# "PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION"

Submitted By

**DR.V.JOTHI BASU**

Dissertation submitted to


**Tamil Nadu Dr.MGR University,**

**Tamil Nadu, Chennai**

In partial fulfillment of the requirements for the degree of

**MD**

In

**General Medicine Branch 1**


**DEPARTMENT OF MEDICINE**

**COIMBATORE MEDICAL COLLEGE HOSPITAL,**

**COIMBATORE**

# DECLARATION BY THE CANDIDATE

I**, Dr.V.Jothi Basu** hereby declare that the dissertation entitiled **"PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION"** is my bonafide and genuine research. It was done under the guidance of professor **DR.CHANDRASEKARAN** $_{MD}$ Chief., Department of medicine.

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**Dr. S. CHANDRASEKARAN. M.D.**

**Professor and Chief Department**

**of Medicine**

**UNIT V**

Date: Coimbatore medical college hospital,

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Name of the Candidate : V. JOTHIBASU

Course : M.D. GENERAL MEDKINE

Period of Study : 2012 - 2015

College : COIMBATORE MEDICAL COLLEGE

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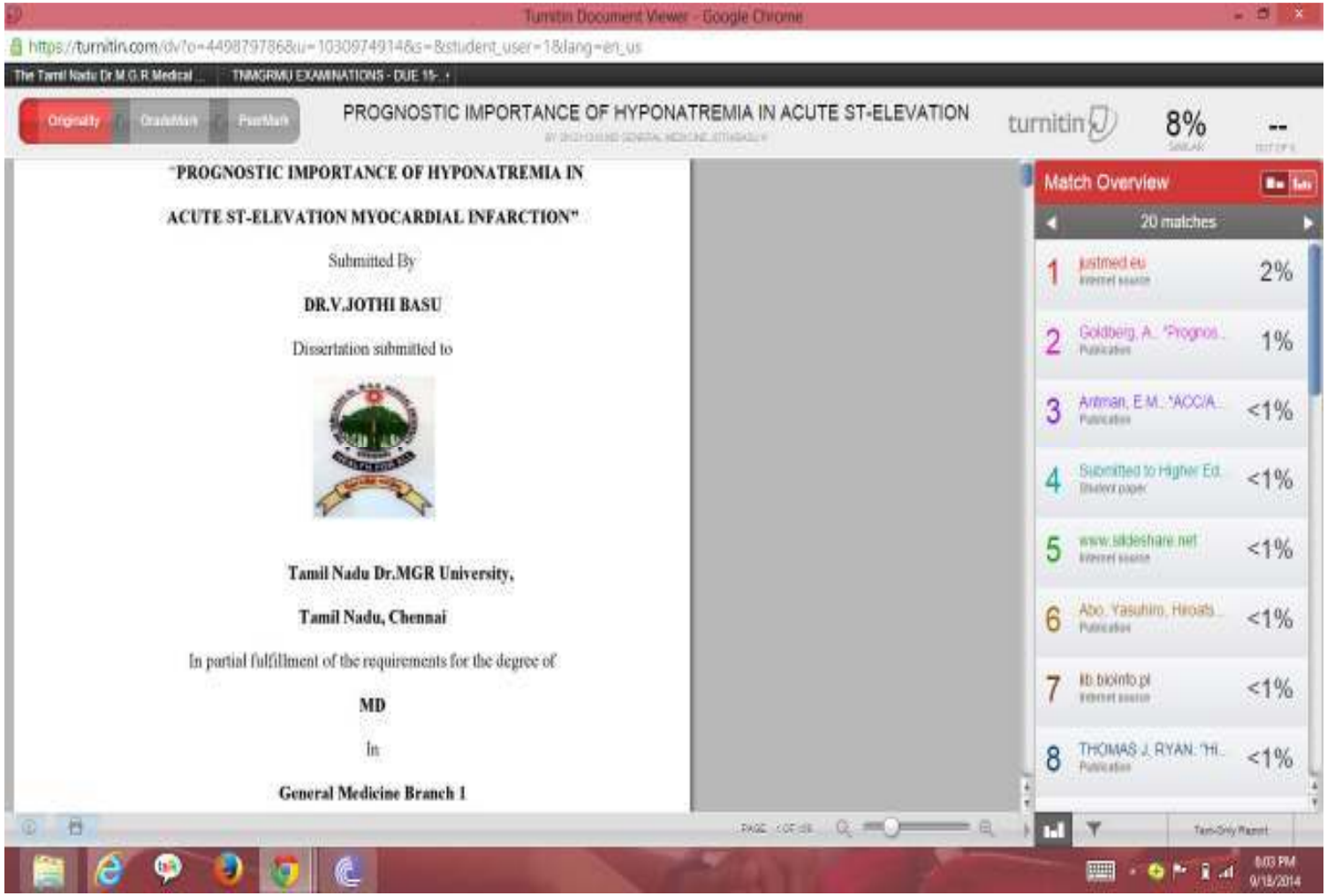
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**Dr. N. KUMAR NATARAJAN. MD.**

**Professor and Head of Department**

**of Medicine**

Date: Coimbatore medical college hospital,

Place: Coimbatore Coimbatore.

# ENDORSEMENT FROM THE DEAN

This is to certify that Dr.V.Jothi Basu has done this thesis by the title "**PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION"** is a bonafide research done under the guidance of **Dr. S.CHANDRASEKARAN. M.D.** Professor & chief department of medicine, unit V.

**Dr. S. Ravwathy..MD. DNB OG**

**Dean**

Date: Coimbatore medical college hospital,

Place: Coimbatore Coimbatore

# ACKNOWLEDGEMENT

*On completing this document it gives me immense pleasure to thank and acknowledge the aspiring guidance provided by my distinguished professors.*

*With great respect, I like to use this opportunity to express my deepest gratitude and special thanks to my Guide* ***DR.S.CHANDRASEKARAN*** $_{M.D}$***,*** *Professor and My Chief., Department of Medicine. Coimbatore Medical College Hospital, Coimbatore, for his invaluable encouragement, support and friendly advice, which he rendered on preparing this thesis as well as on my post-graduate studies, which was priceless.*

*I am forever thankful to* ***DR. N .SUNDAR***$_{M.D}$***, DR. RAVEENDIRAN***$_{M.D}$***,***

***DR. USHA***$_{M.D}$***, DR.ISAAC CHRISITAN MOSES***$_{M.D}$***,*** *and also to Asst professors*

***DR.S. AVUDAIAPPAN*** $_{M.D}$***, DR.NILAVAN***$_{M.D}$***, DR. SIVAKUMAR***$_{M.D}$***,***

***DR. CHAKRAWARTHY***$_{M.D}$***, DR.B.VETRIVEERAN***$_{M.D}$ *for guiding me and for giving valuable comments and suggestions during my study and thesis.*

*I am extremely grateful to* ***DR.S. REVWATHY*** *MD DNB OG ,Dean of Coimbatore Medical College Hospital, Coimbatore, for allowing me to utilize resources in completing my dissertation.*

*I would especially like to thank all Medicine Department Staff, Nurses, Library Staff and all Hospital staffs who have co-operated with me when I recruited patients and collected data for my thesis.*

*I must render my special thanks to my seniors and friends* ***Dr.Mahendravarman*** *M.D,* ***Dr.Rahul, Dr.Karthikeyan, Dr.Govindaraj, Dr.Suresh*** *for their valuable advice whenever I request for and incented me to strive towards my goal.*

*I should specially thank my family. Words cannot express how grateful I feel to my parents and my family members for all sacrifices and prayers that they have made on my behalf.*

*Last but never the least; I would like to convey my heartfelt thanks to all my patients for their co-operation, without which my study would have been incomplete.*

*Date :*

*Place : Coimbatore* **DR.V.JOTHI BASU**

# LIST OF ABBREVIATION

AMI- Acute Myocardial Infarction

AF- Atrial Fibrillation

AVP- Arginine Vasopressin

CAD- Coronary Artery Disease

CCF- Congestive Cardiac Failure

CK-MB – Creatinine Kinase-MB

CVD- Cardiovascular Disease

ECF- Extra Cellular Fluid

ECG- Electrocardiogram

IHD- Ischemic Heart Disease

ICF- Intra cellular Fluid

LV- Left Ventricle

LVF- Left Ventricular Failure

MR- Mitral Regurgitation

PSVT- Paroxysmal SupraVentricular Tachycardia

SIADH- Syndrome of Inappropriate Antidiuretic Hormone Secretion

TR- Tricuspid Regurgitation

VF- Ventricular Fibrillation

VPC- Ventricular Premature Complex

VT- Ventricular Tachycardia

# ABSTRACT

**Background and objective:** Hyponatremia is the most common electrolyte disorder in clinical settings and in hospitalized patients, and is found to be the most important predisposing factor of cardiovascular mortality among patients with heart failure. The fact is that the neuro humoral activation is similar to both acute myocardial infarction and heart failure. So our aim is to investigate the prognostic importance of hyponatremia in acute ST elevation MI and to establish its usefulness in predicting short term survival.

**Material:** From June 2013 to June 2014, around 100 patients who presented with acute ST-elevation MI admitted in ICCU of Coimbatore Medical College Hospital, Coimbatore was studied.

**Method:** 100 consecutive patients who were selected underwent detailed history and clinical examination. Their Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours after that. The end point was to find the cause which caused mortality within 30days following myocardial infarction.

**Results:** The result of this study was found to be that, the proportion of patients who presented with acute ST elevation MI were hyponatremic at the time of admission or developed hyponatremia after admission. The

30days mortality ratio was found to be high in hyponatremic group than normal group. There was also evidence that the severity of hyponatremia and mortality were having significant linear relationship. Multivariate analysis performed also showed that the significant independent predictor of 30days mortality was identified as hyponatremia on admission or early development of hyponatremia.

**Conclusion:** By this study we conclude that hyponatremia at the time of admission or shortly after that in patient with acute ST elevation MI is an independent predictor of 30days mortality. A simple marker to find patients at risk is Plasma Sodium Levels.

**Key words:** Hyponatremia, Acute myocardial infarction, Heart failure.

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# INTRODUCTION

Myocardial infarction is well known clinically and it is one of the major cause of death and disadilty worldwide, affecting all races and nationalities. It is found to affect any individual and can have profound deleterious, psychological and economic complication.

Acute coronary syndrome is a major public health problem in both developed and developing countries, and its gaining more importance in developing countries inspite of studies in the diagnosis and management for past 4 decades. Nowadays studies reveal that there is reduction in disease caused due to infection, and there is fast rise in ischemic heart disease and acute myocardial infarction in developing countries like India due to increased economic development and life style modification which promotes atherosclerosis.

Major efforts are necessary to strengthen primary prevention programmes at community level though there is wide disparity of available resources to treat AMI in developing countries like India.

Hyponatremia is one of the most common electrolyte disorder. In case of heart failure hyponatremia is the main predisposing factor for cardiovascular mortality. It is commonly found in inpatients, mostly in

surgical postoperative period and in patients with congestive cardiac failure, chronic glomerular nephritis and cirrhosis of liver.

Hyponatremia is commonly found after myocardial infarction, the fact is that the neurohumoral activation is similar to both acute myocardial infarction and heart failure.

The clinical improvement in hyponatremia is by rise in plasma sodium concentration. In the setting of acute myocardial infarction it is found that the data for the prognostic value of hyponatremia is lacking, even though in chronic heart failure the prognostic importance of hyponatremia is well established.

My concept of this dissertation is to study the prognostic importance of hyponatremia in acute ST elevation myocardial infarction and also to determine its usefulness in finding its short term survival.

# AIMS AND OBJECTIVES

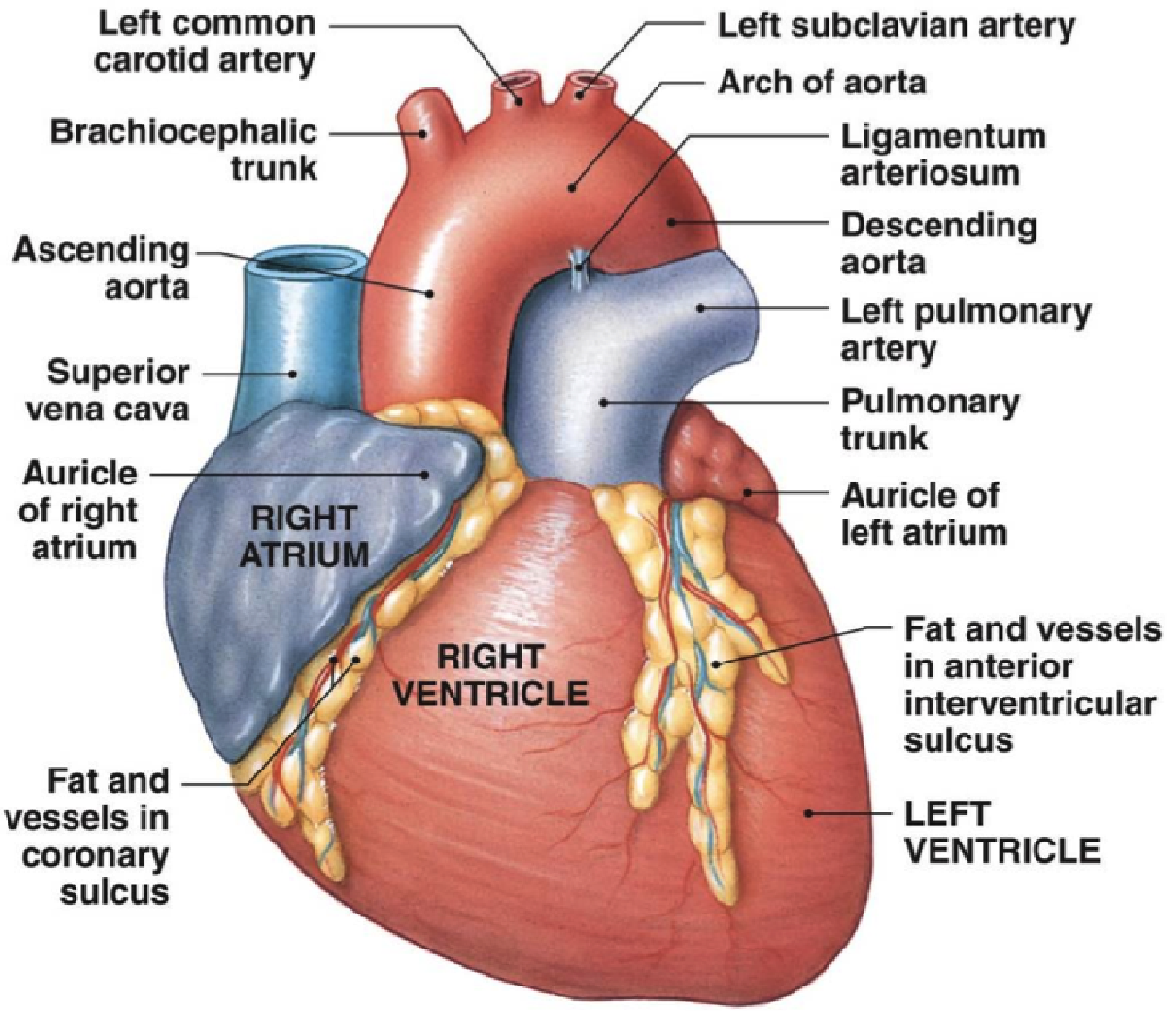
To determine the prognostic importance of hyponatremia in acute ST segment elevation myocardial infarction and to find out its usefulness in predicting its short time survival.

# REVIEW OF LITERATURE

## ANATOMY OF HEART

**Heart and Vessels**

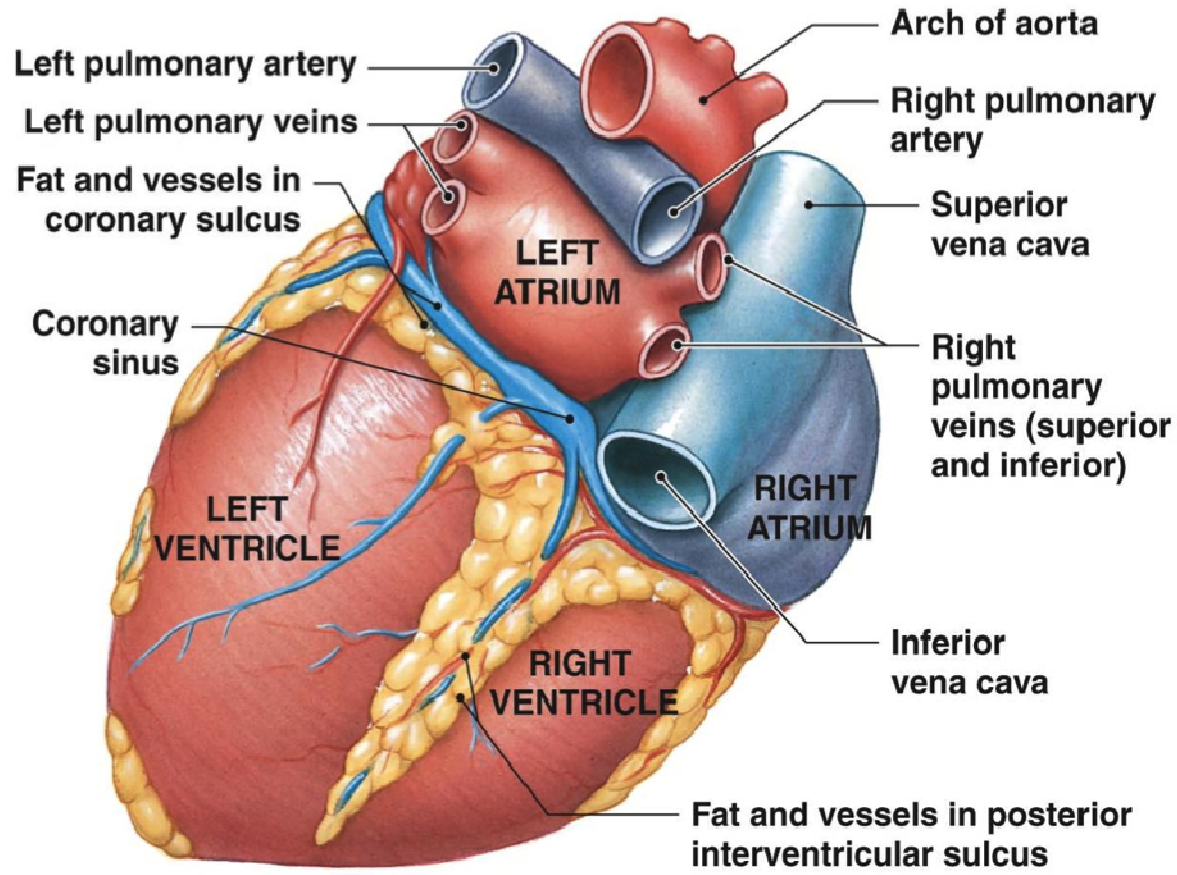
**Fig-1**




(a) Anterior (sternocostal) surface

# Heart and Vessels

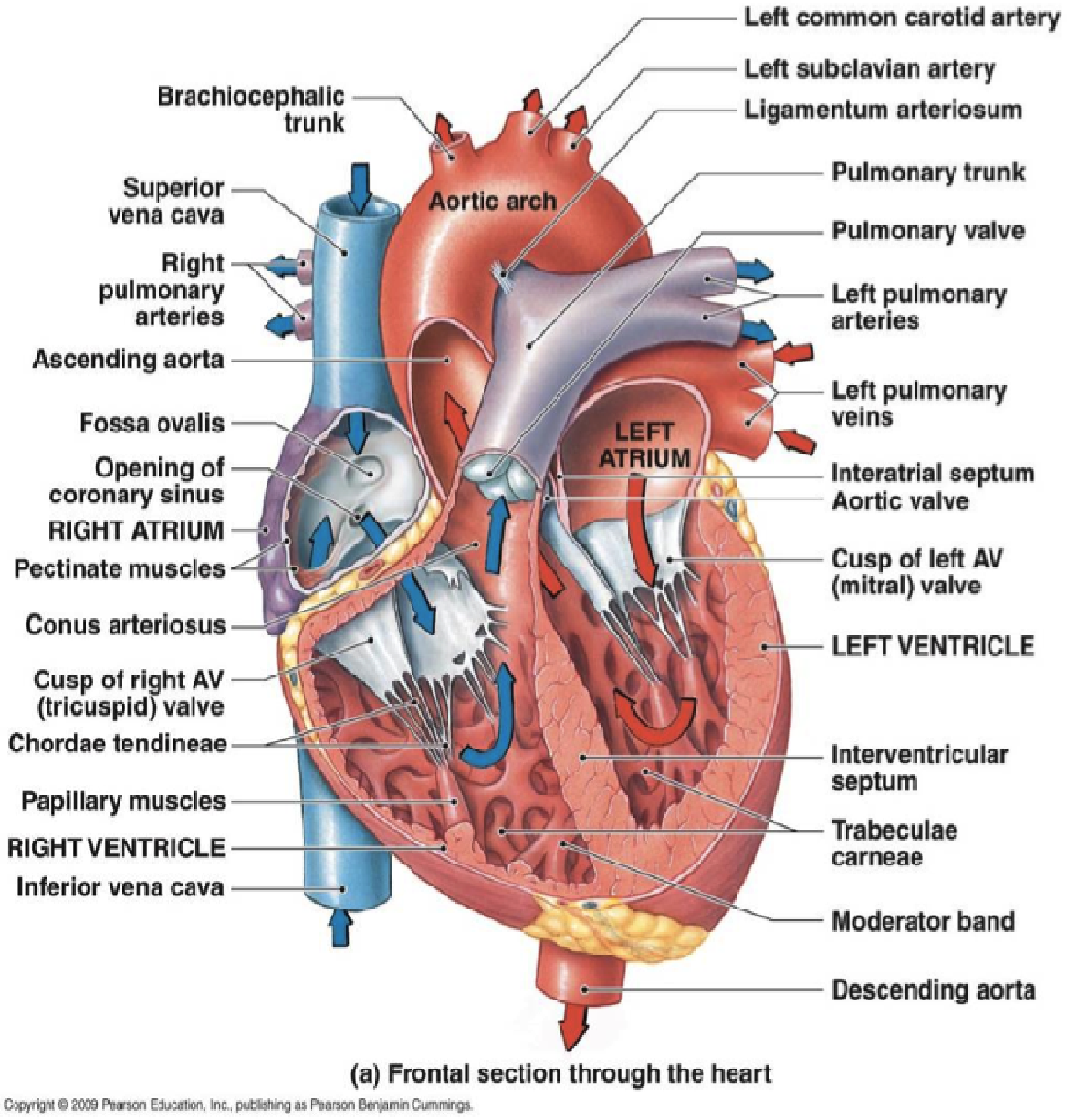
**Fig-2**




(b) Posterior (diaphragmatic) surface

# Heart and Vessels

**Fig-3**




(a) Frontal section through the heart



**Fig-1, Fig-2 and Fig-3 shows:**

- ✓ **Right border -** it is found slightly convex and is long formed by right atrium above and right ventricle below, it is in line with superior vena cava.

- ✓ **Left border -** is formed majorly by left ventricle and a small portion by left auricle.

- ✓ **Inferior border -** is formed by right and left ventricle.

- ✓ **Superior border -** is formed by right and left atrium and great vessels.

- ✓ **Ligamentum arteriosum-** it extends from the origin of left pulmonary artery to the arch of aorta.

- ✓ **Arch of aorta-** it gets arched into two planes, superiorly and to the left. The pulmonary artery bifurcates inferior to it.

- ✓ **Pulmonary artery-** it get divided into right and left branch inferior to arch of aorta. Right branch passes under the arch. He branches lie just superior and parallel to the pulmonary vein.

