A STUDY ON THROMBOLYTIC EFFECT OF STREPTOKINASE INFUSION BETWEEN DIABETIC AND NON-DIABETIC MYOCARDIAL INFARCTION PATIENTS WITH ECG AS A TOOL

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CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **"A STUDY ON THROMBOLYTIC EFFECT OF STREPTOKINASE INFUSION BETWEEN DIABETIC AND NON-DIABETIC MYOCARDIAL INFARCTION PATIENTS WITH ECG AS A TOOL"** is the bonafide work of **Dr R.RAMKUMAR ,** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **April 2015.**

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DECLARATION

I, **DR.R.RAMKUMAR**, solemnly declare that this dissertation titled **"A STUDY ON THROMBOLYTIC EFFECT OF STREPTOKINASE INFUSION BETWEEN DIABETIC AND NON-DIABETIC MYOCARDIAL INFARCTION PATIENTS WITH ECG AS A TOOL"** is a bonafide record of work done by me at the Department Of General Medicine, Government Rajaji Hospital , Madurai, under the guidance of **PROF.Dr.S.Vadivel Murugan,M.D.,** HOD, Department Of General Medicine, Government Rajaji Hospital, Madurai Medical College, Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the rules and regulations for the award of **M.D Degree General Medicine Branch- I**; examination to be held in **April 2015.**

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ABSTRACT

INTRODUCTION

Diabetes Mellitus, being a major risk factor for cardiovascular disease is associated with myocardial infarction (MI) and sudden death at a higher level. In diabetic patients, morbidity and mortality are higher following MI than non-diabetic subjects, with one-year mortality as equal to 50%. The rate of re-infarction is also higher. Diabetes has its impact on the short term as well as long term morbidity of myocardial infarction patients.

Platelet activation is enhanced; Diabetes is associated with a procoagulant state. The likelihood of thrombotic events is increased. Thrombus propagation is encouraged; the efficacy of thrombolytic drugs is impaired . The chance of re-occlusion is also increased.

Measures which are simple as well as inexpensive are needed to assess the thrombolytic efficacy both in clinical practice as well as in clinical trials . Several studies have shown the utility of ST segment monitoring as a simple and rapid means of assessing reperfusion status in patients receiving fibrinolytic therapy for acute ST elevation myocardial infarction.

It is necessary to achieve successful recanalization of the epicardial vessel but microvascular flow strongly correlates with outcome. ST-segment changes are better than coronary angiogram in assessing myocardial perfusion.

AIMS AND OBJECTIVES :

To study the thrombolytic effect of streptokinase infusion between diabetic and non-diabetic myocardial infarction patients with ECG as a tool.

MATERIALS AND METHODS

SELECTION OF STUDY POPULATION:

This study is to be conducted among patients , admitted in coronary care unit with the diagnosis of ST elevation myocardial infarction.

STUDY POPULATION:

100 patients

STUDY PROTOCOL:

Patients who are diagnosed with ST elevation myocardial infarction are included in the study. Random blood sugar values are obtained on admission. Electrocardiogram is obtained on admission and 90 min after streptokinase infusion.

Fasting and post prandial glucose values are recorded from all patients , in the morning of day following admission, or once the patients are stable. The results are then analysed.

RESULTS:

On comparing the ST segment resolution among Diabetic and non-diabetic myocardial infarction patients , by using Chi square test, it is found that failed thrombolysis (<30% resolution) is more in diabetics than non-diabetics (p value is 0.004) which is significant whereas successful thrombolysis (>70% resolution) is more in non-diabetics than diabetics (p value is 0.020; significant).

In diabetic MI patients(n=60), the number of people with successful thrombolysis(>70% ST resolution) is 11 (18%), whereas failed thrombolysis (< 30% ST resolution) is 40 (67%). p value is 0.001, which is significant.

In non-diabetic MI patients (n=40), the number of people with successful thrombolysis (>70% ST resolution) is 21 (52%), whereas failed thrombolysis (<30% ST resolution) is 7 (17.5%) . p value is 0.038 which is also significant.

CONCLUSION:

On comparing the thrombolytic effect of Streptokinase , it is observed that failed thrombolysis (< 30% ST resolution) is more in diabetic STEMI patients when compared to non-diabetic STEMI patients. Successful thrombolysis (>70% ST resolution) is more in non-diabetic than diabetic STEMI patients.

Among diabetics, failed thrombolysis (67%) is more than successful thrombolysis (18%). Among non-diabetics, successful thrombolysis (52.5%) is more than failed thrombolysis (17.5%).

So, the outcome of thrombolysis of acute ST elevation myocardial infarction patients is affected by type 2 diabetes mellitus .

Key words: Diabetes mellitus, STEMI, myocardial infarction, thrombolysis, electrocardiogram.

INTRODUCTION

Diabetes Mellitus, being a major risk factor for cardiovascular disease is associated with myocardial infarction (MI) and sudden death at a higher level. In diabetic patients, morbidity and mortality are higher following MI than non-diabetic subjects, with one-year mortality as equal to 50%. The rate of re-infarction is also higher. Diabetes has its impact on the short term as well as long term morbidity of myocardial infarction patients.

Platelet activation is enhanced; Diabetes is associated with a procoagulant state. The likelihood of thrombotic events is increased. Thrombus propagation is encouraged; the efficacy of thrombolytic drugs is impaired . The chance of re-occlusion is also increased.

Measures which are simple as well as inexpensive are needed to assess the thrombolytic efficacy both in clinical practice as well as in clinical trials . Several studies have shown the utility of ST segment monitoring as a simple and rapid means of assessing reperfusion status in patients receiving fibrinolytic therapy for acute ST elevation myocardial infarction.

It is necessary to achieve successful recanalization of the epicardial vessel but microvascular flow strongly correlates with outcome. ST-segment

changes are better than coronary angiogram in assessing myocardial perfusion.

This study is being done to compare the efficacy of thrombolytic drug, Streptokinase between diabetic and non-diabetic acute myocardial infarction patients using ST segment resolution in ECG as a simple tool.

Zairis et al conducted a study which concluded that even though diabetic patients receive prompt thrombolysis, the outcome is not as good as in non diabetics who receive thrombolytic therapy for acute myocardial infarction. Left ventricular function after thrombolysis is impaired in diabetics.

Acute coronary events are nowadays , more common in general population because the risk factors causing such events are on the increasing verge. Without prompt treatment , either in the form of fibrinolysis or percutaneous coronary intervention, the mortality as well as morbidity is very high. In golden hour for reperfusion therapy , that is the initial 1-1.5 hours is very important because myocardial tissues before they die have to be salvaged since death is irreversible.

Also, the surrounding viable cells will also be in a state of ischemia and injury. In order to save these also, effective treatment is needed at the earliest possible time.

Streptokinase , the first thrombolytic drug discovered , although is associated with some allergic reactions and to some complications like hemorrhage and hypotension, is readily available and cost- effective also. A lot of newer thrombolytic drugs have come after streptokinase.

ECG, being a simple and readily available tool is cost effective as well. The diagnosis of acute myocardial infarction is made on presentation of the patient in emergency room with the classical history of angina and ECG.

