremia increases as the age advances with highest incidence in the 61 – 70 yrs age group.

4. Assessment of serum sodium levels, thus must be carried out in all cases of acute STEMI so as to correct hyponatremia if present and there by preventing treatable complications and reducing mortality.