- ✓ **Pulmonary veins-** the right and the left pulmonary veins drain into left atrium.

- ✓ **Azygos vein-** it begins from the abdomen and it arches over the right pulmonary vessels (and bronchus) and drain into SVC

## Coronary Arteries

**Fig-4**

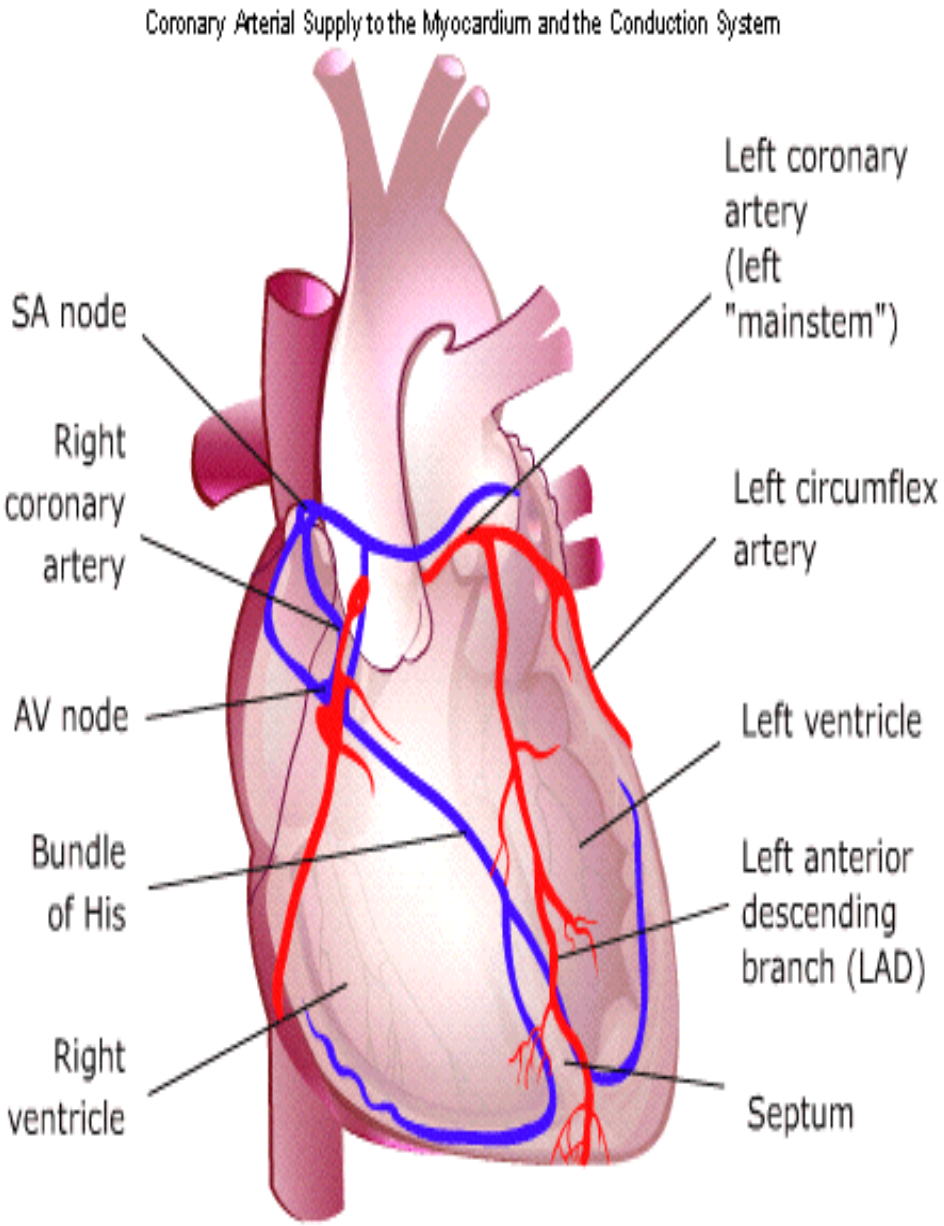
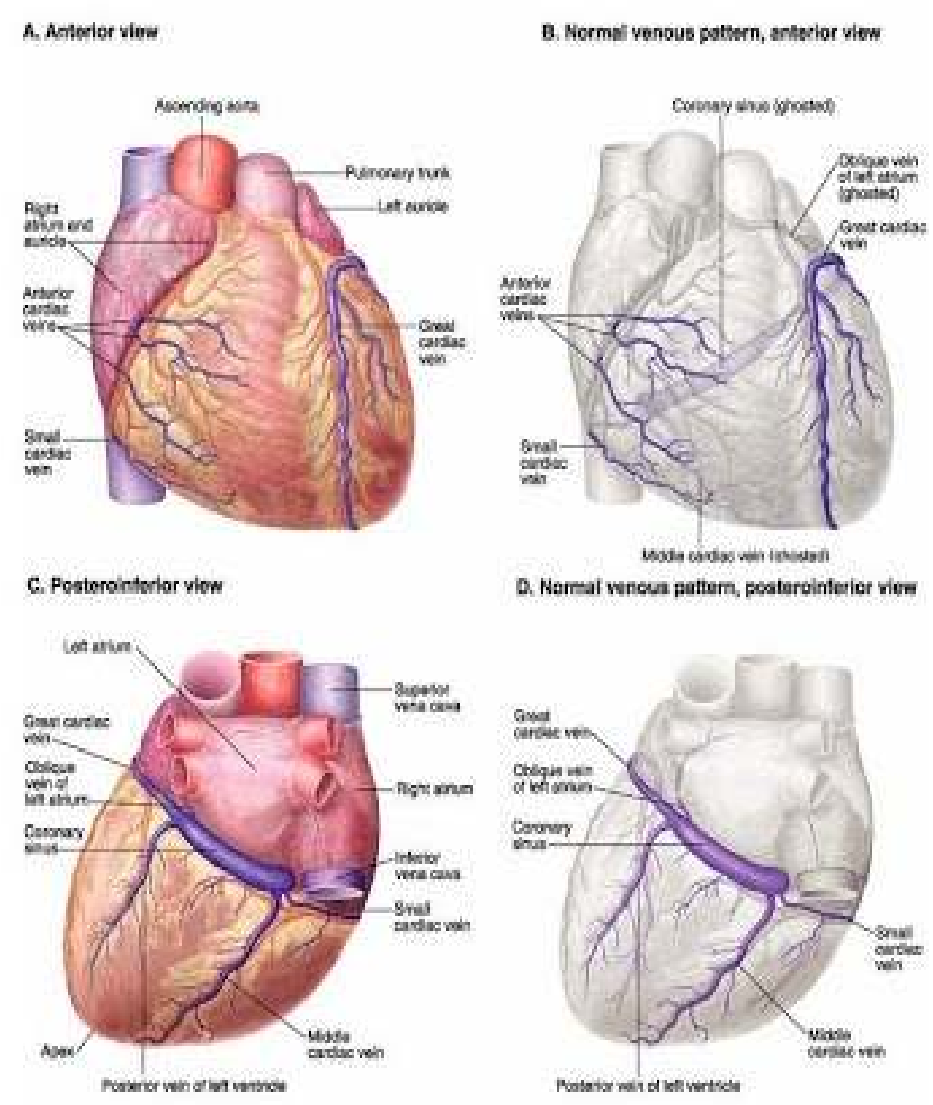


**Fig-5**


A. Anterior view
Ascending aorta
Pulmonary trunk
Left auricle
Right atrium and auricle
Anterior cardiac veins
Great cardiac vein
Small cardiac vein
B. Normal venous pattern, anterior view
Coronary sinus (ghosted)
Oblique vein of left atrium (ghosted)
Great cardiac vein
Anterior cardiac veins
Small cardiac vein
Middle cardiac vein (ghosted)
C. Posteroinferior view
Left atrium
Superior vena cava
Great cardiac vein
Oblique vein of left atrium
Right atrium
Coronary sinus
Inferior vena cava
Small cardiac vein
Middle cardiac vein
Apex
Posterior vein of left ventricle
D. Normal venous pattern, posteroinferior view
Great cardiac vein
Oblique vein of left atrium
Coronary sinus
Small cardiac vein
Middle cardiac vein
Posterior vein of left ventricle

# CORONARY ARTERIES

**Fig-4 and fig-5 shows:**

- ✓ **Coronary artery-** both right and left coronary artery oginate from left side of heart at the beginning of aorta.[11]

- ✓ **Right coronary artery-** it is a smaller branch which arise from right aortic sinus and reaches the posterior surface of the heart by traveling in the coronary sulcus or groove, here it anastomose with the circumflex branch of left coronary artery. It gets lodged in anterior IV groove. It mainly supplies Right Atrium, small part of Left Ventricle near posterior IV groove, posterior part of IV septum, conducting system of heart except a part of LBB. In its course it gives off sinoartrial(SA) nodal branch which supplies right atrium and SA node; the marginal branch is a major branches which supplies anterior wall of right ventricle, in the posterior interventricular groove the posterior interventricular artery anastomose with anterior interventricular artery which is a branch of left coronary artery, near the posterior interventricular septum it gives off arteriventricular nodal artery.

- ✓ **Left coronary artery-** it's a larger branch which arise from left posterior aortic sinus, it gets lodged in the posterior IV groove. It mainly supplies Left Atrium, great part of Left Ventricle, Anterior part of IV groove, RBB, part of LBB and 35% SA node. It gives a circumflex branch which get anastomose with right coronary artery on the posterior surface of heart by running posteriorly, in the interventricular groove it gives an anterior descending branch.

- ✓ Anterior 2/3$^{rd}$ of interventricular septum is supplied by ascending branch of left anterior descending artery, while posterior part of interventricular septumis supplied by right coronary artery.

# ACUTE MYOCARDIAL INFARCTION

**Prevalence of AMI:**

CVD is the most common cause of death worldwide nowdays and it causes around 15 million deaths in a year. CAD is found to increase in developing countries like India though there is decrease in incidence in the industrialized world for the past 3 decades. Compared to all other ethnic groups CAD is the major disease burden and death in Asian Indians. The disease occurs more commonly in younger age groups in India when compared to North America and Western Europe, and is found to be very severe, diffuse, complicated and with increased mortality.[15,16]

In Asian Indians CVD is found as a malignant form due to the underlying genetic susceptibility with abnormality in lipid and lifestyle factors. In Ethnic group the relevant risk factors are metabolic syndrome X, insulin resistance syndrome, lipoprotein(a), dyslipidaemic phenotype and few emerginf factors such as homocysteine, tissue plasminogen activator, fibrinogen, factor VII, PAI-1, infections and inflammations.

More than half of world's population resides in India. In this most of them lives in rural world, around 30% of mortality is found to be due to cardio vascular disease. CVD is found to be more in urban than

rural society, when there 2 fold increase in cases in CVD cases in rural areas there is 9 fold increase in urban areas, as the risk factors such as obesity, hypertension, truncal obesity, low HDL, high cholesterol and diabetes mellitus are more in urban areas. In India most dominant form of CVD is Coronary Artery Disease. Nowadays in India death due to CVD is more when compared to other disease such as stroke. It is found to be four time higher than stroke, which is due to intake of high calories diet from fat, more of diary products with low level of activity which is more in India than other parts of the world.

**MYOCARDIAL INFARCTION (MI) - Revised Definition**

**Acute, Evolving or Recent Criteria Of MI:**

1. Atleast one among the following given below, and biochemical markers of myocardial necrosis must show typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB)[12]
    - Typical anginal symptoms
    - ECG shows pathological Q wave
    - Ischemic ECG changes (ST segment elevation or depression)
    - Post coronary arterial intervention like CAG
2. Acute MI- pathological findings.

**Established Myocardial Infarction Criteria:**

1. Serial ECG reading shows appearance of new pathological Q waves. Depending upon the time since the development of infarct the biochemical markers may have normalized. Previous symptoms of patients may or may not be remembered.

2. ECG finding suggestive of healing or healed MI

Either one of the above criteria must get satisfied for established MI.

**ACUTE MYOCARDIAL INFARCTION- Causes**

Coronary atherosclerosis with coronary thrombosis is the most common cause of MI.

Due to the development of rich collateral network, even high grade stenosis of epicardial coronary arteries which progress to occlusion does not cause STEMI.

Lipid laden atherosclerotic plaque can cause abrupt change, which leads to plaque disruption, which leads to platelet activation and aggregation due to exposure to certain substance which promotes it, which leads to thrombotic generation and finally leading to formation of thrombus. There is disruption of blood flow due to the thrombus formed which causes myocardial necrosis due to severe imbalance between

oxygen supply and demand. In few cases independent traditional risk factor may predispose to plaque rupture.

**Myocardial Infarction- Causes other than Coronary Atherosclerosis**

**Arteritis**

- Chronic granulomatous disease( takayasu disease)
- Leutic
- Polyartheritis nodosa
- Disseminated lupus erythematosus
- Mucocutaneous lymph node (kawasaki) syndrome
- Rheumatoid arthritis
- Seronegative spondylo arthritis like ankylosing spondylitis(AS)

**Coronary arteries trauma**

- Iatrogenic
- Laceration
- Thrombosis
- Post radiation( treatment for malignancies )

**Mural thickening of coronary vessels with metabolic disease**

- Homocysteinuria
- Amyloidosis
- Mucopolysaccharidoses ( Hurler disease )
- Intimal sclerosis juvenile pattern
- Fabry's disease
- Contraceptive steroids leading to intimal hyperplasis
- Post partum period
- Pseudoxanthoma elasticum
- Radiation therapy leading to coronary fibrosis

**Other mechanisms leading to Luminal narrowing**

- Transient spasm of coronary vessels in case of prinzmetal angina
- Coronary artery dissection
- Post nitoglycerine withdrawal spasm
- Aortic dissection

**Coronary artery embolism**

- Infective endocarditis
- Mitral valve prolapsed
- Nonbacterial thrombotic endocarditis
- Prosthetic valve replacement
- Left atrium, left ventricle or pulmonary vein mural thrombus
- Paradoxical emboli
- Cardiac myxoma
- Post CABG and CAG
- Fixed embolus due to fibroelastoma of aortic valve
- After intracardiac catheterization

**Congenital anomalies to coronary artery**

- Left coronary artery arising from sinus of vasalva especially anteriorly
- Left coronary artery arising from pulmonary artery
- Aneurysm of coronary artery

**Disproportion in the oxygen demand and supply in the myocardium**

- Aortic valve stenosis
- Aortic regurgitation or incompetence
- Incomplete differentiation of aortic valve
- Thyrotoxicosis
- Poisoning with carbon monoxide
- Prolonged hypotension

**Hematological causes of in situ thrombosis**

- Thrombocytosis
- Polycytemia vera
- Consumtive coagulopathy
- Hypercoagulable state, thrombocytopenic purpura

**Miscellaneous**

- Cocaine usage
- Contusion of myocardium
- Cardiac catheterization complication
- Normal coronary arteries leading to infarction

**Risk factor of CAD in Asian Indian**

**Fixed**

- Male – more than 25yrs
- Female – more than 45yrs
- Family history- premature CAD less than 5yrs

**Modifiable factors- Non lipid**

- Systemic hypertension
- Type II diabetes mellitus
- Smoking
- Morbid obesity or BMI more than 22
- Serum homocysteine more than 10 micro mol/lit

**Modifiable factors – Lipid**

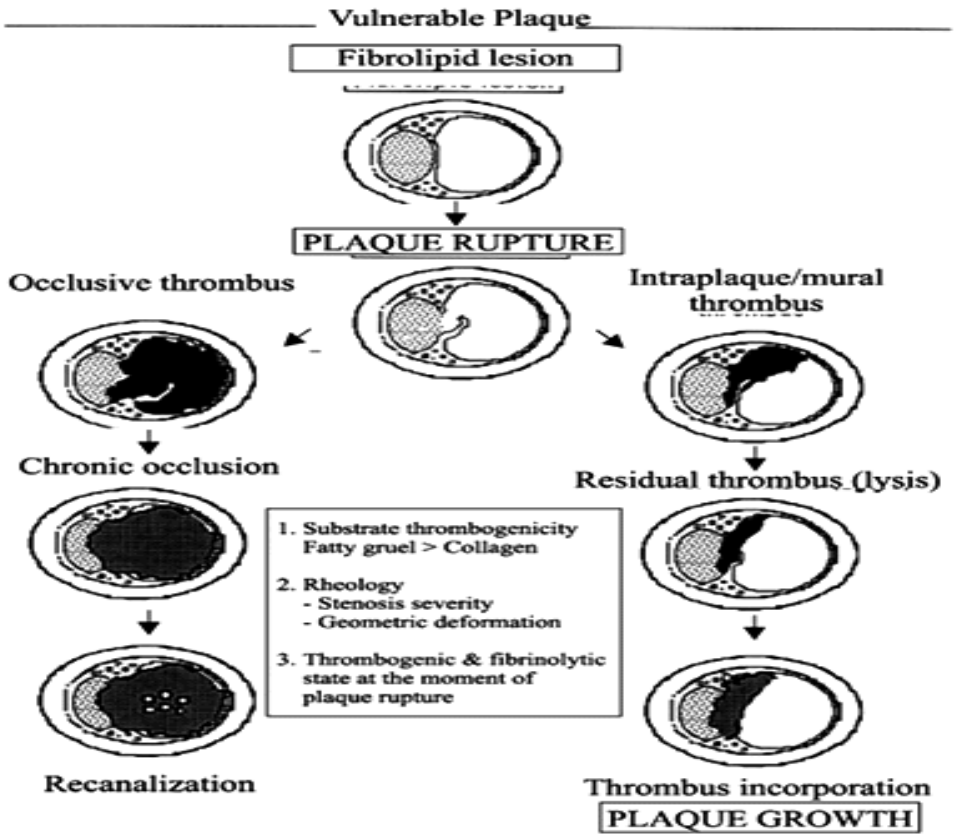
- Serum total cholesterol- more than 150mg%
- Serum triglycerides- more than 150mg%
- LDL cholesterol- more than 100mg%
- HDL cholesterol- Males->less than 40mg%,

  Females->less than 50mg%
- APO lipoprotein b- more than 100mg%

## MYOCARDIAL INFARCTION- Pathophysiology:

Infarcts occur due to prolonged ischemia and hypoxia[1]. All acute infarcts is commonly caused by thrombosis which occlude coronary artery developed due to atherosclerotic plaque rupture, which leads to coronary vasospasm , when vessels get completely occluded, there is ischemia and hypoxia. The major initiating factor for unstable angina is thrombosis (i.e., blood clot) especially when there is recent and increasing rest pain. Thrombus formed in the coronary artery is the cause of sudden death in 50-60% of patients. Pre existing atheromatous lesion is the site usually where thrombus develops.[13]

A plaque is found to be dangerous when the lipid core occupy around 50% of plaque, when the macrophage density is more, when the smooth muscle density is very low, when the tissue factor is high and when the plaque cap is very thin. The rich lipid core and thin fibrous cap is found to have inflammatory reactions[1]. Proteolytic effect of the enzyme metalloproteinase's on thin fibrous plaque cap is the reason for plaque rupture. There is accumulation of RBC's, platelets, macrophages due to such rupture which leads to sudden occlusion and RBC's are rich in the thrombus formed. Thromboxane A2 is a powerful vasoconstrictor which is liberated from platelets, which leads to further vasoconstriction.[13]




Acute coronary syndrome may be of non ST- elevation MI or ST elevation MI. Non ST elevation MI or non Q wave MI or unstable angina occurs there is partial or complete lysis of clot due to natural fibrinolytic substance in the body leading to partial restoration of blood flow. ST elevation MI or Q wave MI occurs when there is no such fibrinolytic activity in the body.

The pathophysiology of acute myocardial infarction is complex and there are many other factors leading to infarct.

**The pathology of myocardial infarction by time after obstruction**

15

| **Onset** | |
|---|---|
| 1 - 3 Hours | Wavy myocardial fibers |
| 2 - 3 Hours | Staining defect with tetrazolium or basic fuchsin dye |
| 4 - 12 Hours | Coagulation necrosis with loss of cross striations, contraction bands, edema, hemorrhage, and early neutrophilic infiltrate |
| 18 - 24 Hours | Continuing coagulation necrosis, pyknosis of nuclei, and marginal contraction bands |
| 24 - 72 Hours | Total loss of nuclei and striations along with heavy neutrophilic infiltrate |
| 3 - 7 Days | Macrophage and mononuclear infiltration begin, fibrovascular response begins |
| 4 - 21 Days | Fibrovascular response with prominent granulation tissue |
| 7 Weeks | Fibrosis |
| | |

The above table shows the pathological changes in myocardial infarction according to the time of obstruction.

No changes in gross examination or by light microscopy in histopathology occurs in the first 30minutes of MI. Sometimes mitochondrial swelling and glycogen loss can be seen in electron microscopy.

Myocardial fibers become wavy within 3 hours of infarct. Staining defect is seen between 2-3 hours of infarct. Within 12 hours of infarct there is loss of cross striation, coagulation necrosis, hemorrhage and edema. Within 24 hours of infarct there is ongoing coagulation necrosis, contraction band necrosis in the margins, pyknosis of nuclei, beginning of neutrofil infiltration and hypereosinophilia of myocytes. There is continued coagulation necrosis, loss of nuclei and striations and heavy neutofil infiltration occurs within 3days of infarct. Within 7 days of infarct there is necrosis of neutrofil, beginning of disintegration of dead muscle fibers and macrophage removal. Within 10days of infarct there is beginning of granulation tissue formation and increased phagocytosis of dead cell at border. Within 21 days there is mature granulation tissue with type 1 collagen. Within 8 weeks of infarct there is increased collagen deposition and decreased cellularity. More than 2 months there is dence scar formation. Once scar formed the actually age of infarct cannot be found.

## MYOCARDIAL INFARCTION- Clinical features

**Precipitating factors-** vigorous physical exercise, emotional stress, medical or surgical illness is found in more than half of the patient with MI. Circadian variations is found between 6am- 12noon is reported in many cases, it can also occur in any time of the day or night.[19]

**Clinical symptoms –** The clinical hallmark is chest pain which is a deep visceral pain, similar in character and distribution to angina pain, very severe and prolonged lasting more than 20mins, it is present at rest and not responding to nitrates. The pain is heavy, squeezing, crushing type and sometime stabbing or burning[19]. Pain involves mainly the substernal region or in the epigastrium commonly radiate to the left shoulder or left arm. It may also get radiated to abdomen back and neck, abdomen, back and lower jaw. It does not radiate below the umbilicus. There may be weakness, sweating, nausea, vomiting, anxiety and feeling of impending death associated with pain.

In patients with diabetes mellitus, prior heart failure, previous stroke and in older age group myocardial infarction may be painless[19]. Loss of consciousness, confusional state, profound weakness, arrhythmic appearance, peripheral embolisation or sudden drop in arterial pressure are the other features found in with or without pain in some patients.

Sudden onset of breathlessness which progresses to pulmonary edema is found in increasing age group.

In cases of inferior wall myocardial infarction patient can presented with abdominal pain diarrhea and giddiness due to activation of parasympathetic nervous system.

**MYOCARDIAL INFARCTION- Physical findings**

Patients usually try altering their position, stretching, moving around in the bed to relieve pain. They are anxious and restless. Common physical findings include pallor, peculiar facial expression, sweating, cyanosis, hypotension, arrhythmias (ventricular ectopic beats are more common), basilar rales, sinus tachycardia, pericardial friction rub, basal crepitations, raised JVP are seen. Sympathetic nervous system hyperactivity, tachycardia or hypertension are seen in patients with anterior infarct and parasympathetic hyperactivity, bradycardia or hypotension are seen in patients with inferior wall infarction.