ST segment elevation is a marker of myocardial injury ; T wave is a marker of ischemia . After prompt thrombolysis, the elevated ST segment returns towards baseline. This can be identified by serial ECG monitoring. ECG taken at 90 minutes after thrombolysis is a reliable indicator of the effect of thrombolytic drug. This percentage of ST resolution correlates with the success of thrombolytic therapy. In our study, the effect of diabetes on the ST segment resolution is compared with non diabetics.

AIMS AND OBJECTIVES :

To study the thrombolytic effect of streptokinase infusion between diabetic and non-diabetic myocardial infarction patients with ECG as a tool.

REVIEW OF LITERATURE

Diabetes is an independent risk factor for coronary heart disease. Death from cardiovascular causes is 3 times more in men with Diabetes than without it. The risk of death in acute myocardial infarction is twice in people with diabetes. An increase in HbA1C of 1% has a 14% increase in independent risk of MI.

Most common manifestations are:

1. Acute MI
2. Angina
3. Heart failure
4. Sudden death

In Diabetics, during acute phase of MI, there is increased mortality risk and in post infarction period, there is increased risk of morbidity.

There is higher incidence of acute coronary events in diabetic patients.

Diabetes mellitus is a metabolic disorder in which the rate of progression of atherosclerosis to occlude vessels increases.

Even after promptly thrombolysing, the aftermath is worse in Diabetics than non-diabetics. There is impaired function of Left ventricle after thrombolysis.

FACTORS ASSOCIATED WITH CAD IN DIABETES:

TRADITIONAL CARDIAC RISK FACTORS:

1. Hypertension
2. Lipid abnormalities
    A. Decreased HDL - C
    B. Increased triglycerides
    C. Presence of oxidized and small dense LDL-C
3. Obesity
4. Physical inactivity
5. Cigarette smoking.

NON-TRADITIONAL RISK FACTORS:

1. Microalbuminuria
2. Homocysteine
3. Hemostatic abnormalities

A. Factor VIII

B. vWF

C. PAI-1

D. Platelet reactivity

4. Inflammatory markers

A. CRP

B. Fibrinogen

C. Soluble cell adhesion molecules

DIABETES SCREENING:

Early screening and early diagnosis of diabetes have potential values. There are a lot of socio economic as well as personal harm because of diabetes.

On diagnosis itself, about 20-30% patients have diabetic complications like retinopathy. The estimated time is that even before 5-6 years of diagnosis of diabetes, complications begin to develop. So the onset of diabetes is about 10-12 years before the diagnosis of diabetes is made clinically.

HIGH RISK GROUPS:

1. People with truncal obesity

2. Siblings or Parents with diabetes mellitus type 2

3. > 45 years of age

4. People with CVA, CAD , peripheral vascular disease, hypertension

5. Dyslipidemia patients

6. Women with gestational diabetes or macrosomic babies

7. Obese women with PCOD

8. Known impaired glucose tolerance or impaired fasting glucose

It is necessary for early diagnosis and early treatment of diabetes to prevent complications.

A targeted screening programme is necessary to find the high risk people. A general health programme at primary health care level is very effective.

The recommended screening test is 2 hour plasma glucose after OGTT.

Disadvantages are :

1. Executional difficulty

2. Impracticability

3. Expensive

People who are screened to have diabetes should undergo a formal confirmatory test.

A large study concluded that diabetes should be considered as an equivalent of coronary artery disease. Aggressive management is therefore necessary. Asymptomatic hyperglycemia which remains unidentified precedes the diagnosis of diabetes. This is the reason why sometimes diabetes is diagnosed after the coronary event.

DIFFERENTIAL DIAGNOSIS OF TYPE 2 DIABETES:

1. Drug induced hyperglycemia

2. GDM

3. Endocrine causes

4. Latent autoimmune diabetes in adults

5. Slowly evolving variant of type 1 DM

NATURAL HISTORY OF TYPE 2 DM:

Glucose homeostasis is normally maintained by a balanced interaction between insulin sensitivity and secretion. There is defect in both insulin secretion and action in Type 2 DM.

An early feature is insulin resistance. It is genetically determined compounded by environmental factors.

Important sites for insulin resistance are:

1. Liver
2. Peripheral tissue
3. Skeletal muscle
4. Fat

INSULIN SECRETION DEFECT:

In type 2 diabetes, beta cells are not functioning normally . At the time of diagnosis, insulin secretion is already decreased. After about 7-10 years of type 2 diabetes, the percentage of patients who need insulin treatment is 60% . This is because of the ineffectiveness of oral anti-diabetics by that time.

C-peptide is a more stable marker of beta cell reserve than insulin. Initially, type 2 diabetics are positive for C-peptide. In response to a challenge with secretagogue, the C-peptide levels can be raised above a threshold.

The plasma insulin levels are high enough in type2 diabetics to prevent diabetic ketoacidosis.

Insulin secretory defect is preceeded by insulin resistance generally. Beta cell failure has an inherent component. When there is a progressive decline in beta cell secretion, a person progresses from normal to IGT to finally type 2 diabetes.

Some reasons for beta cell failure are:

1. Glucotoxicity

2. Amyloid fibril deposition within islet.

But, all type 2 diabetes cannot be attributed to amyloid fibril deposition. Initially, the adaptive capacity of beta cells compensates for insulin resistance.

At some point in time , insulin secretion reaches a plateau, at this stage , there is impaired glucose tolerance.

IGT can be reversible by measures such as :

1. Loss of weight

2. By increasing physical activity

3. Drugs which are insulin sensitizing

Finally, hypoinsulinemia develops.

DIABETES EFFECT ON ATHEROSCLEROSIS:

Complex plaques, when disrupt trigger the formation of arterial thrombus. Tissue factor plays an important role in extrinsic clotting pathway . In the plaque core, it is highly expressed.

After disruption, Factor VII binds to tissue factor and complexes are formed. Finally clotting cascade leads to fibrin formation. In case of insulin resistance or diabetic patients, tissue factor is over expressed.

Plasminogen activator inhibitor 1 is increasingly expressed in diabetics which prevents the nascent thrombi dissolution.

Subclinical plaque burden is increased in diabetics because plaque ruptures are more common in them. In diabetic patients, most of the vessels such as cerebrovascular, coronary as well as peripheral vessels are involved at

an age earlier than non diabetic individuals. The signs and symptoms of accelerated atherosclerosis should be considered with great alert by clinicians.

CORONARY ARTERY DISEASE :

The incidence of CAD is two times more in diabetic males and four times more in post menopausal diabetic females when compared to respeective non- diabetics.

CAD contributes one-third to the death in diabetics after the age of 40. It is characrerized by premature age of onset.

Coronary atherosclerosis in women with diabetes is almost as equal as that of diabetic men. But in non diabetic patients, males have a higher incidence of CAD than females.

Premenopausal women who do not have diabetes have a relative immunity from CAD mortality.

Final complications of diabetes such as renal failure, microalbuminuria, autonomic neuropathy, foot ulcers and blindness contribute to increased

Cardiovascular risk. In diabetics, the incidence and prevalence of triple vessel disease is more. The distribution of fibrous plaques is relatively more.

It is not yet established whether there is a correlation between severity of atherosclerosis in coronary arteries with diabetes duration. Coronary atherosclerosis is diffuse in diabetics.