Any one or more of the finding may be present such as rise in blood pressure and heart rate, presence of fourth heart sound, paradoxical splitting of second heart sound, decreased intensity of first heart sound, murmur of mitral regurgitation due to papillary muscle dysfunction, due to dysfunction of mitral valve apparatus a transient midsystolic, late

systolic apical murmur, dyskinetic segment around the apex, relief of pain by carotid sinus massage (Levine test) are seen. Apical impulse may be difficult to palpate in some cases. Decreased carotid pulse and raise in temperature to $38^0$c maybe observed.

**MYOCARDIAL INFARCTION- Investigations**

Investigations includes electrocardiogram, laboratory findings of cardiac injury enzymes and imaging.

**1. Electrocardiogram:**

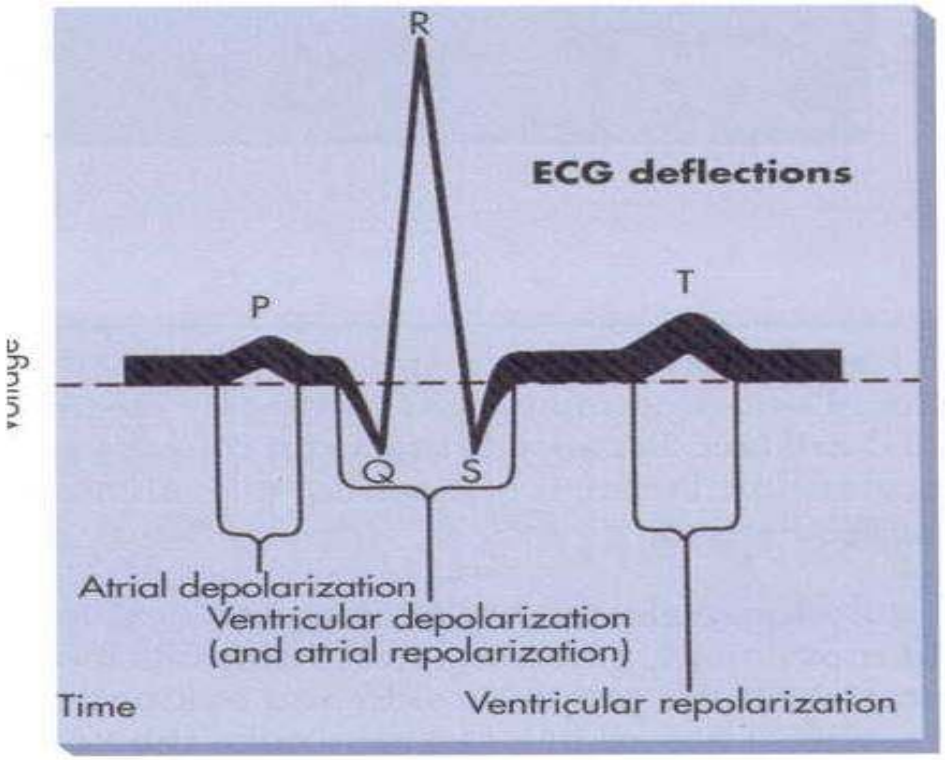
ECG is useful in confirming the diagnosis in both acute and chronic coronary syndrome. Depending on the factors given below the findings may get altered.

- Duration-acute or evolving / chronic
- Extent – transmural /nontransmural
- Topography- anterior / inferior / posterior / right ventricular

Classic pattern may get altered or masked in the presence of underlying abnormalities like bundle branch blocks and arrhythmias.

ECG remains the most cost effective investigation in the diagnosis of acute as well as in chronic myocardial infarction. The ECG changes depends upon duration of ischemic process, extend of infarction. ECG leads are very helpful in localization of involved vessels.

**Normal ECG formation**




- ✓ **P wave -** upright wave in limb leads, biphasic in lead V1& V2. It occurs due to atrial depolarization. It always precedes the QRS complex.

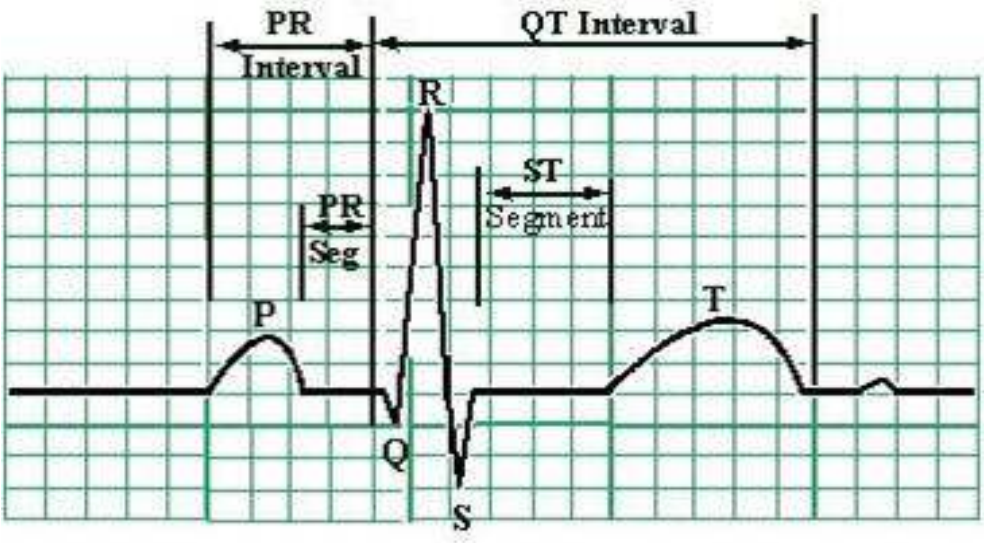
- ✓ **Q wave** -occurs due to septal depolarization. First there is negative deflection, it always precedes the R wave.

- ✓ **R wave** -it is first positive deflection of QRS complex and it occurs due to ventricular depolarization

- ✓ **S wave** - follows R wave, it is negative deflection of QRS complex

- ✓ **T wave** -it occurs due to ventricular depolarization it is usually upright

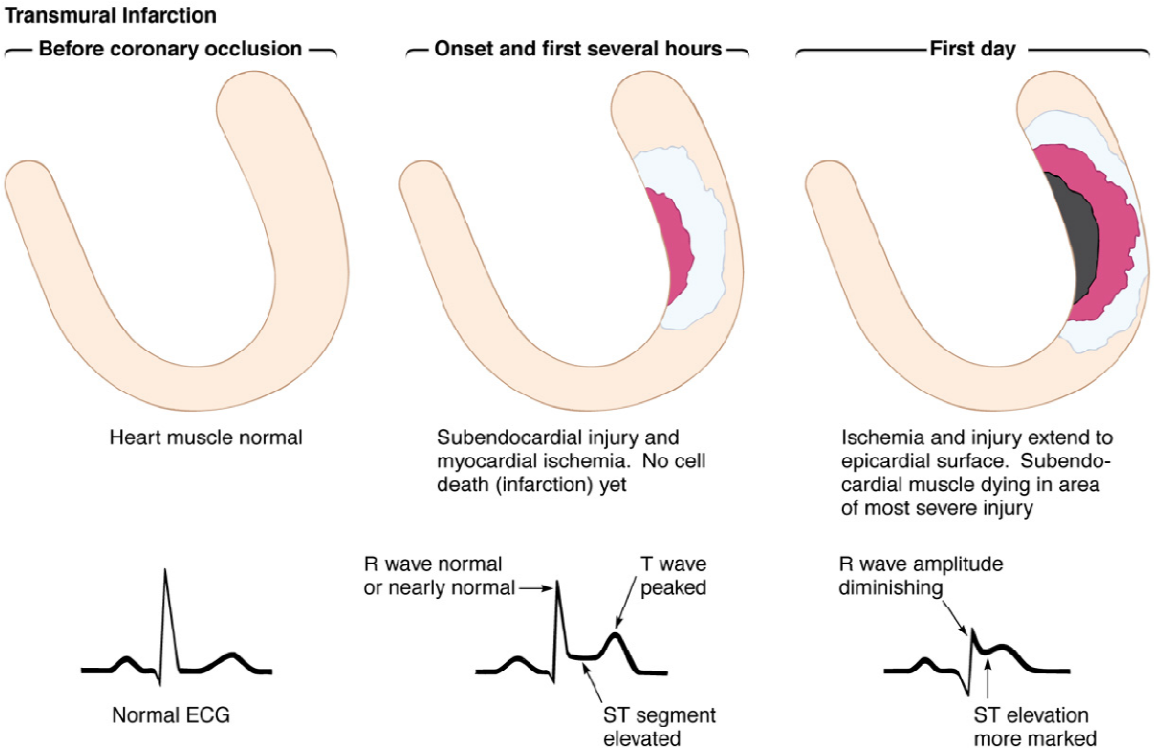
- ✓ **U wave** - it occurs due to late ventricular repolarization of purkinje fibers.




- ✓ **PR interval-** Impulse travel from SA node to both ventricles, the time taken is called PR interval, it indicated AV nodal period of conduction. It can be measured from starting point of P wave to starting point of QRS. Normal PR interval is 0.12-0.21 sec.

- ✓ **RR interval**- useful in counting the heart rate.
- ✓ **QT interval**- it occurs due to ventricular depolarization as well as repolarisation. Normal QT interval is 0.35-0.45 sec.
- ✓ **QRS complex**- the normal QRS occurs due to ventricular depolarization. Normal QRS duration is 0.10-0.12 sec

**ECG changes in myocardial infarction according to the time of infarct:**



The above picture shows the ECG changes in myocardial infarction according to time.

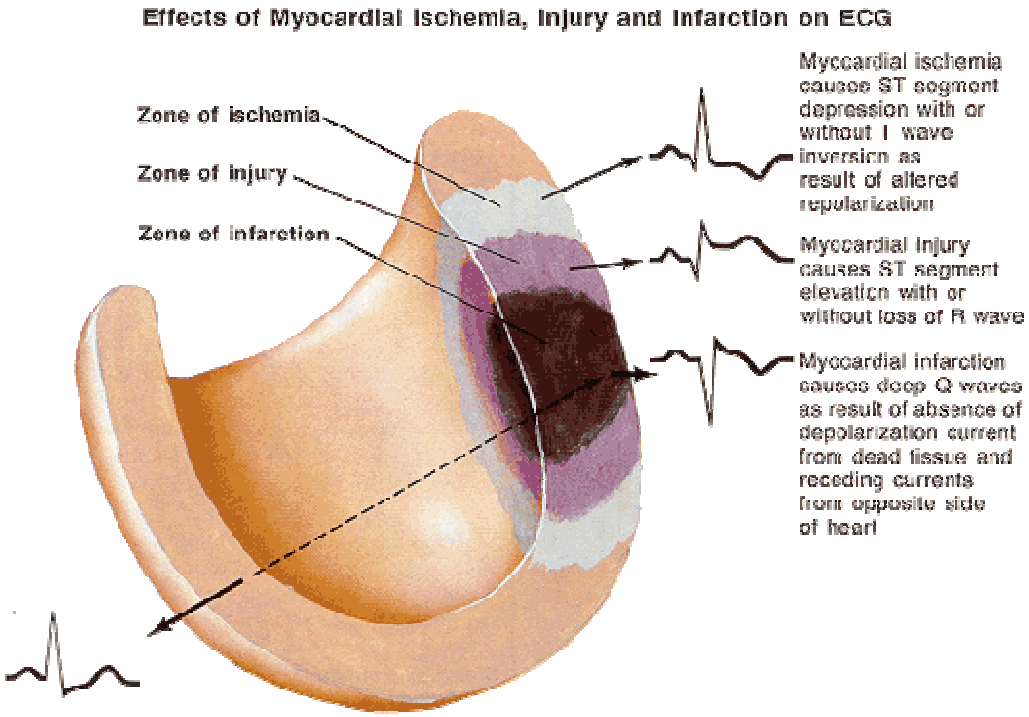
There is subendocardial injury and myocardial ischemia from the onset and within 24 hours if infarction, in this there is ST segment elevation and T wave is peaked, R wave appears nearly normal.

In the first day of infarction the ischemia and injury extend to the epicardial surface and at the site of severe injury there is area of subendocardial muscle dying, there is marked ST segment elevation and diminishing of R wave amplitude.

**Role of ECG in myocardial infarction:**

There are 3 zones of injury occurring- ischemia, injury and necrosis.

- *Ischemia*- is always reversible, the usual manifestation in ECG are ST segment depression and symmetrical T wave inversion. The horizontal and down going ST segments are relatively more specific for ischemia than up going ST segment.




- *Injury*- it is the next degree of ischemia which is severe. Its manifestation are hyper acute T waves and ST segment elevation (especially coving in type in upward convexity). It occurs in impending or ongoing infracted patients.

- *Infarction* – due to ST-T changes of injury the manifestation of infarction in ECG is usually pathological Q wave. (>0.04 seconds, i.e., 1mm wide or >1/4 the size of the following R wave). [17]

It is emphasised that diagnosis of myocardial infarction is usually based on the diagnostic triad such as history and clinical finding, ECG features and raised cardiac enzymes rather that one of the above parameter.

## The Evolution Of An Infarct

As time passes from hours to days to weeks to month there are series of changes in ECG pattern in myocardial infarction. This is called as evolution of ECG. Therefore it is important to take serial ECG's t evaluate the stage or age of infarct. It is clinically and prognostically important to know the age to infarct as the risk of mortality and complications increases with passage of time.[17]

## The Site Of Infarct

It is important to know the site of infarct from ECG. Most infarction occurs in the left ventricle (20-25% occurs in the atria or right ventricle). Sites of infarction are divided into three- anterior, inferior and posterior.

- *Anterior infarcts:* precordial leads $L_1$ and aVL reflects anterior wall infarction. Extensive area is covered by anterior infarct so it is quite common, and is further divided into anteroseptal, anterolateral and extensive anterior infarcts.

When changes are confined to lead $V_1$ and $V_4$ anteroseptal infarction is diagnosed, if confined to lead $V_5$ and $V_6$ anterolateral infarction is diagnosed and extensive when all the chest leads shows the changes.

- *Inferior infarcts:* $L_{II}$, $L_{III}$ and aVF are the leads that reflect inferior wall or diaphragmatic infarction( as the inferior wall faces aVF)

- *Posterior infarcts:* it is difficult to diagnose this infarct in ECG. It may be associated with inferior wall myocardial infarction manifesting only as reciprocal changes (ST-T changes opposite in direction to the changes seen in the area of infarction) in the anterior leads $V_1$ to $V_4$.

For a complete diagnosis of infarction from ECG, 3 parameters are required to be mentioned.

(a) site of infraction

(b) age or stage of infarction

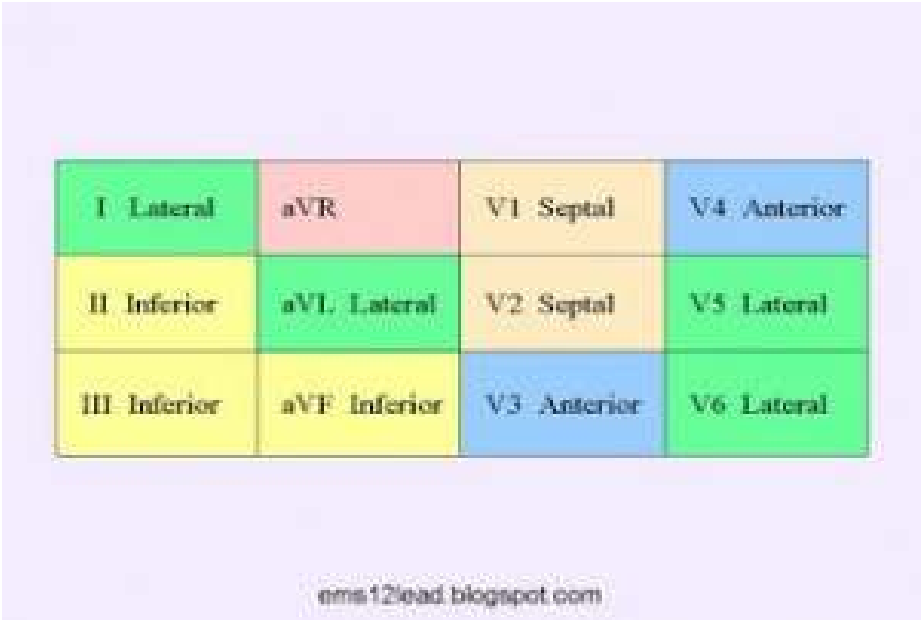
(c) complications if present such as bradycardia, arrhythmia, heart block ,etc.

In about 20-25% of true infarct ECG is absolutely normal. The causes of ST segment elevation are as follows

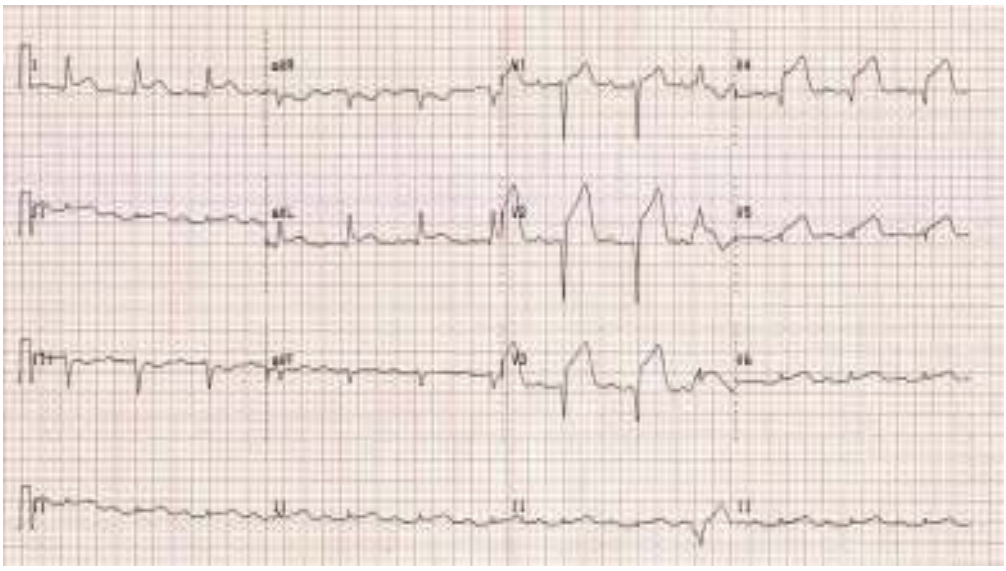
- ✓ Pericarditis
- ✓ Left bundle branch block(LBBB) and WPW syndrome
- ✓ Cor pulmonale

- ✓ Digitalis effect
- ✓ HOCM
- ✓ Quinidine therapy
- ✓ Cardiac tumors
- ✓ LV aneurysm
- ✓ Juvenile T inversion, ERS
- ✓ Prinzmetal's angina
- ✓ Non cardiac lesion with CVA
- ✓ Trauma
- ✓ DC cardio version.

**Localization of infarction by ECG:**



- *Anterior wall (anteroseptal):* ST segment elevation in $V_1$ and $V_4$



- *High lateral wall infarction (apical):* ST segment elevation in aVL, $V_5$ and $V_6$ .

- *Inferior wall infarction:* ST segment elevation in II, III, aVF

- *Inferolateral wall infarction:* ST segment elevation in II, III, aVF and in lead $V_5$ and $V_6$

- *Right ventricular infarction:* always suspect right ventricular infarction when inferior wall MI occurs without any reciprocal changes.

Diagnostic criteria are as follows:

(a) ST segment elevation in $V_3R$ or $V_4R$ or $V_5R$.

(b) Elevated ST segment in $V_1$-$V_3$

(c) ST segment elevation in $V_6R$ or $V_7R$

(d) ST segment elevation in $V_1$ and ST segment depression in $V_2$

(e) Regression of R wave from $V_1$-$V_4$

(f) ST segment elevation more in lead III than lead II

(g) ST segment depression in $V_2$

- *Atrial infarction:*

  - Always occurs with extensive ventricular infarction
  - Usually associated with atrial arrhythmias with large ventricular infarction
  - Incidence : 5-15% in right atrial infarction
  - Isolated atrial infarction is very rare, usually occurs in CCF patients
  - Rarely occurs in aluminum phosphide poisoning

ECG criteria to diagnose atrial infarction

(I) Major criteria[14]

(i) >0.5 mm elevation of negative deflection of Pwave in $V_5$ and $V_6$ with reciprocal changes in $V_1$ and $V_2$

(ii) Elevation of negative deflection of P wave >1.5mm in one precordial leads (or) elevation of PTa >1.2mm in limb leads with occurance of atrial arrhythmias

(iii) Elevation of PTa in lead 1, with reciprocal changes in other limb leads

(II) Minor criteria

(i) Presence of abnormal P wave, it may be irregular or notched

(ii) Depression of PTa with reciprocal changes

- *Posterior wall MI*- occurs due to ST depression with tall R and upright T wave in right precordial leads in a case of inferior wall MI

**Site Of Occlusion Of Coronary Arteries:**

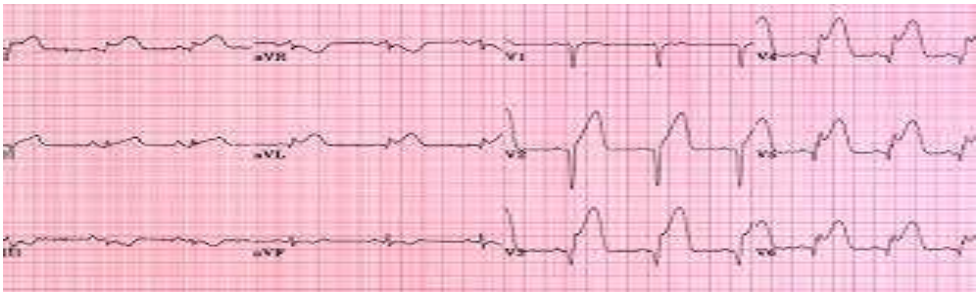
- Occlusion of right coronary artery

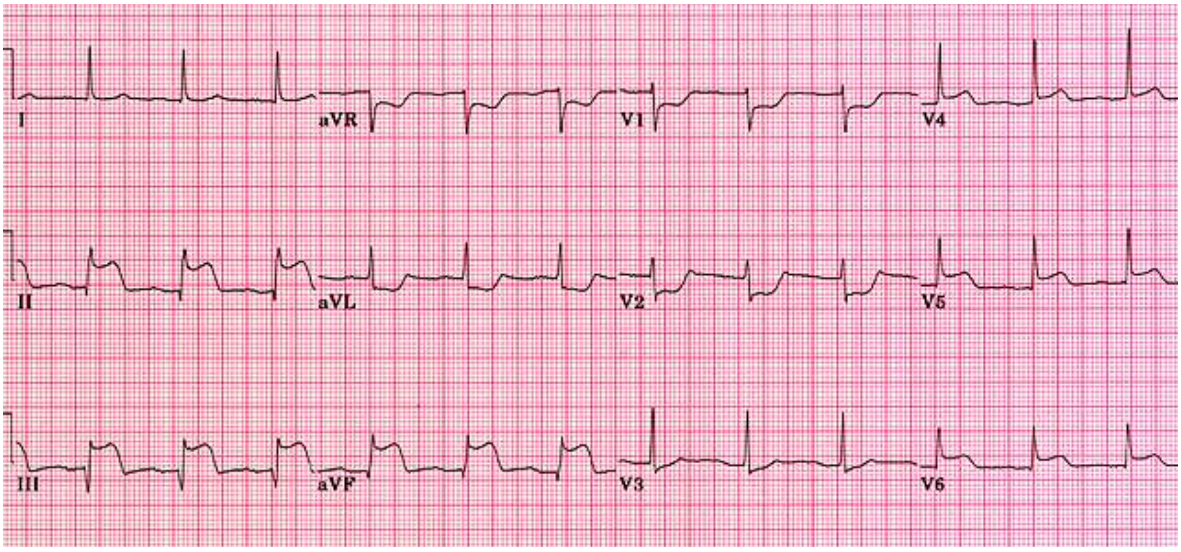
  - Right ventricular MI

- Inferior wall MI
- Posterior wall MI
- Infero posterior wall MI

- Left circumflex occlusion
  - Posterior wall MI
  - Lateral wall MI
  - High lateral MI

- LAD occlusion
  - Anteroseptal MI
  - Extensive anterior wall MI and can present with BBB






***To differentiate RCA and LCA occlusion in case of inferior wall MI***

- Elevation of ST segment in lead III > lead II- indicates RCA occlusion.
- Elevation of ST segment in lead II > lead III- indicated LCA occlusion
- Inferior wall MI with following changes always suggestive of LCA occlusion

  (a) ST depression $V_3$: lead III ST elevation >1.2

  (b) ST depression in $V_1$- $V_3$

  (c) ST depression in aVL

  (d) ST elevation in aVL or $V_5$ and $V_6$

- Inferior wall MI with following changes suggestive of RCA occlusion

Proximal→ ST segment elevation in $V_1$

***Detection of LAD occlusion in a case of anterior wall MI***

(a) Anterior wall MI with ST depression of >1mm in lead II, III, aVF- indicates proximal LAD occlusion

(b) Anterior wall MI with no ST depression in lead II, III, aVF- indicates distal LAD occlusion

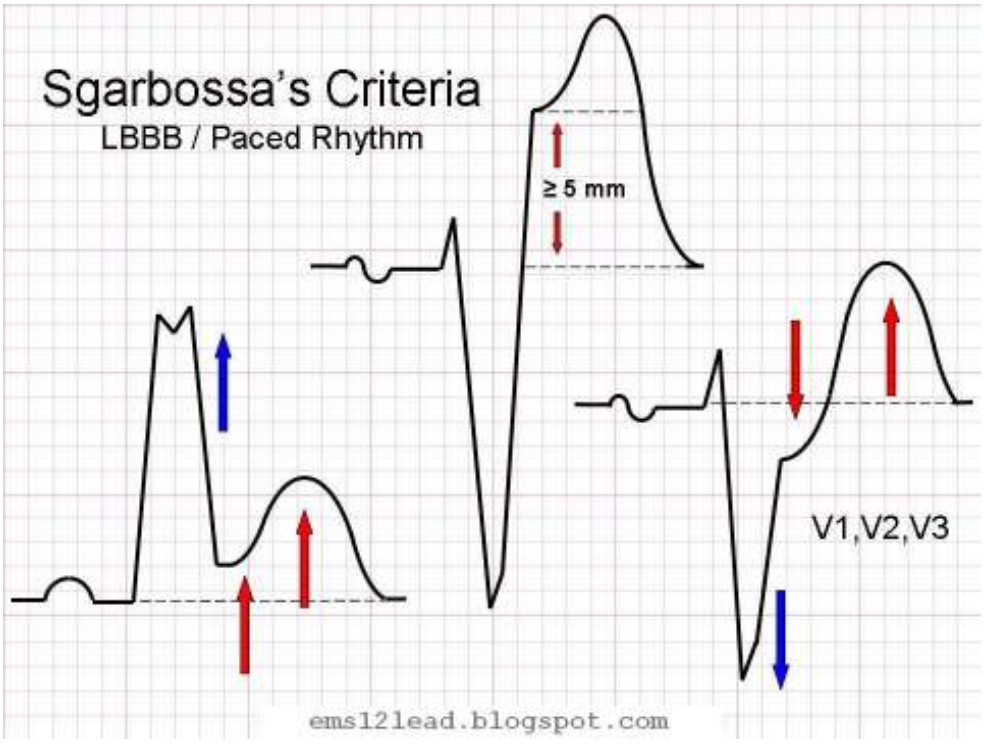
(c) LAD occlusion proximal to septal branch

- ST elevation in $V_1$ >2.5mm
- ST elevation in aVR
- ST depression in $V_5$
- MI and right bundle branch block

(d) Proximal to diagonal branch

- Abnormal Q wave in aVL
- ST elevation lead I and aVL

***Diagnosis of MI in the presence of LBBB***




*Sgarbosa criteria:*

- Elevation of ST segment >1mm + positive QRS complex- 5 points
- Elevation of ST segment >5mm + negative QRS complex- 2 points
- Depression of ST segment >1mm in $V_1$-$V_3$- 3 points

Total points ≥3 indicates MI

*Other criteria*

- Presence of QS pattern in $V_1$-$V_4$
- Regression of R wave from $V_1$-$V_4$
- Q wave in two consecutive precordial leads or in two consecutive limb leads
- Presence of positive T wave in lead $V_5$ and $V_6$
- Left axis deviation
- Presence of prominent S wave in $V_5$ and $V_6$

***Diagnosis of MI in the presence of RBBB*** **-**Presence of RBBB will never mask the ECG changes of MI **.**

**A) Repolarisation (ST-T wave) abnormalities**

The changes of ST segment is the earliest ECG finding found as a result of injury current of rest and injury current of activity. In acute myocardial infarction there is tall T wave with J point elevation and elevation of ST segment with upward convexity are the earliest manifestation. If the ischemia is dominantly transmural, deviation of ST segment towards the injured epicardial layer causing ST segment elevation, it indicates indicative change. In reciprocal changes there is ST

segment depression sometimes T wave inversion, which occurs when the leads get deviated towards uninjured surface eg., in AWMI there is reciprocal changes in inferior lead II, III, aVF. If it is a dominant subendocardial injury the reverse happens, the lead get shifted to uninjured layer which shows ST segment depression and lead aVR shows ST elevation.

T wave become tall in very early MI, and peaked hyperacute MI. It last only for few hours and it is transient.ST segment change is accompanied by deep symmetrical inversion of T wave indicates myocardial injury. The T wave inversion may be associated with iso electric ST segment or sometimes with upward convexity or sometimes with ST segment depression.

**B) QRS changes**

The lead over the infracted region shows QRS negativity and/or loss of QRS positivity. Repolarisation (ST-T) abnormality is accompanied by depolarization (QRS) changes. As a result of loss of electromotive force, sufficient myocardial tissues necrosis in the anterior, lateral or inferior leads show decrease R wave amplitude or Q wave. In subendocardial infarcts and transmural infarcts there is abnormal Q wave and in some cases there is no Q wave found. In these region rarely there

is increase R wave in $V_1$ and $V_2$ without Q wave in any leads due to depolarization forces.

**C) Evolution of ECG changes**

Within hours to days of infarction there is ischemic ST elevation and hyper acute T wave by formation of inversion of T wave and sometimes Q wave in the diagnostic leads. QT prolongation is found associated with these changes. The height of R wave is reduced. Superimposition of ST elevation on the pattern of an old infarction signifies a fresh infarction in the region ofprevious involvement. In days or weeks these changes in the ECG can resolve or may persist indefinitely. Complete normalization of ECG is not common but can take place.

**Mechanism involved in ECG changes**

The ST elevation seen in ECG can be explained by two basic mechanisms. (i) *Diastolic current of injury*- there is primary TQ depression in this case due to the ST vector which will be directed away from the ischemic, negative, partly depolarised region during electrical diastole. For this baseline shift there is compensatory conventional alternating-current electrocardiogram, resulting in ST elevation. (ii) *S*ystolic *current of injury*- in this case the cells are repolarised early and

the amplitude and velocity of the action potential is decreased so the ischemic zone is relatively positive. There is primary ST elevation as the injury current is oriented towards the electropositive zone.

**Current of injury pattern with acute ischemia:**

(*i*) *Subendocardial ischemia*- in this the overlying leads record ST depression as the ST vector is directed towards the inner layer of affected ventricle and the ventricular cavity

*(ii)Transmural or epicardial injury*- in this the leads record ST elevation as the ST vector is directed outward, in the contralateral leads reciprocal ST depression may occur.

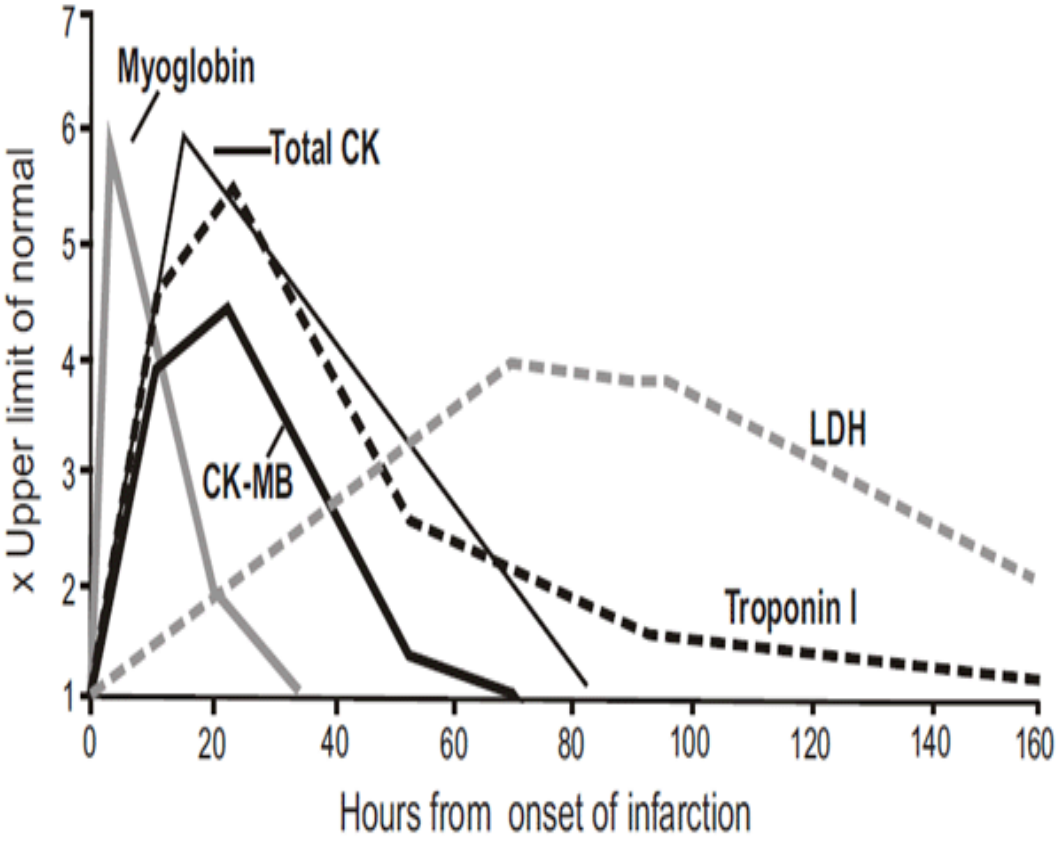
**2) Laboratory findings:**

**i) Creatine kinase MB (CKMB)**

Measurement of the myocardial isoenzymes of CK-MB is more specific in myocardial infarction. Creatine kinase starts to rise at 4-6 hours of the infarct, peaks at 12hours and declines to normal within 2-3 days. CK-MM, CK-MB, CK-BB are the three isoenzymes of creatine kinase. CK-BB is present in brain and kidney, CK-MM is present in skeletal muscles, CK-MB and CK-MM both are present in heart. The value for elevation of CK-MB is set few units above the upper limit as

CK-MB is present in healthy people also. CK value is also elevated in skeletal muscle disease, cardioversion, hypothyroidism, skeletal muscle damage and stroke. CK-MB release in Skeletal muscle is detected for longer period than myocardial release, so a serial measurement showing rise and fall is very important which produces a plateau over several d ays, where skeletal muscle elevation lasts only for a short time

. Figure 1: Cardiac Marker Pattern Associated with Myocardial Infarction (5)




**ii) Cardiac specific Troponin (I and T)**

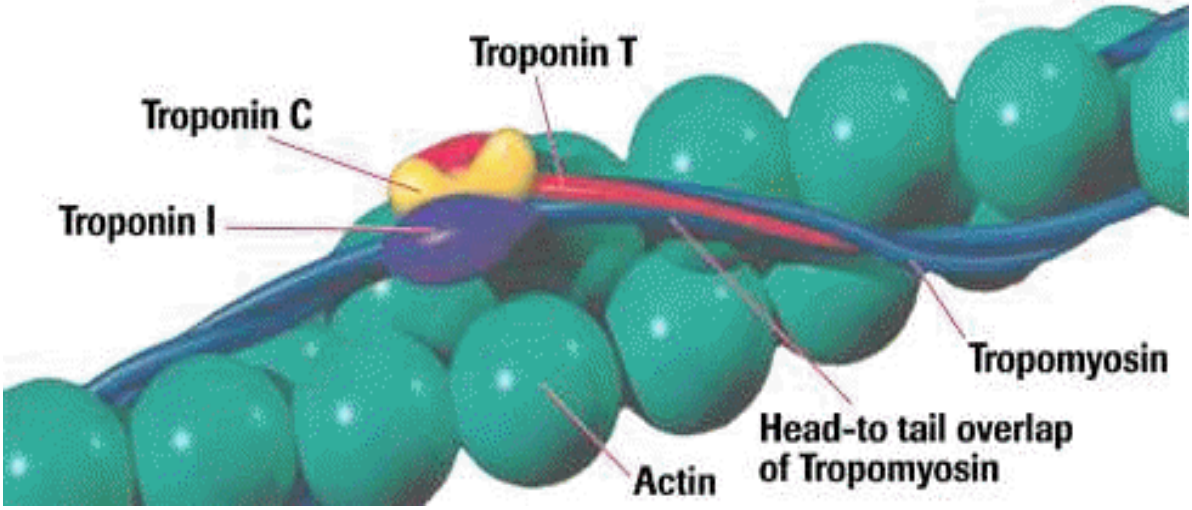
Cardiac and skeletal muscle contraction is under the control of specific protein troponin. Actin and myocin are the two other chief

protein involved in contraction-relaxation cycle of muscle. Through troponin complex, calcium initiates the contraction of muscle.

Troponin C (calcium binding), troponin T (tropomyocin binding protein) and troponin I (inhibitory) are the protein which comprises the troponin complex.

**TROPONIN T**

**A regulatory protein released when cardiac cell necrosis occurs.**




Cardiac TnI and TnT, though it is present in both cardiac and skeletal muscles, the gene and the aminoacid encoding differ so the antibodies formed also differ[18]. Troponin I is highly specific for cardiac muscle injury and it does not represent damaged skeletal muscles.

The biomarker of choice for diagnosis of myocardial infarction is cardiac troponin. In myocardial injury, cardiac isoenzymes such as

cardiac troponin T and I has high sensitivity and high specificity. Monoclonal antibodies against epitopes is used in the detection, as they have negligible cross reaction with troponin of skeletal muscle origin.

By 3hours of chest pain, cardic troponin begin to rise above the reference limit, so only after 4 hours of coronary event cardiac troponin can be detected.after 12 hours test must be repeated to confirm the diagnosis. TnT peaks by 12 hours to 2 days and persist for 10-14days, TnI peaks by 24hours and persist 7-10days.

Troponin T level is used for comparision with different laboratory as TnT can be measured by a single assay. 0.1ng/ml is the usual cut off point for cardiac muscle damage.

Troponin I differ in their cut off value, sensitivity and specificity as there is variety of assay. To obtain uniform concensus and to minimize the difference mentioned above, coefficient variance of less than 10% of $99^{th}$ percentile of normal should be determined by each laboratory. 0.1-2 ng/ml is the cut off point set for myocardial injury.

Troponin is similar to CKMB in its sensitivity, as cardiac troponin remain elevated for 100-200 hours after acute MI and so this assay may be utilized for the evaluation of patients who present long after the episode of chest pain.

| | |
|---|---|
| **Cardiac diseases and conditions** | |
| 1. Myocardial damage | Coronary vasospasm |
| | Cardiac contusion |
| | Cardiac surgery |
| | Percutaneous coronary intervention |
| | Post cardiac transplantation |
| | Closure of atrial septal defects |
| | Supraventricular tachycardia |
| | Cardioversion |
| | Implantable cardioverter defibrillator shocks |
| | Radiofrequency ablation |
| | Myocarditis |
| | Pericarditis |
| | Cardiac amyloidosis |
| 2. Heart enlargement | Dilated cardiomyopathy |
| | Heart failure |
| | Hypertrophic cardiomyopathy |
| | Left ventricular hypertrophy |
| **Noncardiac diseases** | |
| 1. Organ-specific conditions | Primary pulmonary hypertension |
| | Pulmonary embolism |
| | Pulmonary edema |
| | Chronic renal insufficiency |
| | Stroke |
| | Subarachnoid hemorrhage |
| 2. General conditions | Critically ill patients |
| | High dose chemotherapy |
| | Sepsis and septic shock |
| | Sympathomimetic agents |
| | Heavyendurance exercise |
| **Methodological causes** | Fibrin clots |
| | Heterophilic antibodies |
| | Rheumatoid factor |

There is better prognosis and lower risk for adverse cardiac outcome if the cardiac troponin is not detectable after 12 hours of pain. Cardiac muscle injury can be detected but the cause cannot be detected by troponin level measurement alone, clinical assessment is required to determine the cause.

Patients previously negative for other conventional cardiac biomarkers, cardiac troponin is found to be elevated, this is the most important advantage of cardiac troponin. Even when there is absence of ST segment elevation cardiac troponin is used in early and prompt diagnosis of acute myocardial infarction and can be treated early.

It may also get elevated in sepsis, hypotension, atrial fibrillation, intracranial haemorrhage, myocarditis, pulmonary embolism and chronic cardiac failure[18] . Other causes are shown below

**iii) Other cardiac injury enzymes**

Aspartate aminotransferase(AST), Lactate dehydrogenase (LDH), myoglobin. CK and troponin are the first to rise, followed by AST and LDH.

**iv) Laboratory measurement**

- Leucocytosis develop within 2hours, reaches peak by 1day after MI and return to normal by 1week.
- Within 1-2 days of MI lipid profile must be estimated, as total and HDL cholesterol remains near baseline and fall after that.
- ESR usually remains normal for 1 or 2 days and get raised after 4-5days and remain raised for days.
- Due to hemoconcentration, hemotocrit may rise after MI.

**3) Imaging**

**i) 2D Echocardiography**

Regional wall motion abnormality and ejection fraction can be assessed. For establishing prognosis, LV function is found after MI. Patients at risk of developing congestive cardiac failure, mechanical complications after MI and viable but stunned myocardium residual provocable ischemia can be detected in a early state.

**ii) Doppler Echocardiography**

Blood flow in the cardiac chamber and cardiac valves can be assessed. It is also useful in the assessment of the site of acute ventricular

septal rupture, acute cardiac tamponade, detecting the severity of MR or TR after MI and for finding the shut flow across the defect.

**iii) Nuclear Imaging**

In MI radionuclide scanning, perfusion imaging, positron emission tomography, infarct avid scintigraphy are used in evaluation. Radionuclide scanning shows the site of necrosis and the extent of impairment of ventricular function**.** When clinical history, ECG findings and serum markers are not available cardiac radionuclide imaging is done for diagnosis.

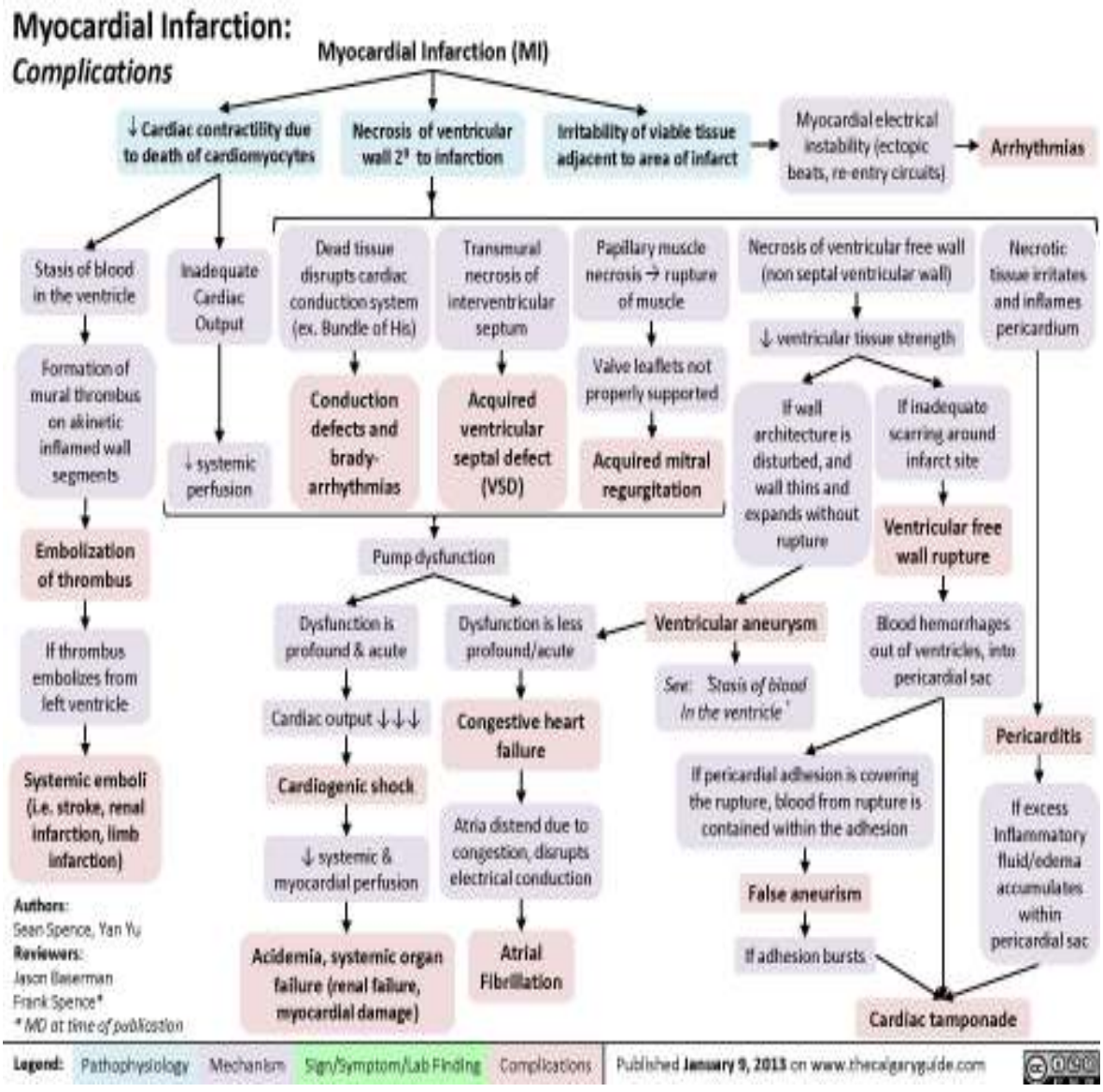
**MYOCARDIAL INFARCTION- Diagnosis**

Atleast two of the following is required to diagnose MI

- Presence of ischemic chest pain.
- Changes in the ECG pattern
- Cardiac enzyme rise and fall

## MYOCARDIAL INFARCTION- Complication

Myocardial damage leads to various adverse consequence and complications.




- **Recurrent chest pain-** it occurs in 20-30% of patients after MI. Ischemia in the territory of original infarction, pericarditis, myocardial rupture, or pulmonary embolism may be the cause of pain.

- **Acute pericarditis-** it occurs in 10-15% of patients after 24-96hours of MI. Dressler syndrome is a autoimmune process with malaise, fever,pericardial pain.,which occurs in contrast to acute pericarditis after 1-8 weeks of MI.