In diabetic subjects, CAD is characterized by premature onset and clinically asymptomatic disease. 75 % of people suffering from acute MI before the age of 45 years have glucose intolerance.

Resting ECG is abnormally documented in about 40% diabetic subjects who are ambulant and normotensive. It doubles on exercise testing when compared to non diabetics.

There is greater prevalence of silent myocardial infarction in diabetics. One etiology advocated is autonomic neuropathy. But, diabetics who have already developed severe form of autonomic neuropathy have suffered from painful form of MI.

RISK FACTORS:

1. **HYPERGLYCEMIA:**

It is an important independent risk for CAD. There is an association between hyperglycemia and increased mortality.

2.LIPIDS:

Increased triglycerides, decreased HDL are more commonly seen in Type 2 DM. The levels of LDL are not much different from that of non diabetics.

3. INSULIN RESISTANCE:

It is mostly associated with obesity, increased BP, increased triacylglycerol, and decreased HDL, all of which contributes to increased risk of CAD.

4. OBESITY:

When energy intake exceeds energy expenditure, the excessive body fat is stored. This results in obesity. BMI is a frequently used parameter . When fat accumulates centrally in upper body areas, there is an increased risk of

co-morbidities. In this aspect, the waist- hip ratio is a stronger predictor of CVD than BMI.

The mortality rate is increased to 85% when acute MI is associated with DKA. Intracoronary streptokinase restores the occluded vessels' patency in two- third diabetics. Coronary angiography can precipitate acute renal failure in diabetics who are dehydrated.

PRIMARY PREVENTION:

1. Diet and exercise.

2. Reduction of weight.

3. Smoking cessation.

4. Hyperglycaemia control

5. Dyslipidemia management

6. Hypertension control

Most cost effective and safest modes of modifying vascular risk factors are lifestyle measures such as weight reduction and exercise. These lifestyle interventions are effective in reducing HbA1C also. Treadmill fitness is improved.

Blood pressue, both systolic as well as diastolic are improved. High density cholesterol and triglycerides are also improved.

Diabetes support and education reduces low density lipoprotein cholesterol to a greater extent.

These life style measures will benefit for both non- diabetic as well as diabetic population.

SECONDARY PREVENTION:

1. Beta blockers have a risk of hypoglycemia unawareness. But it's beneficial effect in cardiovascular disease overweighs the risk.

2. ACE inhibitors are effective in the prevention of acute events. HOPE study concludes this.

3. Diabetics have abnormal platelet activity. Aspirin is beneficial for this. In primary prevention also, aspirin is useful.

4. Statins confer protection from acute coronary events on a long term basis. Also used for primary prevention.

ETIOLOGY:

The traditional risk factors and the physiologic abnormalities recently recognized are attributable to the accelerated atherosclerosis in diabetic patients.

PATHOLOGY:

CAD will be widespread by the time diabetic patients present to medical personnel with cardiac symptoms/ myocardial infarction demanding coronary angiography.

There is a balance between vasoconstritory and vasodilatory mediators of vascular endothelium. Nitric oxide is vasodilatory; endothelin, prostaglandins and angiotensin converting enzyme are vasoconstrictory .

Some other mechanisms are:

1. Adipose tissue is increased.
2. hs-CRP level is elevated.
3. MAP kinase pathway is up regulated.
4. NF kappa B pathway is also increased.

In diabetes , there is endothelial dysfunction due to nitric oxide underproduction due to hyperglycemia. There is impairment in vasodilation.

Through ‘ toll like receptors’ hyperglycemia activates innate immunity leading on to leukocytosis. The result is ischemic reperfusion injury and atherosclerotic plaque is formed.

Stenoses are significant in multiple coronary vessels and >= 1 obstructive lesion can be found in each vessel . Obstruction of left main coronary artery is potentially dangerous. It is much more common in diabetic patients.

Long segment atherosclerotic disease or atherosclerosis involving distal arteries are also common. These kind of diffuse disease processes make the vessels unsuitable for PCI/ CABG. In this case , anti - ischaemic medications are the best treatment modality.

Collateral vessels develop as a compensatory response to coronary artery stenosis . But, in case of diabetic patients , the development of collateral vessels is lesser when compared to non-diabetics . So they are more vulnerable to ischaemia.

In diabetics, coronary atherosclerosis involves all kinds of vessels from large , medium to small vessels . So, in diabetics even small vessel disease can produce ischaemia.

During exercise or stress periods , because of already present endothelial dysfunction in diabetics, the ability of vasodilatation and blood flow augmentation are impaired.

PREVENTION:

A multifaceted approach is needed to prevent the cardiovascular disease in diabetic patients.

Use of aspirin daily is a primary prevention measure for cardiovascular disease in diabetics . A highly effective measure in preventing the microvascular complications is maintaining normal blood glucose . This also reduces triglycerides. The treatment target is to maintain HbA1C < 7%

Exercise is an important as well as a neglected aspect which reduces cardiac risk in diabetes. Exercise also benefits for control of hyperglycemia, dyslipidemia, hypertension and weight. But, recommendations are required individually.

Exercise should be initiated at low levels and the intensity of exercise should be increased gradually.

Even, non- specific symptoms such as chest tightness/ constriction should be considered as equivalent to ischaemic pain and consultations should be sought accordingly.

High intensity regimens should be avoided because these may precipitate unrecognized coronary artery disease which will not have classical angina symptoms.

Individualized glycemia target is very useful and will avoid the adverse effects of hypoglycemia in many patients treated for diabetes.

Young individuals have usually shorter diabetes duration and have lesser complications. In them, an aggressive glycemic control can be beneficial.

Older patients have longer duration of diabetes, along with more number of complications . An aggressive control of blood sugar levels is not warranted in these patients.

ASYMPTOMATIC ISCHEMIA:

1 in 5 asymptomatic diabetic patients have inducible ischemia. Its significance lies in the extent of compromised myocardium. Prior myocardial infarction is of particular concern in case of asymptomatic ischemia.

Subsequent cardiac events are more common in patients with prior myocardial infarction.

After the development of cardiac autonomic neuropathy, heart rate variability to deep breathing as well as valsalva maneuvre is diminished.

Orthostatic hypotension is common in advanced cases. There may be a > 15-20 mmHg fall of systolic blood pressure on standing position.

Any diabetic patient whose ECG shows evidence for ischemia or myocardial infarction Q waves or deep inversion of T waves should be subjected to exercise testing with perfusion imaging or echo. LBBB in

diabetic patients raises the possibility that prior myocardial infarction could have occurred.

Inducible ischemia screening should be done in asymptomatic patients who are diabetics with occlusive disease involving carotid or peripheral arteries. ; autonomic neuropathy or microalbuminuria.

Some of the inducible ischemia predictors are :

1. Increasing age
2. Higher cholesterol level
3. Male gender
4. Proteinuria
5. Cardiac autonomic neuropathy
6. ST/T wave abnormalities on resting ECG.

Prior identification of asymptomatic cardiac patients improves the care. It helps to motivate patients to take additional medications to treat those risk factors. Patients can be motivated to stop smoking, reduce weight . Regular exercise can be recommended.

REVASCULARISATION:

The clinical history, anatomy of coronaries, medical condition are taken into account in making a decision about by what means, a diabetic patient has to undergo revascularisation or intervention.