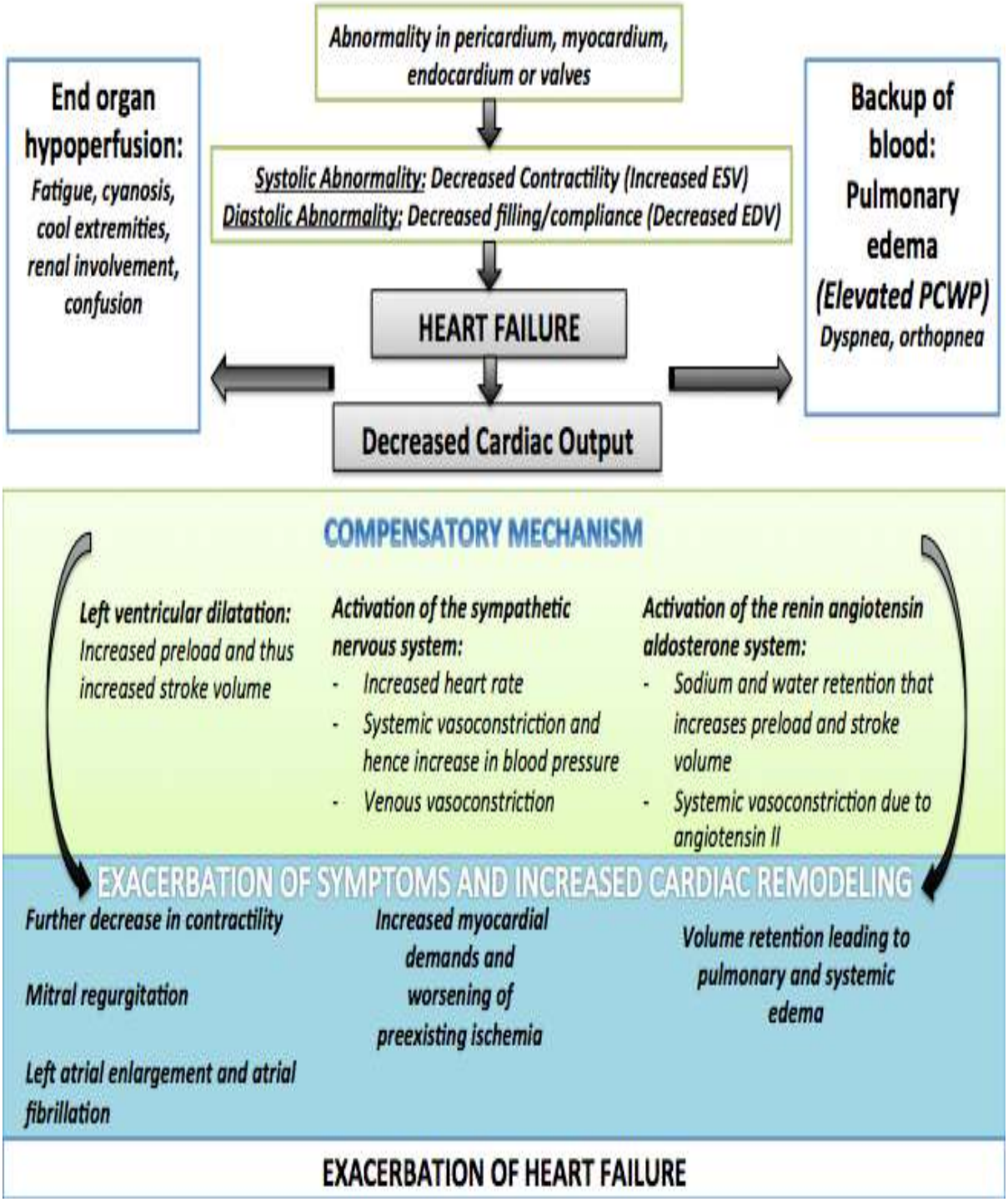
- **Arrhythmias-** cardiac rhythm abnormalities are common after MI

    - ✓ Intraventricular conduction delay, sinus bradycardia, AV block, accelerated junctional rhythm are the bradyarrhythmias and conduction disturbance seen.

    - ✓ Ventricular premature depolarization (VPDs), ventricular fibrillation(VF), ventricular tachycardia(VT) are due to electrical instability

    - ✓ Atrial fibrillation, paroxysmal ventricular tachycardia (PSVT) , sinus tachycardia occur due to pump failure or excessive sympathetic stimulation.

- **Cardiogenic shock-** is an infrequent but serious complication of MI. Mortality is more than 50% in these cases.
- **Mitral regurgitation**
- **Hypotension**
- **Left ventricular failure**


Abnormality in pericardium, myocardium, endocardium or valves
End organ hypoperfusion:
Fatigue, cyanosis, cool extremities, renal involvement, confusion
Systolic Abnormality: Decreased Contractility (Increased ESV)
Diastolic Abnormality: Decreased filling/compliance (Decreased EDV)
HEART FAILURE
Backup of blood: Pulmonary edema (Elevated PCWP)
Dyspnea, orthopnea
Decreased Cardiac Output
COMPENSATORY MECHANISM
Left ventricular dilatation:
Increased preload and thus increased stroke volume
Activation of the sympathetic nervous system:
- Increased heart rate
- Systemic vasoconstriction and hence increase in blood pressure
- Venous vasoconstriction
Activation of the renin angiotensin aldosterone system:
- Sodium and water retention that increases preload and stroke volume
- Systemic vasoconstriction due to angiotensin II
EXACERBATION OF SYMPTOMS AND INCREASED CARDIAC REMODELING
Further decrease in contractility
Mitral regurgitation
Left atrial enlargement and atrial fibrillation
Increased myocardial demands and worsening of preexisting ischemia
Volume retention leading to pulmonary and systemic edema
EXACERBATION OF HEART FAILURE

Heart failure is the common complication which leads to mortality in patients with acute myocardial infarction. The mechanism involved is as shown in above.

- **Mechanical complications-** aneurysm, ventricular pseudoaneurysm, free wall rupture, papillary muscle rupture, ventricular septal rupture.

**MYOCARDIAL INFARCTION- Management**

**1) Anti ischemic treatment:**

It reduces the oxygen demand and myocardial wall stress by reducing both preload and afterload.

*Nitrates:* In stable patients it is given sublingually 0.4mg every 5min or buccal spray (0.3-0.6mg), if pain persist after 3 doses intravenous nitroglycerine 5-10 micro gram per min is advised.

*Beta blockers:* It reduces oxygen demand by lowering heart rate and blood pressure. It also has antiarrhythmic effect which is useful in controlling tachycardia, hypertension and continued angina.[18]

Beta-blockers can be given orally or intravenously within first few hours of infarction which are useful in reducing mortality. Commonly used drugs are i) *Metoprolol*- 5mg IV over (1-2 min) repeated after 5min

for a total dose of 15mg, after 1-2hours followed by 25-50mg orally 6th hourly. ii) E*smolol*: 50-300 mcg/kg/min

**2) Control of pain:**

*Morphine:* is given in a dose of 3-5mg IV, may be repeated every 10-30min along with anti-emetic to control of chest pain. Beta-blockers, nitroglycerine, thrombolysis may also help in relieving pain.

**3) Antiplatelet therapy:**

*Aspirin:* it is administered in a dose of 162-325mg non-coated formulations, early administration in patients with acute MI has great benefits, initial dose is followed by 75-160mg per day.

*Clopidogrel:* in patients less than 75 years, loading dose of 300-600mg followed by 75mg per day is given. In patients above 75years, 75mg per day without loading dose is given.

**4) Thrombolytic or fibrinolytic therapy:**

It should be initited before 30min. Thrombolytic agent includes streptokinase(STK), urokinase(UK), tissue plasminogen activator(t-PA or alteplase), reteplace, tenecteplace, anisoylated plasminogen streptokinase activator complex(APSAC, antstreplase). It leads to generation of plasmin that lyses the clot. These drugs are not recommended in patients

with NSTEMI and unstable angina. In STEMI, when ST elevation is more that 2mm in two contagious precordial leads and 1mm in two limb, patients should be considered for reperfusion therapy.

(i) *Tissue plasminogen activator(tPA)* -is give as 15mgIV bolus 0.75mg/kg(max 50mg) over 30min followed by 0.5mg/kg over 60min (max 35mg) over next 30min.

(ii) *Streptokinase(SK)*- 1.5 million units IV over 60min

(iii) *Tenecteplace(TNK)*- 0.50 mg/kg IV bolus(total dose30-50mg)

(iv) *Reteplase(r-PA)*- two 10 units IV boluses administered 30min apart.

These drugs are absolutely contraindicated in active bleeding, haemorrhagic shock, intracranial aneurysm, aortic dissection, ischaemic stroke within 3months, etc..,

**5) Antithrombin therapy:**

It is required before the completion of infusion of t-PA or tenecteplace, also in patients receiving STK.

*(i) Heparin(UFH)*- is given as initial bolus dose of 60 IU/kg (max of 4000 units), followed by initial infusiom of 12 IU/kg/hour(max of 1000units/hour)

*(ii) Deltaprin* – given 12$^{th}$ hourly, 120 IU/kg SC

*(iii) Fondaparinux*- 2.5mg IV bolus, 2.5mg SC daily. It has decreased bleeding rates. Should not be used during PCI as it causes catheter thrombosis.

*(iv) Enoxaparin* – given as 1mg/kg SC 12$^{th}$ hourly.

*(v)Direct thrombin inhibitors*- hirudin and bivalirudin is better in patients undergoing PCI than UFH.

**6) Percutaneous Coronary Intervention(angioplasty or stenting)**

It is used in acute MI or in coimbination with thrombolytic therapy when thrombolysis fails or it can be given following thrombolysis.

**7) Calcium channel blockers:**

In patients with STEMI for whom beta blockers are ineffective or contraindicated, Verapamil or diltiazem is used for relief of ongoing ischemia or for control of a rapid ventricular response in the absence of CHF, LV dysfunction or AV block.

**8) Angiotensin converting enzyme inhibitor:** It acts by improving myocardial function by reducing myocardial remodelling, to be given in patients within 24hours with acute MI with or without congestive heart failure.

**9) Activity:**

Patient without complication is advised for bed rest for first 12hours, within 24hours sitting is recommended, after 2-3days patient is advised to walk within the room, can increase walking progressively up to 600ft after 3days, at least for more than 3 times a day.

**10) Diet:**

Nil per oral or clear liquids is given for first 4-12hours. Carbohydrate should provide 50-55% and fat around 30% of total calories. High amount of potassium, magnesium and fiber must be provided with low sodium.

**11) Bowel:**

Rich bulk of diet is given, rather than bed pan bed commode is given and stool softeners are used routinely.

**12) Sedation:**

Drugs such as diazepam 5mg, lorazepam 1mg, alprazoam 0.5-1mg is given for about 3-4 times a day.

## Treatment protocol for acute coronary syndromes

| | MYOCARDIAL INFARCTION | | |
|---|---|---|---|
| | NSTEACS | | |
| | Unstable Angina | NSTEMI | STEMI |
| **Pathophysiology** | Ischemia without necrosis | Ischemia with necrosis | |
| | Partially or transiently obstructive thrombus | | Complete obstruction by intracoronary thrombus |
| **Clinical features**<br>• Physical examination and history | Chest pain (angina and associated features) and presence of risk factors | | |
| • Typical presenting symptoms | Severe angina (new onset, crescendo or rest angina) | Prolonged "crushing" chest pain, more severe and wider radiation than usual angina | |
| **12-lead ECG** * | No abnormalities, transient ST-elevation, ST-depression or T-wave inversion | | Persistent ST-elevation, new left bundle branch block (LBBB) |
| **Cardiac troponin**<br>Measurement on arrival and at 6 h | Negative (2x) | Positive | Positive** |
| **Therapeutic intervention** | Non-invasive (conservative) | Early-invasive | Immediate reperfusion |

* Observation of dynamic profiles is more informative (repeat or continuous monitoring).
** Useful for confirmation, but availability of cTn test result should not delay therapeutic intervention.

The above picture shows the treatment protocol for acute coronary syndrome. Most important of this is STEMI, which cause complete obstruction by thrombus, diagnosed by persistent ST elevation and left bundle branch block and confirmed by positive cardiac troponin. The main stay treatment for STEMI is fibrinolytic therapy, percutaneous coronary intervention or CABG. [18]

# HYPONATREMIA

## DEFINITION:

Hyponatremia is defined as plasma sodium concentration less than 135mEq/L. It indicates that the body fluids are diluted by excess of water relative to total solute. [20]

When the sodium concentration is less than 120mEq/L it is severe hyponatremia, it is mild and asymptomatic in most of the cases[3]. Xubstantial neurological complication and mortality are the serious medical condition associated with severe form. Central pontine myelinolysis and extrapontine myelinolysis is found to be associated with correction of hyponatremia.

## PATHOPHYSIOLOGY:

- Low serum osmolality is usually seen when the plasma concentration of sodium is below 135mEq/L, it occurs due to retention of water or due to loss of sodium.[20]

- In some cases of hyponatremia the plasma osmolality may be increased, it occurs in condition where there is accumulation of solutes in the ECF to become impermeable to glucose when there is insulin deficiency. Glucose is an effective osmole which draws

water from muscle cell, which causes hypertonic hyonatremia. It usually occurs in poorly controlled diabetes mellitus. For every 100mg/dl rise in plasma glucose level there is 1.6 to 2.4mEq/L fall in $Na^+$ concentration.

- Hypotonic hyponatremia is most commonly seen, it is mainly due to primary water gain or primary sodium loss[20]. Normally, suppression of ADH occurs when there is slight reduction in serum sodium, which occurs due to reduction in osmolality, resulting in excretion of dilute urine which normalizes sodium.

- Hyponatremia occurs due to factors such as (i) excessive intake of water, (ii) due to renal failure if there is reduced excretion of water by kidney[3], (iii) due to inappropriate release of ADH [SIADH] or due to increased sensitivity to ADH, (iv) when urine flow in collecting tubule is very slow resulting in reduced excretion of urine, it occurs when there is increased salt and water reabsorption in the proximal tubule, resulting in low urine volume, slow flow and further concentration due to ADH.

## CAUSES OF HYPONATREMIA:

### I. Hypotonic hyponatremia[29]

#### a) Reduced effective blood volume

❖ Increased ECF volume(primary $NA^+$ gain exceeded by secondary water gain)

- Congestive heart failure
- Cirrhosis of liver
- Nephrotic syndrome

❖ Reduced ECF volume(primary $NA^+$ loss followed by secondary water gain)

- Renal loss of sodium: diuretics, osmotic dieresis, ketonuria, Addisons disease, salt-wasting nephropathy, post obstructive dieresis, nonoliguric acute tubular necrosis.
- Extrarenal loss of sodium:

    1) Gastrointestinal loss- vomiting, diarrhoea, tube drainage, fistula, peritonitis, pancreatitis, obstruction.

    2) Integumentary loss- sweating, burns.

**b) Normal or increased effective blood volume** (primary water gain followed by secondary $NA^+$ loss)

- Syndrome of inappropriate secretion of ADH(SIADH)
- Chronic renal failure
- Primary polydipsia
- AVP release- because of pain, nausea, drugs
- Glucocorticoid deficiency
- Decreased intake of solute
- Hypothyroidism

**II. Isotonic or slightly hypotonic hyponatremia**

- Hyperlipidemia
- Hyperprotinemia
- Posttransurethral resection of prostate/bladder tumour.

**III. Hypertonic hyponatremia**

- Hyperglycemia
- Mannitol administration.

Congestive cardiac failure, hepatic cirrhosis and nephritic syndrome are the most common cause of hyponatremia seen in ECF volume expansion which is usually associated with edematous state. Decreased effective circulatory arterial volume which leads increased AVP level and increased thirst are common disorders seen. Reduced GFR, increased proximal reabsorption of $Na^+$ and water leading to delivery of decreased ultrafiltrate to the diluting site and treatment with diuretics are the additional factors which impair the excretion of solute free water. Prognostic factor of hyponatremia depends upon the severity of underlying condition

Increased AVP[2] secretion results in impaired water excretion lead to decreased effective circulatory arterial volume or renal insufficiency, which causes absence of ECF volume contraction in hyponatremia.[25]

Since increased AVP[2] alone is insufficient to produce hyponatremia additional factors such as increased intake of water is also required. This results in rise of TBW, serum concentration of $Na^+$ are decreased. The most common form of this is *syndrome of inappropriate ADH (SIADH)*. This is caused due to nonphysiological release of vasopressin from the posterior pituitary or from some ectopic source. Neuropsychiatric disorder (such as encephalitis, meningitis, CVA, head trauma, psychosis), malignant tumors (such as small cell carcinoma),

pulmonary diseases (such as tuberculosis, pneumonia, acute respiratory failure, positive pressure ventilation), major surgery (postoperative pain) and pharmacological agents (such as SSRIs, narcotics, antipsychotic agents, chlorpropamide, NSAIDs) are the most common cause of SIADH.[25]

Hormonal changes both excess and deficiency lead to hyponatremia. Changes such as adrenal insufficiency, hypothyroidism, decreased mineralocorticoids. Decreased cardiac output and GFR, increased AVP secretion in response to hemodynamic stimuli are the mechanism involved in hypothyroidism which leads to hyponatremia[4]. Renal failure if the kidney is not able to excrete the dietary water load or absence of AVP are the causes which finally leads to hyponatremia. Adrenal insufficiency leads to hyponatremia due to decreased mineralocorticoids, but directly or indirectly it is the cortisol deficiency which leads to this condition.[4]

Compulsive increased consumption of water which exceed the excretory capacity of 12liters/day is the cause of hyponatremia which occurs in polydipsia (psychogenic or primary), increased water consumption is because these patients are mostly having psychiatric illness and taking sensation which increases thirst by causing dry mouth. Diuretics are another important cause of hyponatremia. Thiazide diuretics

is almost always the cause of diuretics induced hyponatremia, it leads to $Na^+$ and $K^+$ depletion and retention of water due to AVP. There is limitation in the ability of AVP to cause retention in loop diuretics due to decrease in the tonicity of medullary interstitium and impair maximal urine concentrating capacity.

Beer potomania results in hyponatremia, it occurs in drinkers who consume beer in large volumes and poor intake of diatary protein and electrolyte.

## CLINICAL FEATURES:

Hyponatremia per se does not produce any major symptoms. It produces osmotic water shift and decreased cellular osmolality which leads to various clinical presentation. This leads to increase ICF volume, which causes brain cell swelling or cerebral edema. Magnitude of the fall in plasma $Na^+$ and rapidity of the disease determine the severity of the disease. The symptoms are fond to be neurological. [33]

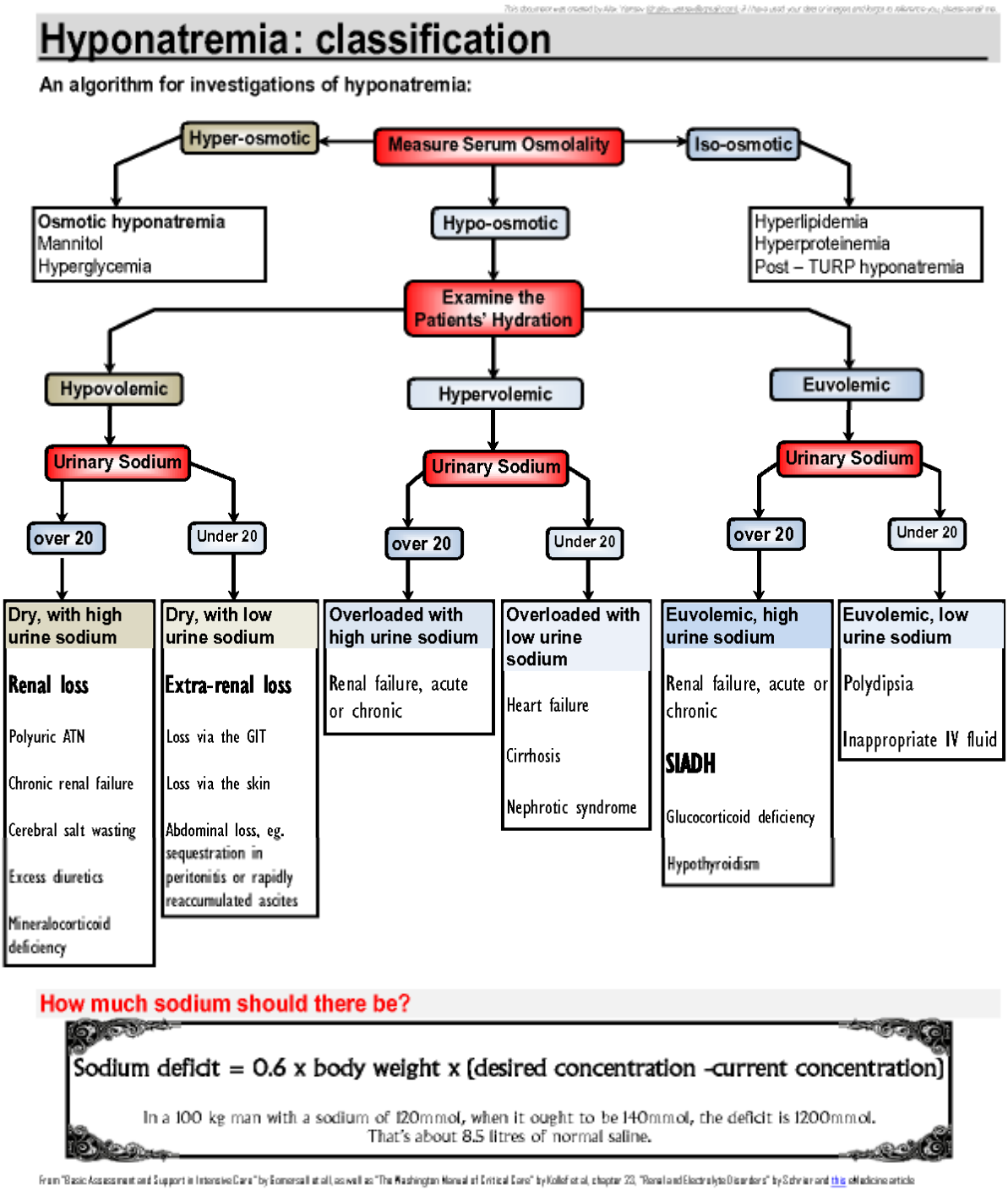
In acute hyponatremia where the symptoms develop within 2 days, nausea and malaise is found when the $Na^+$ concentration is ~125mEq/L. When the concentration falls further below ~120mEq/L there is progression of symptoms to lethargy, headache, obtundation and confusion. When it further fall ~115mEq/L it leads to neurological

symptoms. There is hyponatremic encephalopathy and increased pressure in the skull when the water enters the brain cells. This leads to major symptoms such as nausea, headache, confusion, vomiting, seizures, respiratory arrest, brain stem compression and non cardiogenic fluid accumulation in the lung.

In chronic hyponatremia where the symptoms develop after 3 days, there is adaptive mechanism that tend to minimize the rise in ICF volume and symptoms by defend cell volume.

Development of symptoms depends upon the drop on blood salt level. Because of neuronal adaptation the patients may tolerate if the drop is gradual even to a very low level.