The highest risk patients are those with acute coronary syndrome or ischemic pulmonary edema.

The option of PCI / CABG are determined by

1. Number

2. Location

3. Morphology

4. Extent of coronary stenoses.

PCI with stenting has an important role in treating diabetic coronary artery disease patients . It is favourable along with the intensive platelet therapy such as glycoprotein II b/ III a inhibitors in ACS setting.

Diabetics have an increased rate of intimal proliferation following stent placement , increasing the risk of stent thrombosis over the subsequent 6 months period. Biologically coated stents have reduced risk of restenosis particularly in diabetics.

Factors which favour CABG are:

1. LMCA stenosis

2. Severe multivessel disease

3. Complex calcified lesions.

Some cases have multivessel disease in those , either PCI / CABG may be technically suitable. In these cases , careful analysis should be undertaken comparing the benefits and risks of percutaneous coronary intervention with those of coronary artery bypass grafting.

MYOCARDIAL INFARCTION:

The occurrence of myocardial infarction in diabetic patients increase the risk of complications like :

1. Heart failure and shock

2. Post infarct angina

3. Recurrent MI

4. Heart block

5. Atrial arrhythmias

6. Renal insufficiency

The opening of occluded artery by percutaneous coronary intervention or thrombolysis in ST elevation diabetic myocardial infarction patients is less optimal because of several factors and there is risk of reocclusion.

DIGAMI study showed that factors which predict mortality are previous heart failure, age and glycometabolic state severity on admission ; hypertension and previous myocardial infarction are not the predictors .

These factors are :

1. Increased plasminogen activator inhibitor I

2. Increased fibrinogen

3. Platelet hyperreactivity

4. Endothelial dysfunction

CAD is extensive and at the site of rupture of plaque , the tendency for thrombosis is more in diabetics .

The preferred treatment in Diabetic MI patients with ST segment elevation is primary PCI.

Advantages are :

1. More effective reperfusion
2. Definitve information on the extent of disease

3. No haemorrhagic complications.

Adjuvant treatment should include antithrombotic drugs with clopidogrel and Glycoprotein IIb/and IIIa inhibitors. So, these patients who present within 12 hrs of symptoms onset should be ideally considered for primary PCI.

Particular attention should be given in case of heart failure where establishing the patency of secure vessel is critical.

During primary angioplasty, multivessel disease is often encountered in diabetic MI patients. It poses a challenge for management. The culprit vessel responsible for infarction must be placed with stent. This is the ideal initial treatment.

A smaller section of diabetic patients may require urgent CABG in case of inaccessible lesion / left MCA disease.

After initial revascularisation following acute MI, aggressive medical therapy is necessary.

PLAQUE:

A transition can occur catastrophically in lipid laden atherosclerotic plaques leading to plaque disruption. Some have a predisposition to disruption of plaque. A thrombus results, which occludes flow of blood

which can lead to myocardial necrosis if severe and persistent imbalance develop between supply of oxygen and demand.

Usually complete plaques are associated with an epicardial coronary vessel which has total occlusion. These plaques are less complex in a vessel not related to STEMI.

RED THROMBI	**WHITE THROMBI**
Made up of RBCs, fibrin, platelets,leucocytes	Platelets , fibrin

Certain atherosclerotic plaques overexpress enzymes degrading extra cellular matrix . At the site of disruption of plaques, there is abundant macrophages which are activated as well as mast cells which produce these proteinases.

Also, an increased intraluminal pressure, increased vasomotor tone in the coronaries, tachycardia and the nutrient vessels distribution, all these combined and produce disruption of plaque at the fibrous cap margin at the shoulder regions.

ANATOMY OF CORONARIES AND INFARCTION LOCATION

During STEMI early hours, when angiographic studies are done, it reveals an approximate 90% total occlusion of the vessel related to infarction. spontaneous fibrinolysis can cause recanalization by which total occlusion diminishes angiographically in the period after MI.

Thrombolytic therapy and PCI increases the patency of the artery related to infarction markedly.

When a thrombus superimposes on ruptured plaque, then distal to the occluded artery, a transmural necrosis occurs. Whereas total occlusion which occurs chronically usually do not cause MI.

Factors which affect myocardial viability which is present distal to occlusion are:

1. Collateral vessels.
2. Myocardial metabolism level.
3. Stenosis in other arteries.
4. Speed with which the obstruction develops.
5. Myocardial quantity supplied.

5% of STEMI patients have normal vessels. This can be explained by a lysed embolus, platelet aggregate that has occluded transiently or a severe vasospasm of coronary arteries for a prolonged period.

A well supported concept is that sudden occlusion by thrombus formed by disruption of lipid laden plaques results in STEMI.

INFARCTION OF THE RIGHT VENTRICLE:

Approximately 50% of inferior walls MI are associated with RightVentriclular MI. In those with infarction occurring transmurally of the inferoposterior wall as well as septum (posterior portion), RV infarction exclusively occurs. It also occurs with infarction of inferior walls of left ventricle and adjacent septal infarction.

The incidence of isolated RV infarction is only 3% to 5%. The frequency of occurrence of RV infarction with total occlusion of right coronary artery is less common.

Prolonged ischemia can be sustained by right ventricle and will usually have an excellent contractile fraction recovery after reperfusion.

INFARCTION OF ATRIUM :

By using the PR segment elevation or depression as criteria, 10% of patients with acute STEMI can have atrial infarction . atrial wall is ruptured, mostly in atrial appendages which can lead to formation of thrombus. Atrial arrhythmias can occur.

PRE HOSPITAL MANAGEMENT:

The earliest measure is the restoration of blood flow to the zone of infarction. Usually the preferred option is PCI, when it is timely available and when it can be provided by a experienced personnel.

Necessary steps should be taken in the health care system to deliver some form of reperfusion therapy to STEMI patients in a timely fashion.

These include:

1) educating people about the symptoms of MI

2) contacting medical personnel as early as possible

3) reaching the destined hospitals in right time.

4) apt emergency protocols in emergency department so that time for door

to reperfusion can be minimised

5) ready availability of expert team to deliver reperfusion therapy.

Decision making is a problem in case of

1) Older age

2) Female sex

3) Black race

4) Low socio economic status

5) Low somatic emotional awareness

6) History of diabetes, angina or both.

At risk patients should have a heightened level of awareness.

IN THE EMERGENCY ROOM :

Triaging is an important initial work to be done to assess patients at high risk and those at low risk.

Primary tools are :

1.typical ischemic type of chest pain

2.initial 12- lead ECG

ST segment elevation in the initial ECG with ischemic chest pain is a powerful indicator of occlusion of coronary artery by thrombus.

Preference to invasive strategy if

1. A skilled laboratory available for PCI
2. High risk patients.
    a. Cardiogenic shock
    b. Killip class >= 3
3. Contraindications to fibrinolysis
4. Late presentation.
5. STEMI diagnosis is in doubt

Immediately assess the patient if he / she has any contraindications for fibrinolysis and reperfusion therapy.

FIBRINOLYIC THERAPY – CONTRAINDICATIONS IN STEMI:

RELATIVE:

1. History of poorly controlled hypertension.
2. Uncontrolled hypertension on presentation.
3. Prior thrombotic stroke > 3 months .
4. Prolonged CPR (>10 min) or a major surgery (< 3 weeks).
5. Any recent internal bleed.
6. Bleeding from vascular punctures.
7. Prior exposure to streptokinase (>5 days ago).
8. Previous allergic reaction to streptokinase.
9. Pregnancy
10. Peptic ulcer – active
11. Current anticoagulants use.

ABSOLUTE:

1. Prior ICH
2. AV malformation
3. Intracranial malignancy
4. Thrombotic stroke within 3 months except within 3 hr
5. Aortic dissection
6. Bleeding diathesis or any active bleed (except menses)
7. Significant trauma to head / face within 3 monts

In STEMI patients, lethal arrhythmias occur suddenly, so all STEMI patients should have an intravenous access as well as bedside ECG monitor.

SOME BENCHMARKS ARE :

1. A door to needle time <= 30 mins.
2. A door to balloon time <= 90 mins.

It should be restated as

1. EMS to needle time <=30 mins.
2. EMS to balloon time <= 90 mins.

MEASURES OF GENERAL TREATMENT :

Aspirin :

It is used for primary prevention of cardiovascular events as well as for the entire spectrum of ACS. It also form an important part of initial management suspected STEMI patients. Dose 162 to325 mg . Chewing is better than swallowing for absorption.

FOR CONTROL OF ISCHEMIC PAIN :

One of the aim of treatment is to relieve pain. Underdosage should be avoided for initial control of pain. Some drugs used are nitrates, morphine, o2, beta blockers.

ANALGESICS :

Expect in case of hypersensitivity, the drug of choice is morphine.

Dose 4 to 8 mg i.v, repeat the doses of 2 to 8 mg at 5 to 15 minutes interval till pain subsides (or) toxicity develops.

Consequently, metabolic demands of heart are reduced. It also reduces pulmonary edema.

Hypotension is a problem with administration of morphine, which can be treated with keeping the lower extremities of the patient elevated. Atropine can be given for hypotension and bradycardia. Respiratory depression can occur for which naloxone is used for treatment. For nausea and vomiting, phenothiazine can be given.

BETA – BLOCKERS :

- Ischemic pain is relieved

Exclude patients with

1. Heart failure
2. Hypotension
3. Bradycardia
4. I – degree AV block.

CARDIOVASCULAR DISEASE SCREENING IN DIABETES:

A screening method for early CAD detection must be

1. Simple
2. Widely available

3. Cost effective

4. Applicable to most of the diabetic patients

Diabetes by itself is a cardiovascular disease equivalent. It is challenging to identify high risk people within the population at earliest stage, so that adverse events can be prevented by interventions meaningfully.

In case of diabetic patients presenting with atypical symptoms of coronary artery disease , high index of suspicion is necessary. Some of the evidence based strategies used in diabetic patients are :

CARDIOVASCULAR RISK SCORES:

A few multivariate risk scores are :

1. UKPDS risk engine

2. Diabetes audit and research

3. Hong kong diabetes registry for CAD.

But, none have universal applicability. Framingham risk score relies on age heavily and underestimates the cardiovascular risk in Indians and in young people.

APPROACH BASED ON RISK FACTOR:

Various cardiovascular risk factors are :

1. Dyslipidemia

2. Hypertension

3. Obesity

Higher risk of cardiovascular disease is associated with greater number of risk factors. Several prospective intervention studies have shown that reduction of risk factors aggressively is a strategy very effective for reducing primary as well as secondary risk. This approach is recommended in the guidelines for managing diabetic patients to reduce cardiovascular risk.

RESTING ECG:

This provides important clues to prior myocardial infarction

1. Pathological Q waves

2. T wave inversion

3. LBBB

Non-specific ST/T changes can be predictors of ischemia inducible on stress testing.

MICROALBUMINURIA:

Overt nephropathy has a high risk of cardiovascular events and diabetic patients with this condition should ideally be screened for CAD.

HOPE trial shows that the risk of myocardial infarction and stroke are significantly increased even in patients with mild renal insufficiency.

In patients having Type 2 diabetes as well as chronic kidney disease , about 40% experience a cardiac event within 5 years . Microalbuminuria powerfully predicts risk of cardiovascular events. It is a useful test of risk in the future.

COMPLICATIONS INVOLVING MICRO AND MACROVESSELS:

Complications like neuropathy and retinopathy are risk predictors of coronary artery disease.

Clinical manifestations of autonomic neuropathy are:

1. Unexplained tachycardia

2.Orthostatic hypotension

3.Hypertension

These are also CAD risk factors . Screening for this condition is recommended by American Diabetes Association in all diabetic patients.

Other indicators of CAD are:

1. Peripheral neuropathy

2. Transient ischemic attack

3. Stroke

EXERCISE CAPACITY AND AGE:

When exercise capacity is impaired , it carries an adverse prognosis ; obese diabetics have a high risk of cardiac disease.

Advanced age is a powerful risk factor of cardiovascular events in diabetics. Diabetics of age 65 years or more are highly likely to have positive stress test.

HYPERGLYCEMIA:

It is a well known predictor of microvascular complications and atherosclerosis also. Hyperglycemia which is chronic and untreated is an important risk factor for cardiovascular disease .

SOME NEWER MODALITIES:

1.Cardiac CT

2.Cardiac MRI

3.Carotid intima media thickness (CIMT)

4.Arterial stiffness

5.Brachial artery FMD

1. CARDIAC CT:

The burden of atherosclerosis is determined non-invasively by cardiac CT.

Calcium scoring in the coronaries using CT scan is an important measurement of atherosclerosis extent.

Radiation and cost are two important parameters that limit the use of cardiac CT.

2. **CARDIAC MRI** has similar use but, there is no risk of radiation exposure.

3. **CIMT** is a reliable echocardiography based measurement which correlates better with atherosclerosis extent. Left main disease is even predicted by CIMT.

4. **Flow mediated Dilation** is a simple tool used in bedside to detect dysfunction of endothelium . Vasodilatory response mediated by endothelium in response to increased blood flow is measured. By occluding the artery first, flow is increased and ischemia is produced. It is followed by release.

5. **Arterial stiffness** assessment measures vessel wall function . Intima media thickness measures the structure of vessel wall. Non- invasive measurement of arterial stiffness is possible and pulse wave velocity can be recorded.

Arterial stiffness correlates well with age which is a conventional risk factor for CAD.

Unknown diabetes patient can be identified by Indian diabetes Risk Score with which arterial stiffness correlates well . Pulse wave velocity is an emerging tool as a early marker of CAD.

Peripheral arterial disease can be screened in the bedside by simple measuring of ankle brachial index. Impaired ABI is a CVD risk marker. A value less than 0.9 has an increased mortality risk.

C-REACTIVE PROTEIN:

A powerful inflammatory marker is hs-CRP . It is an independent predictor of diabetes and cardiovascular disease. Conventional risk factors if absent, this is a useful marker of risk of cardiovascular disease.

Excess fat in the body as well as subcutaneously , and physical inactivity are important reasons for high levels of this parameter in the population . But there are no prospective studies on the large scale to show that hs-CRP can be definitely used as a biomarker for cardiovascular risk in diabetics.