# DIAGNOSIS:


Hyponatremia: classification
An algorithm for investigations of hyponatremia:
Measure Serum Osmolality
Hyper-osmotic
Iso-osmotic
Osmotic hyponatremia
Mannitol
Hyperglycemia
Hypo-osmotic
Hyperlipidemia
Hyperproteinemia
Post – TURP hyponatremia
Examine the Patients' Hydration
Hypovolemic
Hypervolemic
Euvolemic
Urinary Sodium
Urinary Sodium
Urinary Sodium
over 20
Under 20
over 20
Under 20
over 20
Under 20
Dry, with high urine sodium
Renal loss
Polyuric ATN
Chronic renal failure
Cerebral salt wasting
Excess diuretics
Mineralocorticoid deficiency
Dry, with low urine sodium
Extra-renal loss
Loss via the GIT
Loss via the skin
Abdominal loss, eg. sequestration in peritonitis or rapidly reaccumulated ascites
Overloaded with high urine sodium
Renal failure, acute or chronic
Overloaded with low urine sodium
Heart failure
Cirrhosis
Nephrotic syndrome
Euvolemic, high urine sodium
Renal failure, acute or chronic
SIADH
Glucocorticoid deficiency
Hypothyroidism
Euvolemic, low urine sodium
Polydipsia
Inappropriate IV fluid
How much sodium should there be?
Sodium deficit = 0.6 x body weight x (desired concentration -current concentration)
In a 100 kg man with a sodium of 120mmol, when it ought to be 140mmol, the deficit is 1200mmol.
That's about 8.5 litres of normal saline.

- To determine the cause of hyponatremia, accurate history and proper physical examination is required. ECF volume status and effective circulatory arterial volume must also be assessed along with it.

- *Differential diagnosis:* congestive heart failure, cirrhosis of liver and nephritic syndrome presents with expanded interstitial space and reduced circulatory volume. In hypothyroidism and adrenal insufficiency present with normal ECF volume and reduced circulatory volume. Euvolemic with SIADH. [21]

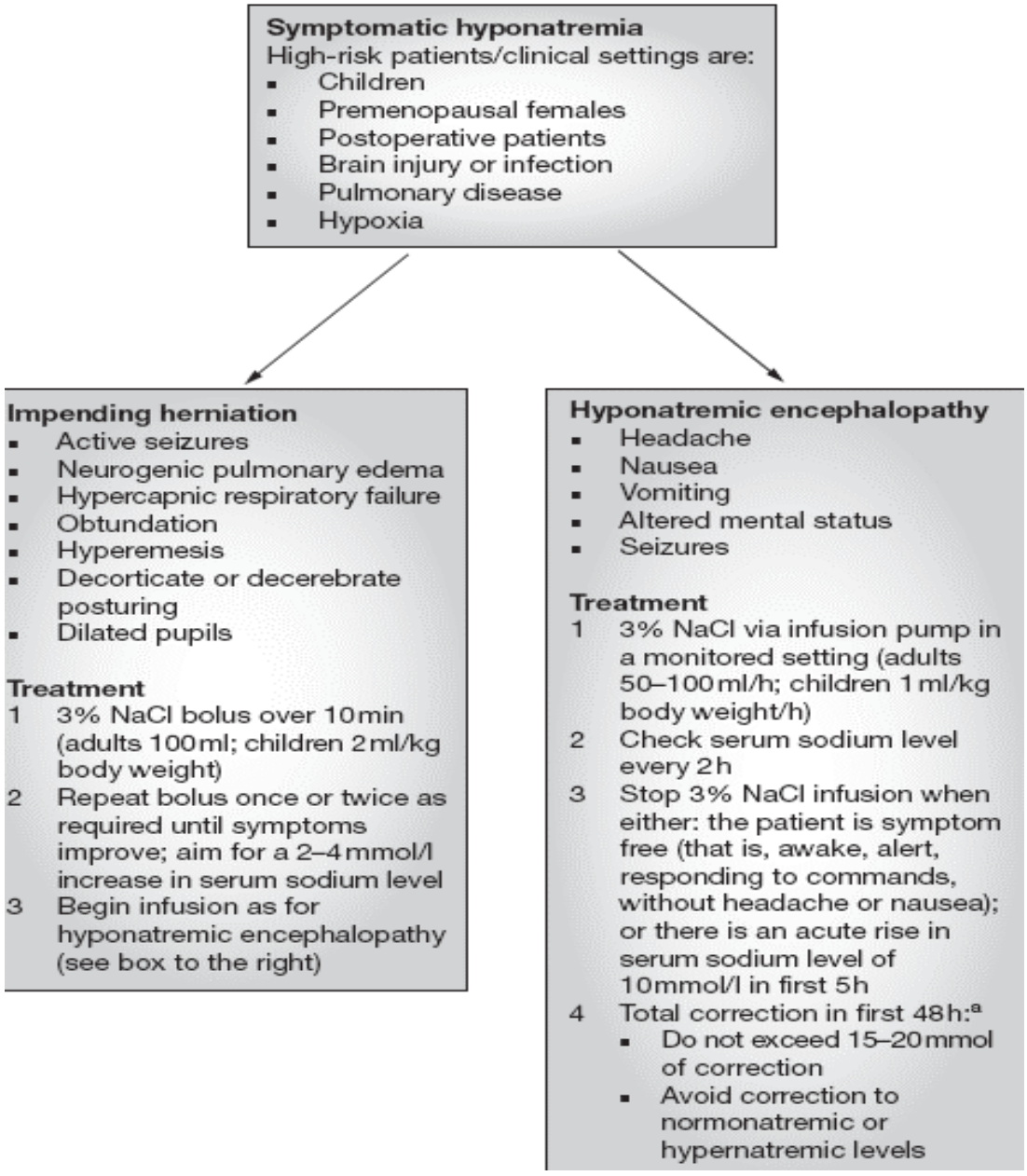
- Differential diagnosis can be narrowed by laboratory analyses such as (i) plasma osmolality, (ii) urine osmolality, (iii) urine $Na^+$

- *Plasma osmolality:* plasma osmolality of <275mOsm/l is found in most of the patients with hyponatremia. If the osmolality is around 275-290mOsmo/l pseudohyponatremia and if it is >290mOsmo/l hyperosmolar hyponatremia can be ruled out.

- *Urine osmolality:* excretion of large volume of dilute urine is the response to hyponatremia , it is around <100mOsmo/l and specific gravity around <1.003. This occurs in primary polydipsia, beer potomania, post -TURP. Impaired free water excretion is suggested if the urine sample is not dilute and it is due to appropriate or inappropriate secretion of ADH.[21]

- *Urine sodium:* it is used in differentiating between extrarenal and renal lose of sodium and to assess effective circulatory volume. There is increased sodium reabsorption in response to decreased circulatory volume, such that the $Na^+$ in urine is <10mEq/l. if urine sodium is >20mEq/l it is due to salt wasting nephropathyincluding cerebral salt wasting, hypoaldosteronism, recent diuersis or ketonuria. If the urine sodium concentration is >20mEq/l and if the urine osmolality is greater than 100mOsm/l (inappropriate urine concentration), but the patient has normal Na+ balance and normal volume and associated with hypouricemia then it is due to SIADH. But due to increased proximal urate reabsorption there is hyperuricemia in patients with hypovolemia contast to hypouricemia in SIADH.[28]

# TREATMENT


Symptomatic hyponatremia
High-risk patients/clinical settings are:
Children
Premenopausal females
Postoperative patients
Brain injury or infection
Pulmonary disease
Hypoxia
Impending herniation
Active seizures
Neurogenic pulmonary edema
Hypercapnic respiratory failure
Obtundation
Hyperemesis
Decorticate or decerebrate posturing
Dilated pupils
Treatment
1 3% NaCl bolus over 10 min (adults 100 ml; children 2 ml/kg body weight)
2 Repeat bolus once or twice as required until symptoms improve; aim for a 2–4 mmol/l increase in serum sodium level
3 Begin infusion as for hyponatremic encephalopathy (see box to the right)
Hyponatremic encephalopathy
Headache
Nausea
Vomiting
Altered mental status
Seizures
Treatment
1 3% NaCl via infusion pump in a monitored setting (adults 50–100 ml/h; children 1 ml/kg body weight/h)
2 Check serum sodium level every 2 h
3 Stop 3% NaCl infusion when either: the patient is symptom free (that is, awake, alert, responding to commands, without headache or nausea); or there is an acute rise in serum sodium level of 10 mmol/l in first 5 h
4 Total correction in first 48 h:[a]
Do not exceed 15–20 mmol of correction
Avoid correction to normonatremic or hypernatremic levels

**Treatment in symptomatic patients**

- Childrens, post operative patients, brain injury, premenopausal females, pulmonary disease and hypoxia are the patients with high risk in symptomatic hyponatremia.

- In this patients with *impending herniation* presents with seizures, obtundation, hyperemesis, neurogenic pulmonary edema, hypercapnic respiratory failure, dilated pupil and must be treated with 3% sodium chloride bolus over 10 min, until symptoms improve repeat bolus once or twice (2-4mmol/l), then continue treatment as for hyponatremic encephalopathy

- *Hyponatremic encephalopathy* presents with headache, nausea, vomiting, altered mental status and seizure, this must be treated in a monitored setting with 3% sodium chloride, for every 2 hours serum sodium must be checked, when patient is symptom free or when rise in serum sodium is 10mmol/l in first 5hours - 3% sodium chloride can be stopped.

- So in the first 48 hour the correction must not exceed 15-20mmol, correction to hypernatremic or normonatremic level must be avoided

**Treatment in acute and chronic hyponatremic patients**

- The rate of correction, the intervention required, and the underlying disorders are the factors which determine the treatment of hyponatremia. The rate of correction depends on the acuity of development of disease and the neurological symptoms present.

- The correction of hyponatremia requires addition of sodium or removal of water or both and also correction of the underlying disorder.

- *Asymptomatic hyponatremia:* in mild asymptomatic patients generally no treatment is required. In general isotonic saline is used for $Na^+$ repletion, when hyponatremia is associated with ECF volume contraction. There is normalization of sodium due to reduction in renal water retention if euvolemic state is restored.

- *Chronic asymptomatic hyponatremia:* it is found to be asymptomatic for more than 3 months[6]. Usually no treatment is required due to risk of treatment induced toxicity is very high in this case, because cells get adapted to hypoosmolar state, so sudden normalization leads to increase in volume over load. The rate of correction in this type of patients is 6-8mEq/l over 24hours

duration. If the underlying cause in this case is life threatening the correction can be done as in acute symptomatic hyponatremia.

- *Asymptomatic hypovolemic hyponatremia:* isotonic saline is used to restore the intravascular volume. If the duration is not known 1L of 0.9% of normal saline can be given over 24 hours. Renal water retention is reduced and sodium level becomes normal if hypovolemic is brought to euvolemic state.

- *Asymptomatic hypervolemic hyponatremia:* most common causes are congestive cardiac failure and cirrhosis of liver. As effective circulatory blood volume is decreased in this case, administration of fluid lead to worsening of volume overload state due to increased interstitial fluid.

- The definitive treatment is to treat the underlying condition with supportive measures such as

    - ✓ Fluid restriction must be done which must be less than the daily urine output

    - ✓ Loop diuretics given to increase the water excretion by diuresis.

- ✓ Vasopressin antagonists such as coivaptan and tolvaptan also promotes dieresis

- ✓ High dietary solute intake like high salt diet, high protein diet or oral urea increases water excretion and normalization of hyponatremia.

- The amount of fluid restriction necessary depends upon extent of elimination of water. Formula used usually is

(Urine $Na^+$ + urine $K^+$) / Serum $Na^+$ → if value <0.5, 1L fluid can be given, if value is 0.5-1.0, 500ml/day can be given, if value >1 the fluid given gets retained so in this patients high dietary solute and medications like diuretics and vasopressin antagonist must be considered.

- *Symptomatic hyponatremia:* can be divided into acute and chronic symptomatic hyponatremia.[22]

- *Acute symptomatic hyponatremia*: this usually presents with neurological dysfunction like cramps, weakness, fatigue, mental confusion, disorientation, coma and convulsion. In this rapid correction should be avoided, the rate of correction must not be more than 0.6mEq/L/hour.

- The most important complication of rapid correction are

    - ✓ Volume overload
    - ✓ Shrinkage of brain – it occurs when there is loss of organic acids leading to normalization of brain volume.
    - ✓ Central pontine myelinolysis- quadriplegia, dysarthria, dysphagia with altered level of consciousness are the major manifestation found in this. It occurs due to rapid osmotic shift leading to neuronal damage. MRI is the investigation of choice. Patient with hypokalemia, malnutrition and alcoholism are more prone to develop CPM. In these cases rapid correction must be done 1-2mEq/l/hr for first 3-5 hours followed by 0.5mEq/l/hr for next 24hours.[22]

- *Chronic symptomatic hyponatremia:* in this case rate of correction must be around 6-8mEq/l over 24hour period.

- *Modalities of treatment:* addition of sodium or removal of excessive water must be done. Removal of excessive water load is required in most of the cases of hyponatremia because excessive water is the cause of hyponatremia. Hypertonic normal saline and loop diuretics are given in this case to remove excessive water and salt, in this

hypertonic saline leads to addition of salt. Loop diuretics administration does not alter the amount of sodium as there is excretion of isotonic urine occurs, so amount of sodium administered can determine the increase in amount of sodium in the serum.

- Restriction of fluid is done if slow correction is requires in volume expanded subjects. Loop diuretics and increase sodium and potassium intake is advised if above is not possible.

- The formula for rate of correction is

$$Na^+ = [\ Na^+_i + K^+_i - Na^+_s] / [TBW+1]$$

Total body water can be calculated by lean body weight in kg×0.6 for men and 0.5 for women. It does not estimate the ongoing water or solute loss, it is only a rough guide.[23]

- *Hypertonic saline:*

  - ✓ It is the main stay treatment for all type of hyponatremia includes acute and chronic symptomatic hyponatremia

  - ✓ The usual indications are seizures, altered mental status, coma, muscle weakness and fatigue.

  - ✓ 3% normal saline is commonly used, if not available 0.45% normal saline can be used.

- ✓ Rate of correction for acute cases is 1-2mEq/l/hr. If 1.2ml/kg hypertonic saline will increases the serum sodium by around 1mEq/l. $2^{nd}$, $3^{rd}$ and $6^{th}$ hourly sodium level must be monitored.

- *Vasopressin receptor antagonist* like conivaptan, tolvaptan can be used in the case of SIADH.

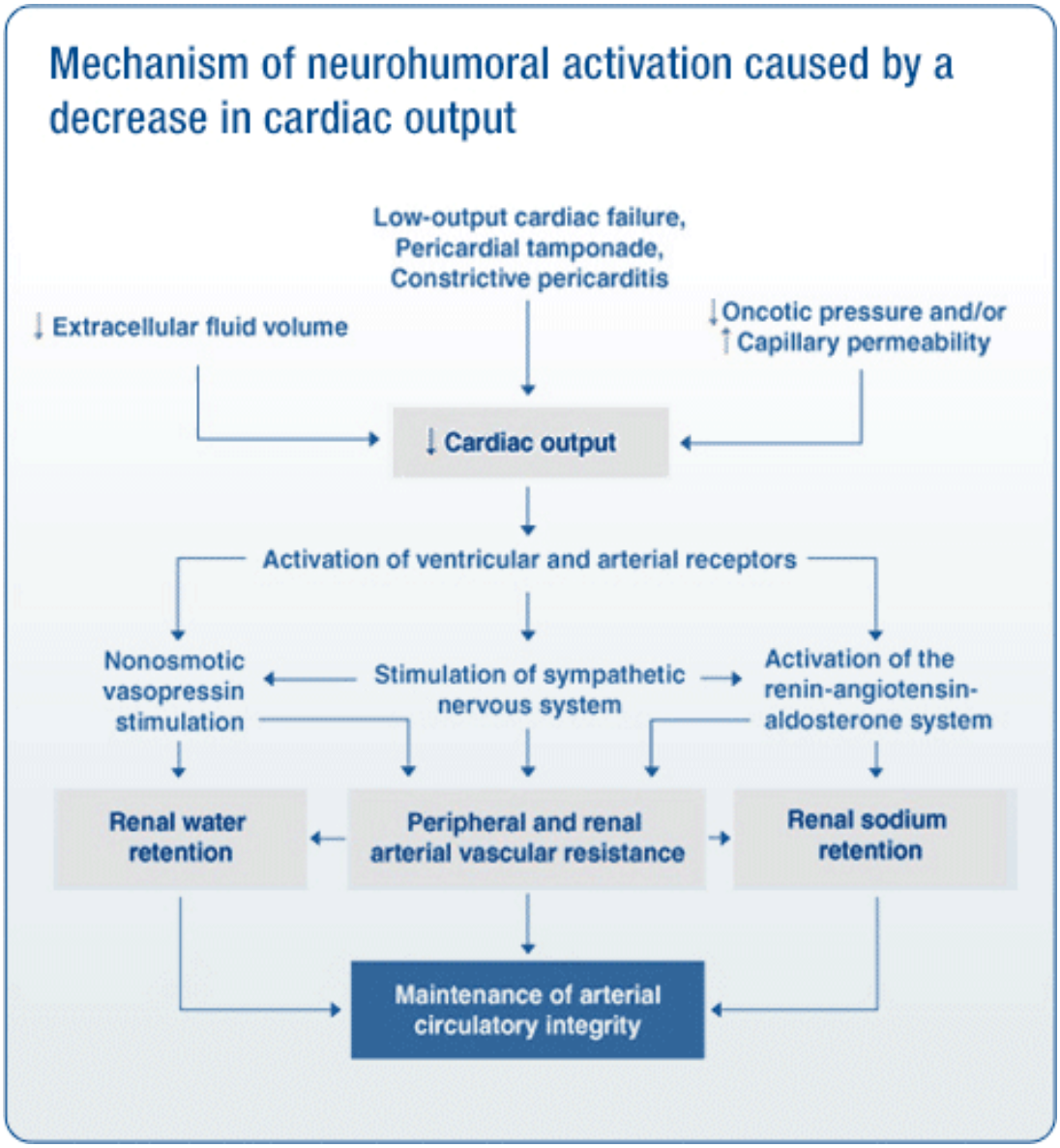
- Lithium and Demeclocyclin can be given if unresponsive to other medications. It is not commonly used due to its side effect.

# NEUROHUMORAL ACTIVATION FOLLOWING ACUTE MYOCARDIAL INFARCTION

Acute myocardial infarction is followed by several systemic metabolic changes in human. Plasma insulin level fall initially which return back to normal values, the plasma concentration of catecholamines[30], cortisol, glucose, glycerol and cyclic adenosine phosphate increases following MI.[35] According to the study done by Hilton P and Flear CT, there is confirmed evidence that hyponatremia, hypochloremia and uremia is present with patients with myocardial infarction and the degree of infarction is related well with these indices. If the sodium level is less than 130mEq/l in patients admitted in coronary care unit, the mortality is found to be higher.[8][35]

Due to the sudden development of left ventricular dysfunction; or due to pain, nausea and stress; or due to analgesic and diuretics administration in acute myocardial damage there is nonosmotic release of vasopressin. This is the most common cause of hyponatremia in adults. In this case serum osmolality does not correlate with level of vasopressin, even though other neurohormones such as rennin or nor epinephrine rises along with vasopressin, this proves the importance of nonosmotic mechanism involvement.[27] Arterial underfilling due to carotid baroreceptors in addition with increased messenger RNA expression in

the hypothalamus are involved in the nonosmotic release of vasopressin. The vasopressin regulated water is up regulated in the collecting duct in heart failure due to the renal effect of vasopressin.[26]




Renin-angiotensin system is activated and catecholamine production is increased in myocardial infarction which may further aggravate hyponatremia. [30,31]There is reduction in renal water excretion

due to the above factors which decreases the glomerular filtration rate and there is delivery of tubular fluid to the diluting segment of nephron.[5]

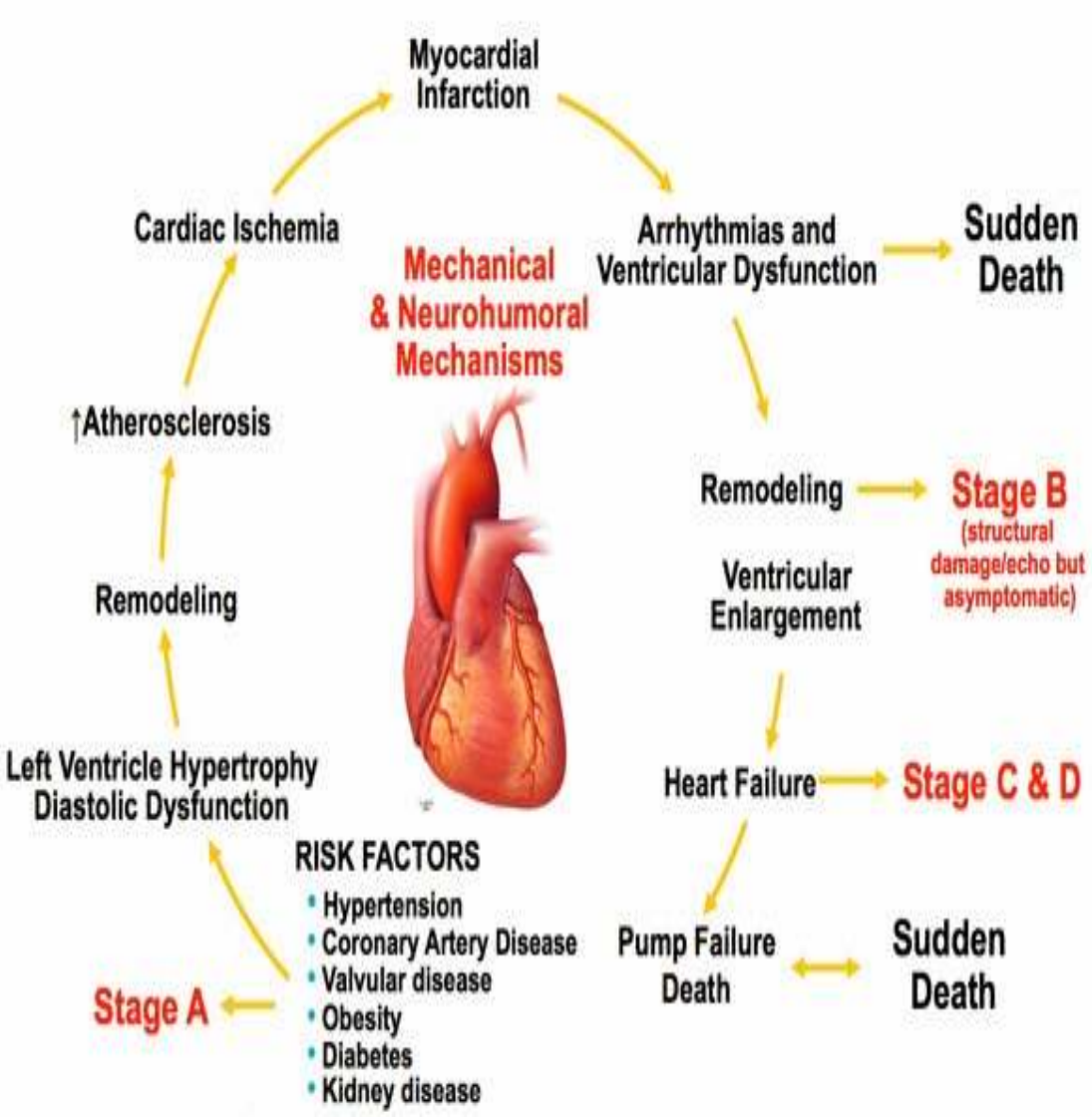
From a study done by Szatalowicz VL, Schrier RW, Arnold PE, Chaimotivz C, Bichet D, Berl T found that the patients with congestive cardiac failure, there were detectable arginine vasopressin levels in 40-45 patients and for the development of hyponatremia vasopressin is essential. In patients with congestive cardiac failure the severity of hyponatremia is directly proportional to the degree of neurohumoral activation. [24]

Another study conducted in around 530 patients by Rouleau JL, the independent sign of poor prognosis in post infracted patient at the time of hospital discharge can be found by neurohumoral activation. [8]

From a study conducted in around 56 patients with acute myocardial infarction by Sigurdsson A, Held P, Swedberg K found that mainly in clinical heart failure patients there is sustained neurohumoral activation after myocardial infarction and even in patients without clinical heart failure it is related to the magnitude of myocardial damage.