ECG CHANGES IN MYOCARDIAL INFARCTION:

MI evolves through three recognizable phases:

1.Hyperacute,

2..Fully evolved ,

3..Chronic stabilized

HYPERACUTE PHASE:

With in a few hours of infarction , this phase occurs . It is one of the frequently un recognized or ignored phase in literature.

Four principal manifestations are :

1.Ventricular activation time is increased.

2. R wave amplitude is increased.

3. ST segment is elevated.

4. T waves are tall and widened.

In the leads facing uninjured surface, reciprocal changes occur . An identical presentation can be seen in the hyperacute phase of prinzmetal angina. But, there is a resolution of changes within 20 minutes.

Primary ventricular fibrillation is an important complication during this phase. There is a need for vigilant monitoring during this phase.

FULLY EVOLVED PHASE:

1.QS complex represents myocardial necrosis.

2. ST segment is convex upward which represents myocardial injury.

3. Inverted , symmetrical T wave represents myocardial ischemia.

MYOCARDIAL NECROSIS:

QRS negativity or positivity loss reflects loss of myocardium.

Early and complete reperfusion of myocardium is the main aim behind thrombolysis. There is elevated risk of complications after incomplete or also failed thrombolysis.

In STEMI, ST segment resolution following fibrinolysis, assessed on ECG is a cost effective measure of assessing reperfusion of coronary vessels. The outcome depends on microvascular flow , for which resolution of ST segment is a better reflector. Coronary angiogram can not assess myocardial microvascular reperfusion.

Schroeder et al had reported that the most important early mortality predictor is the absence of resolution of ST segment. We can also identify patients for PCI at the earliest. So, ECG is the cheapest and an effective tool to assesss reperfusion.

In diabetics, failed reperfusion is more than complete reperfusion whereas complete reperfusion is more in non diabetics. The occurrence of complications is also more following thrombolysis in diabetics than non diabetics.

Recurrent ischemic pain is more common in diabetic patients because of more residual lesion in the artery related to infarction.

Heart failure and arrythmias are also more common in diabetic myocardial infarction patients.

THROMBOLYTIC THERAPY VS PCI :

Failure of reperfusion in diabetics is mainly because of increased aggregation of platelets, reduced vasodilation which is endothelium mediated.

Thrombogenicity is enhanced and fibrinolysis is impaired. So, PCI is a better option in diabetic myocardial infarction patients.

So, attention must be directed to the above mentioned factors by secondary preventive measures like adequate control of glycaemic status and lowering of lipid levels.

Derangements in metabolism occur at the time of infarction. This leads to anaerobic metabolism of glucose and a shift towards utilisation of free fatty acids. This affects both non-ischaemic and ischaemic areas. Infarct size is increased. The viable myocardial tissue has a compensatory response which is reduced.

Therapy with Insulin in acute MI counteracts the above said adverse effects. The pro thrombotic state is also improved.

THROMBOLYTIC THERAPY:

During acute MI, a well recognized and effective treatment is intravenous streptokinase. This has mortality benefits on cardiovascular events. The ongoing infarction process is interrupted and there is also reversal of metabolic derangements of viable cells.

STRESS HYPERGLYCEMIA:

There is a detrimental effect of stress hyperglycemia on the outcome of thrombolysis. This entity can be differentiaated only after acute phase with certainty.

Compared to non-diabetics, the use of thrombolysis is less frequent in diabetics. The reason is the less frequent presentation of ST elevation in ECG of diabetic patients.

CLINICAL PRESENTATION:

In diabetic patients , ischaemic chest pain may be absent or blunted. In Framingham Heart study, unrecognized MIs account for 25% .

In non diabetics, silent infarctions account for 22%. In diabetics, it is 39%. It is mainly because of autonomic neuropathy in diabetic patients.

Usually , atypical symptoms like dyspnoea, vomiting, confusion, fatigue may lead to delay in diagnosing acute MI in diabetics. These may lead to increase in cardiac mortality and morbidity.

STEMI patients are in considerable distress whereas angina patients often remain still because activity increases pain. In LV failure , patients appear pale and propped up. Bradycardia or tachycardia can occur.

More specific cardiac markers are now available which help in the diagnosis of MI very accurately. But, the treatment should not be delayed for the results to come. This is because of the golden period of reperfusion therapy.

STEMI:

STEMI naturally occurs in early morning hours because of circadian variation of various endogenous factors. Clinically silent episodes of infarction occur because of adequate collaterals.

Complete occlusion of an artery by thrombus produces myocardial injury transmurally and leads to STEMI. Acute coronary events presenting without ST elevation in ECG are diagnosed as UA / STEMI

STEMI patients are the ideal candidates for reperfusion therapy. UA/STEMI patients should not receive pharmacologic reperfusion therapy but are treated with anti thrombotics and later by PCI.

All patients of ACS must receive therapy with anti platelets and anti coagulants.

Factors contributing to increased occurrence of cardiovascular problems in diabetes are:

1. Atherosclerotic process is accelerated.
2. A specific form of cardiomyopathy develops.
3. Microvessel disease.
4. Autonomic neuropathy develops.

SMALL VESSEL DISEASE:

Occlusion of smaller vessels is the hallmark in the heart disease due to diabetes. The resultant ischemia leads to interstitial fibrosis resulting in

impaired LV function. The chest pain due to small vessel disease lasts longer than classical angina .

When it involves the smaller supplying sino atrial or atrio ventricular node , syncope , arrhythmias, conduction blocks and also sudden death can occur.

DIABETIC CARDIOMYOPATHY:

It is myocardial derangement with abscence of atherosclerosis in coronaries. It is a functional disturbance . In the myocardium which surrounds the small intramural vessels , there is increased accumulation of connective tissue . This diffuse myocardial fibrosis is analogous to the micro infarcts present in DR.

Saccular aneurysms can occur in arterioles in any layer of myocardium. Due to accumulation of glycoprotein , ventricular wall becomes less complaint . Response to catecholamines is diminished and calcium uptake is reduced .

Glucose is the source of energy for contraction of myocardium . The accumulation of substances which are osmotically active like fructose and sorbitol extracellularly impedes oxygen supply and by way , the underlying ischemia due to microvessel disease is accentuated.

Very early changes of diabetic cardiomyopathy in ECG are ST/ T wave changes . In insulin resistance states , there is hyperinsulinemia which has a growth promoting effect on the ventricular septum.

A very sensitive index for LV dysfunction is systolic time interval. Pre ejection period / Left ventricular ejection time (PEP / LVET) value increases in diabetic subjects and correlate with increased blood glucose values. LV relaxation is also prolonged . Diastolic dysfunction , that is due to relaxation failure , is a predictor for morbidity and mortality.

In diabetic subjects , congestive cardiac failure can ocur with a relatively normal size cardiac chambers . It is presumed that , small myocardial infarcts occur frequently which can result in scarring and fibrosis leading to diminished distensibility of ventricles.

HEART FAILURE:

It is more common in diabetic subjects leading on to increased mortality . They have a poor prognosis , mainly due to underlying cardiomyopathy . In diabetic men , heart failure is twice more common . In diabetic women , it is five times more common than the non- diabetics .

The aim of treating the patients is to decrease mortality . This is achieved by slowing down the remodelling process . By using drugs that inhibit Renin Angiotensin System and Sympathetic Nervous System , the remodelling process can be attenuated.

ACUTE CORONARY SYNDROME IN DIABETES:

About 20 to 30 percent of patients who are hospitalized during acute MI are found to have hyperglycemia.

Usually , diabetic myocardial infarction patients are younger in age , have greater mortality risk , face major complications .

DIGAMI study states that glycemic control during acute MI should be achieved intensively . This shifts the use of free fatty acids to glycolysis for the generation of ATP.

The sulfonylurea receptor expressed in cardiac muscle is SUR 2A ; in vascular smooth muscle , it is SUR 2B . Some sulfonylureas (except gliclazide) have benzamido group. The ischemic preconditioning is interferred by these sulfonyl ureas. Ischemic preconditioning is also obviated by hyperglycemia.

For one year following acute coronary event, aspirin and clopidogrel should be given in combination. After one year , one of the two drugs should be continued . In TRITON TIMI trial, prasugrel has been found to have an increased efficacy.

In non-ST elevation MI , Low molecular weight heparin is better than Unfractionated heparin , because the former has more stability , predictable anticoagulation , side effects are lesser , administration is easy and also cost effective .

In OASIS 6 study, Fondaparinux , a selective inhibitor of Factor Xa, has been found to be superior when compared to unfractionated heparin . In OASIS 5 study , it is found to be equally effective and the bleeding is less when compared to enoxaparin .

Hemorrhagic complications are an important cause of failure in the treatment of acute coronary events. This property of lesser bleeding with Fondaparinux is very useful in this acute coronary syndrome setting. But in the setting of PCI for AMI , Fondaparinux alone has an increased risk of catheter thrombosis . So, additional heparin is needed in case of PCI.

Thrombolysis in diabetic myocardial infarction patients is less effective when compared to non- diabetic counterparts.

tPA is superior to streptokinase for thrombolysis in case of survival benefit and quality of reperfusion. Also antibody formation is not there with use of tPA . But since it is costly, streptokinase is mainly used as a thrombolytic agent in most centers.

PCI in diabetics is complicated . Because the disease is extensive , can involve small branches , and risk of re-stenosis is more , drug eluting stents are found to have lesser restenosis with the complication of late stent thrombosis. By dual anti-platelet therapy, this complication can be managed in the long term effectively. CABG is superior to PCI in diabetic MI patients.

STREPTOKINASE:

Dr. William Smith Tillett discovered streptokinase , the first thrombolytic agent.

Fibrinogen is present in plasma , but absent in serum. This fibrinogen is the reason for agglutination of streptococci. As the fibrinogen is used for agglutination of streptokinase , the plasma is devoid of fibrinogen.

Streptokinase produced by streptococci causes lysis of clot. A lytic factor is normally present in plasma in an inactive form. Streptococcal fibrinogen activates this lytic factor which then lyses the fibrin clot.

This fibrinolysin is termed as streptokinase. The inactive lytic factor is plasminogen and its active enzyme is plasmin.

The concept of golden hour in acute myocardial infarction management emerged from the fact that when more than few hours have passed between thrombosis and thrombolysis, heart muscle will die and could not be saved. So , earlier the thrombolysis , the smaller the area of infarction.

GISSI trial established a significant difference in the rates of mortality between the SK and non-SK group at 12 months , SK is especially useful in the 0-3 and 3-6 groups.

EPICARDIAL REPERFUSION:

The major etiology for MI is coronary atherosclerosis . At the ischemia onset , biochemical as well as functional abnormalities begin immediately . Myocardial contractility is lost severely within 60 seconds. After at least 20-40 min of total occlusion , irreversible injury occurs .

Early reperfusion limits the progression of sub-endocardial infarct to transmural infarct. This transmural infarct is linked to remodelling of ventricle and survival rate is decreased.

So , the recommended door to balloon time is less than 90 monutes in hospitals capable of PCI, door to needle time is less than 30 min for thrombolytic administration in hospitals where PCI facility is not available.

MEASURES OF EPICARDIAL REPERFUSION :

TIMI FLOW:

Based on the assessment of contrast opacification rate of the infarct related artery visually, a grading scale is developed for coronary blood flow. TIMI flow grade 3 has reduced morbidity as well as mortality than grades 0,1 or 2.

CHEST PAIN RESOLUTION:

Resolution of ischemic chest pain due to coronary reperfusion is associated with thrombolysis or PCI. But this criteria has several limitations . This indicator is not reliable for successful reperfusion.

It has false positive values that 13% patients relieved of chest pain still have occluded artery. Persistant chest pain is asssociated with TIMI grade 2 but not total occlusion .

ST SEGMENT RESOLUTION IN ECG :

Maroko et al first analysed the efficacy of this non invasive tool in thrombolytic therapy in AMI.

>= 70 % resolution is complete ; 30 % - 70 % is partial and <=30% is failed or no ST resolution . Incomplete resolution has a 10 times more risk of mortality than complete resolution.

ST resolution is a better variable than myocardial blush in prognosis. With regard to availability and simplicity , ST segment resolution is a very useful tool for assessing the efficacy of thrombolytic therapy.

Schroder et al

ST SEGMENT RESOLUTION	**MORTALITY AFTER 180 MIN**
Complete	2.2%
Partial	3.4%
Failed	8.8%

SERUM MYOGLOBIN:

Its measurement has limitations similar to ST resolution.

Since individual measures are inadequate in predicting the success of reperfusion, for identifying candidates for rescue PCI, a combined criteria is used.

COMBINED CRITERIA:
1. <= 50% ST resolution at 90 minutes
2. Persistant chest pain at the time of angiography
3. A ratio smaller than 4 of serum myoglobin at 60 minutes / baseline

REPERFUSION STRATEGIES:

Total ischemic time is defined as the symptom onset time to the time to reperfusion therapy initiation time. So the concept of reperfusion is to minimize this ischemic time.

PCI :

In a hospital capable of doing PCI , STEMI patients should ideally be treated with primary PCI within 90 minutes of contact with first medical personnel.

FIBRINOLYSIS:

In a hospital not capable of doing PCI or in conditions , the patients could not be transferred to a PCI capable center, within 30 minutes of presentation , the fibrinolyic therapy should be given.

FACILITATED PCI:

After full dose fibrinolytic therapy, facilitated PCI is associated with increased rate of vessel closure and death because following fibrinolysis, there is an early prothrombotic condition. So , this may be considered in regimens using other than full dose streptokinase therapy.

In case of failed fibrinolysis, rescue PCI can be undertaken. Survival benefits are demonstrated with rescue PCI for patients in cardiogenic shock, congestive cardiac failure or arrhythmias.

PHARMACOINVASIVE APPROACH:

PCI is done 4-6 hours after pharmacological fibrinolysis. This has a lower risk of bleeding .TRANSFER -AMI trial has shown 30 day mortality reduction with this approach.

MYOCARDIAL INFARCTION:

DIGAMI study shows that factors which predict mortality are previous heart failure, age, and glycometabolic state severity on admission and previous myocardial infarction.

The risk of heart failure is increased in diabetic MI patients because of impaired infarction induced remodelling as well as decompensation by metabolic derangement.

Stress hyperglycemia also increases the risk of mortality as well as heart failure and shock.

From enzyme release and angiographic studies , it is evident that thrombus in the coronary artery of diabetic patients is more resistant to therapy with thrombolysis.