From a study in around 970 patients by Goldberg A, Hammerman found that, during acute phase of myocardial infarction a very simple

marker of neurohumoral activation is hyponatremia and the long term development of heart failure and death can be predicted from this.[36]



The above picture explains the mechanism of neurohumoral activation involved in myocardial infarction similar to hyponatremia. In this there is ventricular remodeling due to various risk factors leading to atherosclerosis causing myocardial infarction, which causes sudden death due to arrhythmias and ventricular dysfunction, if there is remodeling it leads to further ventricular enlargement leading to heart failure and sudden death due to pump failure. [7]

# MATERIALS AND METHOD

## SOURCE OF DATA:

From June 2013 to June 2014, around 100 patients who presented with acute ST-elevation MI admitted in ICCU of Coimbatore Medical College Hospital, Coimbatore were studied.

Studies conducted at Department of Cardiology Rambam Medical Center by Antony Goldberg, Haim Hammerman, Sirouch Petcherski, Alexander Zdorovyak, Sergey Yalonetsky, Michael Kapeliovich, Yoram Agmon, Walter Markiewicz, Doron Aronson and Rappaport Medical School by Haim Hammermam , Walter Markiewicz, Haifa, Israel proved that in ST- elevation myocardial infarction the incidence rate of hyponatremia was found as around 32% . i.e., 447 patients developed hyponatremia among 1047 cases.

The sample size (n) can be calculated by the incidence rate 32% and the allowable error 30% by the formula----> $n=4pq/L^2$,

Where, p---> incidence rate

q---> 1-p

L---> allowable error

## METHOD OF COLLECTION OF DATA

100 consecutive patients who presented with ST elevation MI were selected and they underwent detailed history and clinical examination.

## INCLUSION CRITERIA

All patients with myocardial infarction having following criteria were selected

- More than 20minutes of chest pain
- ECG alteration consisting of new pathological Q waves or ST segment and T wave changes which are diagnostic of MI in ECG
- Elevation of cardiac enzymes such as creatinine kinase (CK-MB) or cardiac troponin T and I levels.

## EXCLUSION CRITERIA

Acute coronary syndrome without ST elevation in ECG must be excluded. Patients who received thrombolytic therapy (tissue type plasminogen activators or streptokinase).Selected patients underwent detailed history and clinical examination. Their Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours after that.

## END OF THE STUDY

Following myocardial infarction the end point was to find all the cause of mortality within 30 days. Within 30 days of discharge of the patients the mortality data were collected from the patients or from their family though post card received, when there was no response telephone or direct visit was done to collect the data of the patients.

Ion selective electrode auto analyzer was used to determine plasma sodium concentration.

## STATISTICAL METHOD

- Odd ratio
- Mean standard deviation
- Confidence interval
- To find the association between 30dys mortality and hyponatremia, logistic regression tests such as univariate ad multivariate were done
- Parametric and non parametric test which was suitable (for non continuous variable Chi square test, for continuous variable Analysis of variance, Z test, etc).

## OBSERVATIONS AND RESULTS

**AGE DISTRIBUTION:**

**TABLE SHOWING AGE DISTRIBUTION OF CASES**

**Table no 1**

| Age group Yrs | Frequency cases |
|---|---|
| 21-30 | 1 |
| 31-40 | 7 |
| 41-50 | 18 |
| 51-60 | 35 |
| 61-70 | 27 |
| 71-80 | 8 |
| 81-90 | 4 |

The youngest age group is - 30 years

The eldest age group is - 85 years

35% of cases were in the age group of 51-60 years which accounts for the maximum number of patients and 27% of cases were found in the age group of 61-70 years which accounts for the next highest number of patients.

SEX DISTRIBUTION:

TABLE SHOWING SEX DISTRIBUTION

Table no 2

| Patients | Cases |
|---|---|
| Males | 80 |
| Females | 20 |
| Total | 100 |

Ratio of Male:Female were found as 4:1 in this study

80% were males, 20% were females among 100 patients studied

## Table no-3

## Table showing baseline characteristic of cases

| Characteristics | Normal sodium level(n=71) | Hyponatremia on Admission (n=11) | Hyponatremia within 72 hrs (n=18) | P value |
|---|---|---|---|---|
| | MEAN ±SD, NUMBER (%) OR MEDIAN | | | |
| AGE(YRS) | 57.8±11.7 | 64.9±13.1 | 56.61±11.54 | F=1.97<br>P=0.145 |
| MALE SEX | 57(71) | 9(81) | 14(77) | $\chi^2$=0.082<br>p=0.962 |
| DIABETES | 9(12.6) | 3(27.5) | 8(44.45) | $\chi^2$=9.466<br>p=0.009 |
| SMOKING | 50(70) | 9(81) | 11(61) | $\chi^2$=4.938<br>p=0.0085 |
| HYPERTENSION | 14(5.6) | 2(18.18) | 4(22.22) | $\chi^2$=0.082<br>p=0.960 |
| ANTERIOR INFARCTION | 45(63) | 8(72) | 15(83) | $\chi^2$=2.754<br>p=0.252 |
| KILLIP CLASS | 1.06±0.23 | 1.18±0.40 | 1.06±0.24 | F=1.18<br>p=0.312 |
| EJECTION FRACTION (%) | 44.63±11.19 | 40.36±6.14 | 50.11±13.26 | F=2.86<br>p=0.06 |

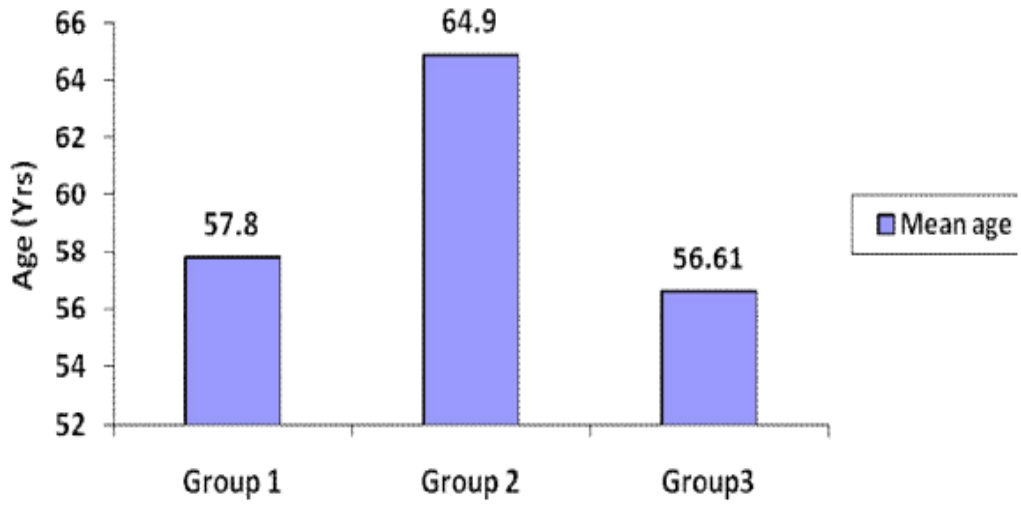
Hyponatremia on admission was present in patients with older age group than patients who presented with normal sodium level.

81% of male patients presented with hyponatremia hyponatremia at the time of admission and 77% of patients who developed hyponatremia after 72hours of admission.

Compared with patients with normal sodium level, patients who were smokers around 81%, who had anterior infarction around 83%, who were diabetic around 44.45%,who were hypertensive around 22.22%, who had lower ejection fraction around 50.11 ±13.26% of patients and who were killip class accounted around 1.06±0.24 were found to present with hyponatremia at the time of admission or 72hrs after admission.

# Graph-1

## Mean age in various groups



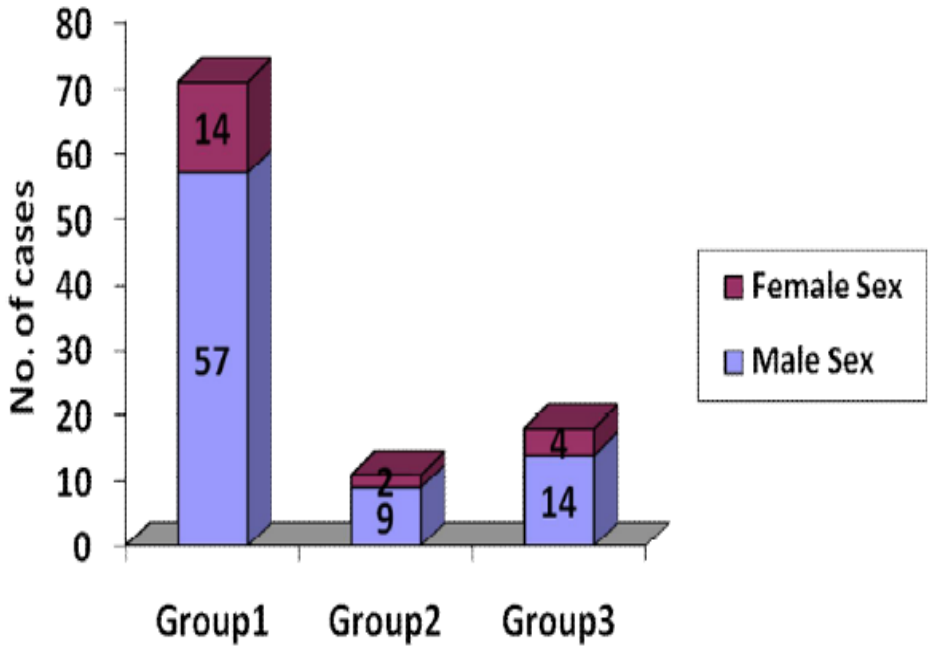

In Group 1 = Patients with normal serum sodium level (57.8years)

In Group 2 = Hyponatremia at the time of admission (64.9 years)

In Group 3 = Hyponatremia with in 72 hours of admission (56.61years)

## Graph-2

### Sexwise distribution



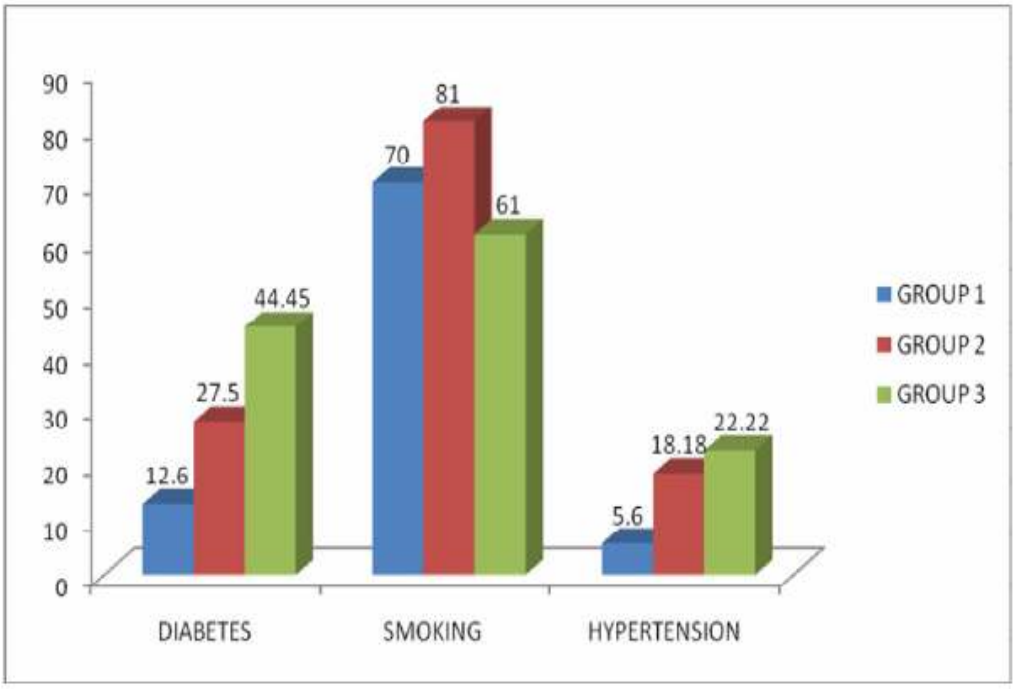

Group 1 = Patients with normal serum sodium level (60-70 cases)

Group 2 = Hyponatremia at the time of admission (10-15 cases)

Group 3 = Hyponatremia within 72 hours of admission ( around 20 cases)

# Graph-3

## Risk factor in various groups



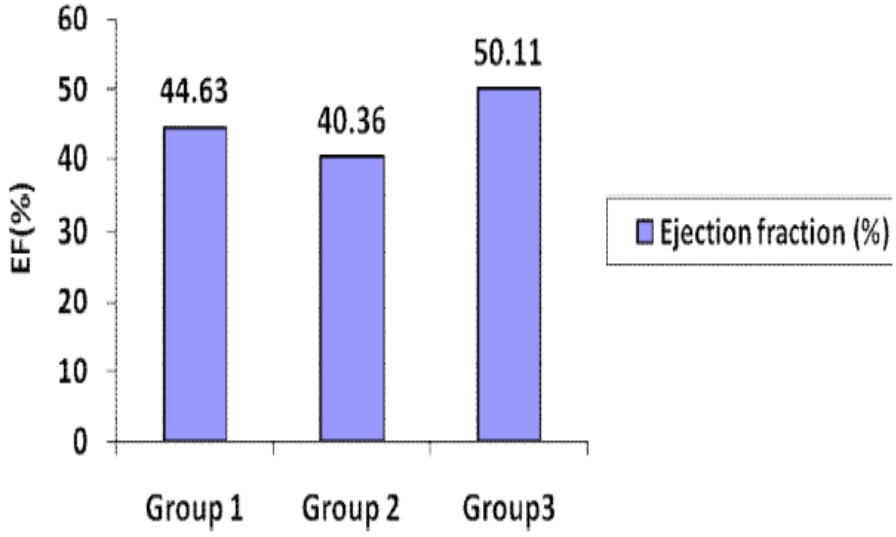

Group 1 = Patients with normal serum sodium level (DM – 12.6, smoking -70, HTN – 5.6)

Group 2 = Hyponatremia at the time of admission (DM –27.5, smoking - 81, HTN – 18.18)

Group 3 = Hyponatremia within 72 hours of admission (DM – 44.45, smoking -61 HTN -22.22)

# Graph -4

## Ejection fraction (%) in various groups




Group 1 = Patients with normal serum sodium level (EF =44.6%)

Group 2 = Hyponatremia at the time of admission (EF=40.36%)

Group 3 = Hyponatremia within 72 hours of admission (EF=50.11%)

## Hyponatremia on admission and at 72 hours and its outcome in terms of mortality

Table no 4

| | Normal sodium levels | Hyponatremia on admission | Hyponatremia within 72 hours | Total |
|---|---|---|---|---|
| No. of patients | 71 | 11 | 18 | 100 |
| Mortality in each group at the end of 30 days | 2 | 3 | 3 | 8 |

Among 100 patients admitted with MI the mortality was found to be 8%

-71 Patients were found to have normal serum sodium level 2 patients died within 30 days of admission

-11 patients were found to have hyponatremia at the time of admission, 3 patients died within 30days of admission

-18 patients were found to develop hyponaremia within 72 hours of admission, 3 patients died within 30days of admission

## Table showing severity of the hyponatremia and its outcome in terms of mortality

**Table no 5**

| Range of Sodium levels in hyponatremia patients | No. of patients | Mortality |
|---|---|---|
| <130 | 3 | 3(100%) |
| 131-134 | 26 | 3(11.11%) |

With serum sodium level of <130mg/dl- the mortality was 100%

With serum sodium level between 131-134mg/dl- the mortlity was 11.11%

# Odd's ratio for 30 days mortality

Table no 6

| | Survivors | Non survivors | Odds ratio | P value |
|---|---|---|---|---|
| Group1 | 69 | 2 | | |
| Group2 | 8 | 3 | 5.03 | 0.01 |
| Group3 | 15 | 3 | 6.9 | 0.02 |

Group 1 = Patients with normal serum sodium level

Group 2 = Hyponatremia at the time of admission

Group 3 = Hyponatremia within 72 hours of admission

When group 1 was compared with other groups, the 30 days mortality Odd's ratio was found to be more in groups with hyponatremia,(Odd's ratio for Group 2=5.03 and Group 3=6.9)

**Survivors and non survivors were also compared for various factors**

**Table no 7**

| | Survivors | Nonsurvivors | T or $\chi^2$ | P value |
|---|---|---|---|---|
| n | 92 | 8 | | |
| Age(yrs) (mean ±SD) | 57.7 ±12.1 | 65.5 ±7.58 | 2.63 | 0.025 |
| Sex M<br>F | 76(82%)<br>16(18%) | 4(50%)<br>4(50%) | 4.89 | 0.027 |
| Hyponatremia (mean±SD) | 136.96 ±1.92 | 134.09±3.53 | 2.27 | 0.057 |
| Smoking | 66(72%) | 4(50%) | 1.65 | 0.198 |
| Diabetes | 16(17%) | 4(50%) | 4.891 | 0.027 |
| Hypertension | 16(17%) | 4(50%) | 4.891 | 0.027 |
| Infarct site<br>Anterior<br>Inferior | <br>63(68%)<br>29(32%) | <br>5(63%)<br>3(37%) | <br>0.002 | <br>>0.05 |
| Killip class I<br>II | 88(95%)<br>4(5%) | 5(63%)<br>3(37%) | 12.426 | 0.001 |
| EF(%) (mean±SD) | 47.7±12.7 | 38.6±10.9 | 2.24 | 0.05 |

Mortality of the patients were significant by statistics by serum sodium level. In patients who survived mean sodium level was found to be 136.96±1.92 and in patients who did not survive the mean sodium was 134.09±3.53.

Other significant factors which determined mortality were age, sex, smoking, diabetes, hypertension,Killip class.

Including variables that had p value of <0.2 in univariate analysis , logistic regression analysis which is a multivariate analysis was performed to identify the factors which were independently associated with 30 days mortality,

**Table No 8**

| Variables | P value |
|---|---|
| Age | 0.025 |
| Sex | 0.027 |
| Smoking | 0.198 |
| Hypertension | 0.027 |
| Daibetes | 0.027 |
| Killip class | 0.001 |
| Hyponatremia | 0.057 |
| Ejection fraction | 0.050 |

Hyponatremia was a important significant risk factor associated with 30 days mortality along with other factors in multivariate analysis, Which is clear from the above table.

# DISCUSSION

From our study we found that the high risk people are patients who presented with hyponatremia at the time of admission or developed hyponatremia shortly after the admission of patients with acute myocardial infarction.

Acute ST elevation myocardial infracted patients who presented in our hospital were found to be hyponatremic at the time of admission or after admission in a substantial proportion of patients in our study. At the time of admission around 11% of patients (11 patients) were hyponatremic and first 72 hours of admission around 18% of patients (18 patients) developed hyponatremia in our study.

Antony Goldberg conducted a similar study and found similar findings, he observed that at the time of admission 12.5%of patients (131 patients) were hyponatremic and 72 hours of admission around 19.9% of patients (208 patients) developed hyponatremia.

Goldberg in his study also found that diabetes, anterior infarction, Killip class and patients with lower ejection fraction where found in most of the patients who developed myocardial infarction and presented with hyponatremia.

We also observed that mortality was found to be increased in patients with hyponatremia in our study. Within 30 days of admission there were total of deaths were 8% (8 patients). In this 2.8% (2/71)of patients presented without hyponatremia, 27.5% (3/11) of patients who presented with hyponatremia at the time of admission and 16.67% (3/18) of patients who developed hyponaremia within 72 hours of admission.

Similarly Goldberg in his study observed that mortality was found to be increased in patients with hyponatremia. Within 30 days of admission there were total of 105 deaths (10%). In this 6.2% (44/708) of patients presented without hyponatremia, 19.8% (26/131) of patients died presented with hyponatremia at the time of admission and 16.8% (35/208) of patients developed hyponaremia within 72 hours of admission.

In our study there was higher mortality in patients who presented with hyponatremia when compared to the above study of Goldberg et al, and the mortality rate were almost equal in patients who developed hyponatremia shortly after admission.

Concordance with the finding of Goldberg the 30days mortality Odd's ratio was high around 5.03 and 6.9 in both patients who presented with hyponatremia at the time of admission and with patients who developed hyponatremia within 72hours of admission in our study.

Goldberg in his study showed that an independent risk factor for 30 days mortality was hyponatremia, which is concordance with our study which showed that significant risk factor determining mortality is hyponatremia, when we compared the outcome among survivors and non survivors, it was found that apart from sex, age, hypertension, diabetes, ejection fraction, killip class of admission; hyponatremia was significant among them. In the multivariate logistic regression analysis, all the variables associated with mortality in survivors and non survivors were included. In this analysis the independent predictor which was significant for mortality was hyponatremia.

Concordance to our study Goldberg et al aso showed that when the hyponatremia is severe mortality is high. In our study, when we divided

patients into two groups depending on the level of sodium. 100% mortality was found in patients with sodium level <130mEq/l and 12% in patients with sodium level around 131-134mEq/l. so it is clear that there is mortality tend to increase with severity of hyponatremia.

Flear CT conducted a similar study in patients with acute myocardial infarction in coronary care unit and absorbed that when plasma sodium was <130mEq/l the mortality was found to be highe

The different prognostic factors of myocardial infarction such as severity of left ventricular function, hemodynamic alteration and the extent of neurohumoral activation was to incorporate by the development of hyponatremia. Goldberg concluded that development of hyponatremia is a marker which associate the above prognostic entities.

The independent predictor of 30 days mortality were hyponatremia at the time of admission or development of hyponatremia within 72 hours of admission, was concluded from our study.

# SUMMARY

The important predictor of cardiovascular mortality in heart failure patients was hyponatremia in most of the patients. As the neurohormnal activation that accompanied were similar in both myocardial infarction and hyponatremia. So, in the setting of acute ST elevation MI and in predicting the usefulness in short term survival, the prognostic importance of hyponatremia was investigated.

From our study it was clear that hyponatremia was present in substantial proportion of patients at the time of admission and developed hyponatremia within 72 hours of admission. When we compared with normal groups the Odd's ratio for 30days mortality was found to be very high in patients who were hyponatremic.

There were also findings which suggested there were linear relationship between hyponatremia and mortality. Among several variables in survivors and non survivors the significant risk factors of mortality was found to be hyponatremia in univariate analysis. Killip class on admission, age, sex, diabetes, hypertension, low ejection fraction were other factors which play significant role in mortality.[34]

Multivate analysis by logistic regression analysis was performed and identified hypontremia as independent predictor of mortality.

# CONCLUSION

From our study we concluded that in patients with ST elevation myocardial infarction patients who presented with hyponatremia at the time of admission and within 72 hours of admission had high mortality and so hyponatremia is a independent predictor of mortality. Patient at risk can be identified by a simple marker plasma sodium level.

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# PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION

## PROFORMA

NAME: IP. NO:

AGE: DOA:

SEX: DOD:

OCCUPATION:

RELIGION:

MARITAL STATUS:

ADDRESS:

TELEPHONE NO:

STATUS AT DISCHARGE:

**PRESENTING COMPLAINTS:**

**I. HISTORY OF PRESENTING ILLNESS:**

**A. CHEST PAIN:**

- Site: Precordial/ Restrosternal Epigastric/ Shoulder/ Neck
- Time of onset:
- Nature: Squeezing/ Crushing/ Compressive/ Tightness
- Radiation: Arm/ Back/ Epigastric/ Neck
- Frequency:
- Severity
- Aggravating Factor:
- Relieving Factor:
- Associated sweating:

**B. BREATHLESSNESS:**

- Onset: Sudden/ Gradual
- Grade: I/II/III/IV
- H/O Orthopnea: Yes/ No

- Wheeze: Present/ Absent
- H/O PND: Yes/No

Associated symptoms

**C. COUGH**

- Onset: acute insidious
- Productive/ Non Productive
- Sputum: Quantity
- Quality
- Colour
- Postural Variation
- Haemoptysis: Yes/ NO

**D. PALPATION**

- Onset: Acute/ Insidious
- Duration
- Nature: intermittent/ continuous
- Aggravating Factors: Exertion/ Excitement
- Relieving Factors

**E. PRESYNCOPE/ SYNCOPE**

- Related to exertion : Yes
- Postural relation : Erect Supine
- Frequency : Isolated Frequent
- Loss of consciousness : Yes No
- Others :

**F. SWELLING OF LEGS/ FACE**

- Onset: Acute/ Insidious
- Duration:
- Associated with pain: yes/ No
- Diurnal Variation: Yes /No

**G. NAUSEA /VOMITING**

H. MISCELLANEOUS Present Absent

- General weakness/ Fatigue
- Altered sensorium
- Oliguria

- Convulsion
- Others

## II. PAST HISTORY

- Past history : Present/Absent
- Duration
- Treatment
- IHD –Angina
- Infarction
- Hypertension
- Diabetes
- Rheumatic
- Syphilis
- Vascular heart disease
- TIA/ Stroke
- Any other

## III. PERSONAL HISTORY

1. Diet Vegetarian Mixed

2. Sleep Sound Disturbed

3. Appetite Good Decreased

4. Bladder Normal Polyuria/ Anuria/Dysuria

5. Bowel Normal Constipated /Loose stools

6. Menstrual history Normal /Irregular

Postmenopausal

7. Habits

a) Smoking : Duration

b) Alcohol : Duration

Type

Quantity

c) Tobacco Chewing: Duration

Quantity

d) History of exposure to STD: Present/ Absent

## IV. GENERAL PHYSICAL EXAMINATION

| | | |
|---|---|---|
| 1) Built | Well/Moderate | Poor |
| 2) Nourishment | Obese/Average | Poor |
| 3) Emotional state | Calm/Anxious | Restless |
| 4) Pallor | Present/ Absent | |
| 5) Cyanosis | Present/ Absent | |
| 6) Icterus | Present/ Absent | |
| 7) Clubbing | Present/ Absent | |
| 8) Pedal oedema | Present/ Absent | |
| 9) Lymphadenopathy | Present/ Absent | |
| 10) Extremities | Warm/ Cold | |

## V. VITAL SIGNS

-Pulse

-Blood pressure

-Respiratory rate

-Temperature

## VI. SYSTEMIC EXAMINATION

CVS EXAMINATION

1) Pulse

-Rate

-Rhythm

-Volume

-Character

-Condition of Vessel Wall

-Radio Femoral Delay

2) JVP –Normal /Raised

### A. INSPECTION

| | |
|---|---|
| Precordium | Normal/Bulged |
| Apical impulse | Visible / Non Visible |
| Other pulsation | |

**B. PALPATION**

| | |
|---|---|
| Apical impulse | Location, Character |
| Palpable | Heart Sounds |
| Thrills | Apex |
| | Parasternal area |
| Any other | |

**C. PERCUSSION**

Cardiomegaly

Pericardial effusion

**D. AUSCULTATION**

Heart sounds

S3/S4 Present/ Absent

Murmur

Timing/Location/Character/Radiation/Grade

Pericardial rub

Basal crepitations

Others

KILLIP CLASS:

RESPIRATORY SYSTEM:

PER ABDOMEN:

CENTRAL NERVOUS SYSTEM

# INVESTIGATIONS

## I. BLOOD

| | |
|---|---|
| HAEMOGLOBIN | gm/dl |
| TC<br><br>DC | Cells/$mm^3$ |
| NEUTROPHILS | % |
| LYMPHOCYTES | % |
| EOSINOPHILS | % |
| BASOPHILS | % |
| MONOCYTES | % |
| ESR | % |
| CARDIAC ENZYMES: CPK-MB | IU/L |
| Or TROPONIN T. | IU/L |

**II.URINE**

| | |
|---|---|
| ALBUMIN | |
| SUGAR | |
| MICROSCOPY | |

**III.BIOCHEMISTRY**

| | | |
|---|---|---|
| RBS | | mg/dl |
| SODIUM LEVELS | ON ADMISSION | mEq/L |
| -AFTER 24 HRS | | mEq/L |
| -AFTER 48 HRS | | mEq/L |
| -AFTER 72 HRS | | mEq/L |
| TOTAL CHOLESTEROL | | mg/dl |
| HDL CHOLESTROL | | mg/dl |
| LDL CHOLESTROL | | mg/dl |
| VLDL CHOLESTROL | | mg/dl |
| TRIGLYCERIDE | | mg/dl |

# IV.ELECTROCARDIOGRAPHY

## V.ECHOCARDIOGRAPHY

| | |
|---|---|
| EJECTION FRACTION | |
| CONCLUSIONS | |

## OTHER RELEVANT INVESTIGATIONS

## DIAGNOSIS

IN HOSPITAL COMPLICATIONS

CCF/LVF

Cardiogenic shock

Arrhythmias

Thromboembolism

Pericarditis

Rupture of Interventricular septum

Rupture of papillary muscle

Aneurysm

Any other

FOLLOW UP UPTO 30 DAYS

## KEY TO MASTER CHART

| | | |
|---|---|---|
| M | – | Male |
| F | – | Female |
| Prior IHD | – | Prior history of ischemic heart disease |
| CK-MB | – | Creatine Kinase MB |
| AWMI | – | Anterior wall myocardial infarction |
| ASWMI | – | Anteroseptal wall myocardial infarction |
| ALWMI | – | Anterolateral wall myocardial infarction |
| IWMI | – | Inferior wall myocardial infarction |
| RVMI | – | Right ventricular myocardial infarction |

OUTCOME **positive(+)** - Means Survivors

OUTCOME negative(-) - Means Non Survivors

# MASTER CHART

| SL NO | NAME | AGE | SEX | SMOKING | DIABETES | HYPERTENSION | PRIOR IHD | PRIOR DIURETIC THERAPY | KILLIP CLASS | CKMB | SODIUM ON ADMISSION | SODIUM AT 24 HOURS | SODIUM AT 48 HOURS | SODIUM AT 72 HOURS | EJECTION FRACTION | DIAGNOSIS | OUTCOME |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | SD | 60 | M | YES | NO | NO | NO | NO | 1 | 179 | 136 | 135 | 138 | 141 | 66 | ASWMI | + |
| 2 | SN | 80 | M | NO | NO | NO | NO | NO | 2 | 69 | 139 | 135 | 136 | 135 | 58 | IWMI | + |
| 3 | MV | 42 | M | YES | NO | NO | NO | NO | 1 | 420 | 138 | 137 | 135 | 137 | 48 | AWMI | + |
| 4 | BB | 64 | M | YES | NO | NO | NO | NO | 1 | 20 | 132 | 134 | 134 | 141 | 39 | IWMI | + |
| 5 | AK | 60 | M | YES | NO | NO | NO | NO | 1 | 219 | 140 | 141 | 141 | 141 | 46 | AWMI | + |
| 6 | BB | 55 | M | YES | NO | NO | NO | NO | 1 | 220 | 137 | 136 | 135 | 140 | 86 | AWMI | + |
| 7 | B | 60 | F | NO | NO | NO | NO | NO | 1 | 89 | 138 | 140 | 136 | 138 | 36 | IWMI | + |
| 8 | VB | 63 | M | YES | NO | NO | NO | NO | 1 | 116 | 137 | 132 | 134 | 135 | 77 | IWMI | + |
| 9 | NJ | 45 | M | YES | NO | NO | NO | NO | 1 | 45 | 137 | 135 | 137 | 135 | 45 | IWMI | + |
| 10 | SK | 60 | M | NO | NO | NO | NO | NO | 1 | 124 | 144 | 140 | 136 | 138 | 36 | ASWMI | + |
| 11 | BV | 60 | M | YES | YES | NO | NO | NO | 1 | 126 | 141 | 137 | 135 | 136 | 36 | AWMI | + |
| 12 | AR | 52 | M | YES | NO | NO | NO | NO | 1 | 110 | 137 | 135 | 146 | 140 | 42 | AWMI | + |
| 13 | SB | 65 | M | NO | NO | NO | NO | NO | 1 | 108 | 139 | 136 | 138 | 135 | 78 | AWMI | + |
| 14 | IM | 65 | M | NO | YES | NO | NO | NO | 1 | 78 | 138 | 132 | 132 | 134 | 38 | AWMI | + |
| 15 | MC | 45 | M | YES | NO | NO | NO | NO | 1 | 34 | 138 | 136 | 136 | 137 | 42 | ALWMI | + |
| 16 | VM | 55 | M | YES | NO | NO | NO | NO | 1 | 35 | 136 | 140 | 140 | 136 | 59 | AWMI | + |
| 17 | BB | 45 | M | YES | NO | NO | NO | NO | 1 | 9 | 141 | 140 | 135 | 138 | 36 | AWMI | + |
| 18 | CR | 58 | M | YES | YES | NO | NO | NO | 1 | 96 | 135 | 134 | 133 | 137 | 44 | AWMI | + |
| 19 | RC | 32 | M | YES | NO | NO | NO | NO | 1 | 37 | 137 | 136 | 134 | 133 | 40 | AWMI | + |
| 20 | SP | 85 | F | NO | YES | NO | NO | NO | 1 | 70 | 133 | 134 | 130 | 138 | 36 | AWMI | + |
| 21 | SJ | 35 | M | YES | YES | NO | NO | NO | 1 | 16 | 138 | 138 | 136 | 138 | 58 | IW+RVMI | + |
| 22 | AS | 30 | M | YES | NO | NO | NO | NO | 1 | 80 | 139 | 137 | 138 | 135 | 49 | IWMI | + |
| 23 | BB | 65 | M | NO | NO | NO | NO | NO | 1 | 90 | 139 | 138 | 137 | 136 | 80 | ALWMI | + |
| 24 | GS | 65 | M | YES | YES | NO | NO | NO | 1 | 16 | 136 | 133 | 134 | 135 | 51 | AWMI | + |
| 25 | SB | 64 | M | YES | NO | NO | NO | NO | 1 | 121 | 135 | 136 | 136 | 137 | 40 | IWMI | + |
| 26 | DB | 52 | M | YES | NO | NO | NO | NO | 1 | 95 | 138 | 136 | 140 | 140 | 30 | AWMI | + |
| 27 | SD | 56 | F | NO | YES | NO | NO | NO | 1 | 65 | 139 | 137 | 138 | 135 | 40 | IWMI | + |
| 28 | P | 44 | M | NO | YES | NO | NO | NO | 1 | 221 | 135 | 135 | 136 | 136 | 51 | AWMI | + |
| 29 | GH | 55 | M | YES | NO | YES | NO | NO | 1 | 48 | 136 | 132 | 130 | 132 | 40 | AWMI | + |
| 30 | MA | 60 | M | YES | NO | NO | NO | NO | 1 | 94 | 136 | 140 | 136 | 138 | 36 | ASWMI | + |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 31 | HR | 70 | M | YES | YES | NO | NO | NO | 1 | 44 | 144 | 138 | 140 | 136 | 44 | AWNI | + |
| 32 | B | 60 | M | YES | NO | NO | NO | NO | 1 | 20 | 138 | 140 | 137 | 136 | 20 | IWMI | + |
| 33 | DR | 32 | M | YES | NO | NO | NO | NO | 1 | 44 | 137 | 131 | 134 | 135 | 58 | AWMI | + |
| 34 | US | 70 | F | NO | YES | YES | NO | NO | 2 | 105 | 135 | 132 | 131 | 130 | 63 | AWMI | - |
| 35 | SH | 65 | M | YES | NO | NO | NO | NO | 1 | 71 | 136 | 138 | 136 | 140 | 45 | AWMI | + |
| 36 | SP | 40 | M | YES | NO | NO | NO | NO | 1 | 179 | 134 | 130 | 138 | 134 | 40 | AWMI | + |
| 37 | NG | 85 | M | YES | NO | NO | NO | NO | 1 | 36 | 140 | 137 | 140 | 138 | 30 | IWMI | + |
| 38 | HJ | 55 | M | YES | NO | YES | NO | NO | 2 | 48 | 136 | 134 | 132 | 134 | 30 | AWMI | - |
| 39 | IR | 49 | M | YES | YES | NO | NO | NO | 1 | 80 | 136 | 132 | 134 | 134 | 42 | AWMI | + |
| 40 | RA | 83 | M | YES | NO | NO | NO | NO | 1 | 130 | 130 | 135 | 134 | 137 | 40 | ASWMI | + |
| 41 | RC | 55 | M | YES | NO | NO | NO | NO | 1 | 55 | 138 | 137 | 139 | 136 | 60 | AWMI | + |
| 42 | SG | 71 | F | YES | NO | NO | NO | NO | 1 | 8 | 138 | 136 | 138 | 140 | 57 | ASWMI | + |
| 43 | VM | 48 | M | YES | NO | NO | NO | NO | 1 | 6 | 136 | 134 | 132 | 135 | 50 | AWMI | + |
| 44 | RA | 56 | M | NO | YES | NO | NO | NO | 1 | 147 | 137 | 138 | 136 | 140 | 30 | IWMI | + |
| 45 | SD | 65 | M | YES | NO | NO | NO | NO | 1 | 26 | 138 | 140 | 142 | 140 | 49 | AWMI | + |
| 46 | SP | 40 | M | YES | NO | NO | NO | NO | 1 | 179 | 136 | 139 | 138 | 137 | 40 | AWMI | + |
| 47 | NG | 75 | M | YES | NO | NO | NO | NO | 1 | 36 | 138 | 138 | 137 | 140 | 30 | IWMI | + |
| 48 | SH | 70 | M | YES | YES | NO | NO | NO | 1 | 38 | 132 | 135 | 134 | 136 | 41 | AWMI | + |
| 49 | AN | 55 | M | NO | NO | NO | NO | NO | 1 | 28 | 137 | 132 | 134 | 134 | 70 | AWMI | + |
| 50 | BR | 69 | M | YES | YES | NO | NO | NO | 1 | 99 | 136 | 135 | 136 | 137 | 63 | AWMI | + |
| 51 | SA | 57 | M | YES | NO | NO | NO | NO | 1 | 14 | 133 | 132 | 134 | 136 | 40 | IWMI | - |
| 52 | SH | 60 | M | NO | NO | NO | NO | NO | 1 | 31 | 136 | 137 | 139 | 135 | 70 | IWMI | + |
| 53 | BG | 47 | M | YES | NO | NO | NO | NO | 1 | 38 | 138 | 133 | 132 | 134 | 60 | IWMI | + |
| 54 | SP | 38 | M | YES | NO | NO | NO | NO | 1 | 128 | 137 | 137 | 136 | 138 | 50 | ASWMI | + |
| 55 | DR | 55 | M | YES | YES | NO | NO | NO | 1 | 49 | 137 | 136 | 135 | 135 | 56 | AWMI | + |
| 56 | LB | 64 | F | NO | YES | NO | NO | NO | 1 | 117 | 136 | 134 | 134 | 135 | 50 | AWMI | + |
| 57 | SA | 65 | M | YES | NO | NO | NO | NO | 1 | 15 | 135 | 135 | 135 | 135 | 30 | IWMI | + |
| 58 | BA | 50 | F | NO | NO | NO | NO | NO | 1 | 45 | 135 | 135 | 135 | 138 | 36 | AWMI | + |
| 59 | SB | 64 | F | NO | NO | YES | NO | NO | 1 | 30 | 140 | 138 | 140 | 138 | 40 | IWMI | + |
| 60 | BP | 60 | M | YES | NO | YES | NO | NO | 1 | 100 | 128 | 130 | 130 | 132 | 36 | AWMI | - |
| 61 | DS | 50 | M | YES | NO | NO | NO | NO | 1 | 40 | 136 | 135 | 137 | 136 | 50 | AWMI | + |
| 62 | MP | 52 | M | YES | NO | NO | NO | NO | 1 | 74 | 136 | 137 | 136 | 138 | 40 | AWMI | + |
| 63 | MB | 70 | F | NO | NO | NO | NO | NO | 1 | 80 | 138 | 139 | 137 | 136 | 50 | ALWMI | + |
| 64 | RB | 73 | F | NO | NO | NO | NO | NO | 2 | 145 | 128 | 130 | 130 | 130 | 40 | IWMI | - |
| 65 | RA | 51 | F | NO | NO | NO | NO | NO | 1 | 50 | 136 | 136 | 136 | 135 | 50 | AWMI | + |
| 66 | BM | 58 | M | YES | YES | NO | NO | NO | 1 | 28 | 137 | 134 | 132 | 134 | 59 | IWMI | + |
| 67 | AS | 60 | M | YES | NO | NO | NO | NO | 1 | 28 | 132 | 132 | 134 | 135 | 52 | AWMI | + |
| 68 | PS | 48 | M | YES | NO | NO | NO | NO | 1 | 298 | 138 | 137 | 138 | 139 | 50 | IWMI | + |
| 69 | KN | 65 | M | YES | NO | NO | NO | NO | 1 | 20 | 135 | 136 | 138 | 137 | 40 | IWMI | + |
| 70 | VN | 60 | M | YES | NO | NO | NO | NO | 1 | 340 | 136 | 137 | 136 | 138 | 76 | AWMI | + |
| 71 | BA | 70 | F | NO | NO | NO | NO | NO | 1 | 127 | 135 | 136 | 138 | 139 | 30 | IWMI | - |
| 72 | VA | 44 | M | NO | YES | NO | NO | NO | 1 | 80 | 136 | 137 | 135 | 138 | 40 | IWMI | + |
| 73 | DA | 50 | M | YES | YES | YES | NO | NO | 1 | 152 | 131 | 134 | 132 | 135 | 50 | AWMI | + |
| 74 | NG | 45 | M | YES | NO | NO | NO | NO | 1 | 96 | 137 | 138 | 139 | 138 | 60 | IWMI | + |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 75 | NN | 45 | M | YES | NO | NO | NO | NO | 1 | 85 | 138 | 136 | 137 | 138 | 60 | AWMI | + |
| 76 | HM | 60 | M | NO | NO | NO | NO | NO | 1 | 78 | 135 | 136 | 138 | 139 | 50 | IWMI | + |
| 77 | KA | 32 | M | YES | NO | NO | NO | NO | 1 | 80 | 137 | 137 | 138 | 139 | 40 | IWMI | + |
| 78 | NN | 72 | M | YES | NO | NO | NO | NO | 1 | 115 | 136 | 135 | 133 | 132 | 60 | AWMI | + |
| 79 | RC | 75 | M | YES | NO | NO | NO | NO | 1 | 55 | 140 | 138 | 142 | 138 | 40 | AWMI | - |
| 80 | RT | 60 | M | YES | YES | NO | NO | NO | 1 | 68 | 140 | 136 | 138 | 136 | 50 | IWMI | + |
| 81 | CH | 45 | M | YES | NO | NO | NO | NO | 1 | 77 | 136 | 137 | 136 | 138 | 60 | AWMI | + |
| 82 | GB | 85 | F | NO | NO | NO | NO | NO | 1 | 43 | 137 | 138 | 138 | 137 | 30 | AWMI | + |
| 83 | BG | 55 | M | YES | NO | NO | NO | NO | 1 | 44 | 138 | 138 | 138 | 137 | 50 | AWMI | + |
| 84 | VT | 44 | M | YES | NO | NO | NO | NO | 1 | 43 | 136 | 137 | 137 | 138 | 58 | IWMI | + |
| 85 | BA | 70 | F | NO | YES | NO | NO | NO | 1 | 18 | 136 | 138 | 137 | 138 | 40 | IWMI | + |
| 86 | SB | 64 | F | NO | NO | NO | NO | NO | 1 | 120 | 136 | 132 | 134 | 134 | 30 | AWMI | - |
| 87 | PS | 56 | M | YES | YES | NO | NO | NO | 1 | 88 | 137 | 136 | 135 | 140 | 40 | AWMI | + |
| 88 | BD | 64 | M | YES | NO | NO | NO | NO | 1 | 54 | 130 | 134 | 134 | 135 | 74 | AWMI | + |
| 89 | BS | 60 | F | NO | NO | NO | NO | NO | 1 | 67 | 136 | 135 | 134 | 134 | 42 | AWMI | + |
| 90 | SP | 67 | F | NO | NO | YES | NO | NO | 1 | 70 | 137 | 133 | 132 | 133 | 40 | AWMI | + |
| 91 | CP | 70 | F | NO | NO | NO | NO | NO | 1 | 40 | 138 | 137 | 139 | 136 | 30 | AWMI | + |
| 92 | DP | 56 | M | YES | NO | NO | NO | NO | 1 | 39 | 135 | 136 | 137 | 137 | 42 | IWMI | + |
| 93 | KH | 59 | M | YES | YES | NO | NO | NO | 1 | 28 | 138 | 138 | 138 | 139 | 45 | AWMI | + |
| 94 | PN | 74 | F | NO | NO | NO | NO | NO | 1 | 45 | 135 | 138 | 137 | 139 | 32 | AWMI | + |
| 95 | SR | 67 | M | YES | NO | NO | NO | NO | 1 | 129 | 137 | 136 | 138 | 139 | 43 | AWMI | + |
| 96 | PD | 72 | F | NO | NO | NO | NO | NO | 1 | 74 | 139 | 138 | 139 | 137 | 42 | IWMI | + |
| 97 | BS | 64 | M | YES | NO | NO | NO | NO | 1 | 36 | 138 | 137 | 136 | 136 | 49 | IWMI | + |
| 98 | MA | 60 | M | YES | NO | NO | NO | NO | 1 | 100 | 135 | 136 | 136 | 136 | 40 | ASWMI | + |
| 99 | HM | 50 | M | NO | YES | NO | NO | NO | 1 | 70 | 137 | 138 | 139 | 140 | 48 | AWMI | + |
| 100 | SH | 63 | M | NO | NO | NO | NO | NO | 1 | 67 | 137 | 138 | 137 | 140 | 46 | AWMI | + |

# INFORMED CONSENT

## DEPARTMENT OF GENERAL MEDICINE

## Coimbatore Medical College, Coimbatore

Principal investigator : Dr. Jothibasu . V

Research guide : Dr. S. Chandrasekaran, M.D.

Organisation : Department of General Medicine

Informed consent : I have been invited to participate in research

Project Titled

**"PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION"**

I understand, it will be answering a set of questionnaire, undergo physical examination, investigations and appropriate treatment.

I also give consent to utilise my personal details for study purpose and can be contacted if necessary.

I am aware that I have the right to withdraw at any time which will not affect my medical care.

Name of the participant :

Signature :

Date :

## ஒப்புதல் படிவம்

பெயர் :

பாலினம் : வயது :

முகவரி :

அரசு கோவை மருத்துவக் கல்லூரியில் பொது மருத்துவத் துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவர் மேற்கொள்ளும் **"கடுமையான மாரடைப்பும் இரத்தத்தின் சோடியம் அளவு குறைப்பாடினால் ஏற்படும் பின் விளைவுகள்"** குறித்த ஆய்வில் செய்முறை மற்றும் அனைத்து விவரங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய அனைத்து விபரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்விலிருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் : கையொப்பம் / ரேகை

நாள் :