GUSTO study showed similar 90 min patency rate in diabetic and non-diabetic subjects. No evidence to state that hemorrhagic complications are more in diabetic than non diabetic subjects.

ECG IN MYOCARDIAL INFARCTION:

1.QS complex

2.Qr complex

3.R wave amplitude loss

Hyperacute phase:

Increased R wave amplitude:

The R wave in the corresponding leads become, indeed very tall .

Extensive anterior – V1 – V6

Anteroseptal - V1-V3

Anterolateral – V4-V6, I , aVL

Antero apical – V5, V6

Inferior – II, III, aVF

Inferolateral – II , III, aVF, I, aVL

Inferoanterior – II, III, aVF, V1, V2

Lateral – I , aVL

Posterior – V1, V2

Anterior – extensive with LBBB.

Subendocardial without Q wave

These changes occur because of acute injury block. The injuried tissue conducts current at a slower rate and is still not necrosed.

Ventricular Activation Time increased:

Onset of intrinsicoid deflection is delayed ; leaning of R wave to the right of observer.

ST segment – slope elevation:

There is loss of concave upward nature of ST segment. First it becomes straightened, then it becomes elevated resembling a slope elevation. The proximal limb of the T wave and this straight ST segment blends. ST segment straightening can be an earliest sign also.

T waves – tall and widened

LOCALIZATION OF TERRITORY :

Always towards the site of ischemia, the ST segment is deviated . Pathology involving anterior wall causes elevation of ST segment in leads in the anterior precordium . That involving inferior wall causes changes on III, aVF, II.

Infarction in right ventricle causes elevation of ST segment in right precordial lead V1. In case of involvement of first septal perforator, lead V1 ‘s ST segment is elevated.

LAD lesion:

ST segment deviation is present in leads I, aVL, V3-V6 in case of anterior MI, occasionally lead II . In inferior leads III, aVF, reciprocal changes are present.

ST segment changes in V1 are less frequent than in V2 / V3 in anterior MI. In case of acute anterior MI , when there is ST elevation in V1 also , it implies that the conal branch is absent/ small enough to reach to interventricular septum . Conal branch is usually a branch of Right coronary artery.

Elevation of ST segment in aVL and III with positive T waves implies that there is wrap around LAD around the apex and is occluded.

Three main areas supplied by LAD :

1) Basoseptal by first septal branches.

2) Lateral basal by first diagonal branches

3) Infero apical by distal LAD

Occlusion of left main coronary artery:

When ST elevation is present in all leads except inferior leads, this lesion should be suspected. When RBBB is associated with posterobasal ischemia signs, this occlusion should be suspected.

When aVR has greater ST elevation than V1 , left main coronary artery occlusion should be suspected.

RCA occlusion / LCX occlusion:

In leads II, III, aVF , also sometimes in leads V5, V6, there is elevation of ST segment. In lead I, aVL, reciprocal ST depression is present sometimes in V2, V3, when the ST segment depression in V2, V3.

When the ST segment depression in V1, a reciprocal change is not present, instead there is elevation, Right ventricular myocardial infarction should be suspected. But ST depression in V1 indicates also posterior wall MI.

In case of occlusion of Right coronary artery , elevation of ST segment in lead III is more than lead II and there is depression of ST segment in lead I.

In left circumflex artery occlusion, there is ST elevation in II, III, aVF, as well as in V5, V6 (or) I and aVL.

INDICATIONS FOR THROMBOLYSIS BASED ON ECG CHANGES:

Evidence of ST elevation of >0.1 mV in two limb leads or two or more precordial leads which are anatomically contiguous indicates there is acute MI and emergent thrombolysis can be instituted.

Recanalization is paralleled by ST segment regression. Incomplete damage also predicts mortality. Extensive myocardial damage is suggested by ST segment re elevation.

In acute coronary syndrome , the most lethal form is STEMI . Here , the artery is completely occluded by thrombus, the territory supplied , suffers total cessation of blood supply and the ECG shows ST elevation . New Q waves typically evolve in 70 % patients.

Only based on ECG alone, STEMI is not diagnosed. Two out of following three elements are necessary:

1. > 30 mins of ischemic chest pain.
2. In serial ECG there is evolutionary changes.
3. Because of myonecrosis, the serum cardiac biomarkers rise and then fall.

It is of paramount importance to accurately diagnose STEMI.

MI COMPLICATIONS:

ACUTE COMPLICATIONS:

1. Arrhythmias
2. Sudden death
3. Cardiogenic shock
4. Fibrinous pericarditis

5. Infarct extension
6. Mural thrombi
7. Embolization
8. Cardiac rupture

ARRHYTHMIAS:

After acute MI , 90% patients at sometime develop, rhythm abnormality.

Reason for tachyarrhythmias are:

1. Reperfusion
2. Altered tone of autonomic nervous system
3. Hemodynamic instability

Tachyarrhythmias associated with increased mortality are:

1) Premature ventricular complexes – subacute and late
2) Late onset non sustained ventricular tachycardia
3) Monomorphic VT – sustained

Initially, arrhythmias evolve from the ischemic zone surrounding the infarcted myocardium because of metabolic abnormalities, later these result from scar tissue which surround viable tissues.

Within 24 hours, cardiac conduction disturbances is experienced by 25% patients . In inferior wall MI, bradyarrhythmias developing within 24 hours are usually benign. But those occurring later than 24 hours needs to be monitored carefully and treated.

In case of anterior wall MI, there is higher mortality rate associated with conduction disturbances such as left anterior hemiblock and right bundle branch block . The occurrence of Atrial Fibrillation is only 5 to 10%

CARDIOGENIC SHOCK :

When there is atleast 40% loss of left ventricular mass, cardiogenic shock follows MI. This constitutes about 44% of short term deaths.

MYOCARDIAL RUPTURE:

An early catastrophic and fatal event is rupture of free wall of LV. Hemodynamic collapse occurs . A late complication is aneurysmal dilatation.

VENTRICULAR SEPTAL RUPTURE:

Delayed or failed thrombolysis is associated with ventricular septal rupture.

MITRAL REGURGITATION:

Mechanisms are:

1. Severe LV dilatation

2. Papillary muscle dysfunction due to IWMI

3. Papillary muscle infarction

DRESSLER SYNDROME:

More common in anterior wall STEMI. With thrombolysis , it's incidence has been decreased.

LIFE STYLE MODIFICATIONS AFTER ACS:

Cardiac rehabilitation programme should be implemented.

1. Mediterranean type of diet is advisable.

2. Moderation of alcohol drinking

3. Physical activity

4. Smoking cessation

5. Weight reduction

6. Hypertension control

7. Glycemic control.

ST segment resolution :

It is advantageous to monitor ST segment resolution continuously.

Finding ST segment resolution at some point in time after fibrinolysis helps to identify patients for resue PCI.

Non invasive diagnosis of failed thrombolysis:

1) Chest pain – non resolution

2) Non resolution of ST elevation at 90 mins after thrombolysis

3) Post/pre thrombolysis enzyme levels

< 5 at 1 hour

< 10 at 11/2 hour.

In case of failed thrombolysis, the following options can be tried.

1. With a newer agent, repeat thrombolysis can be tried.

2. Abciximab, tirofiban or either GP II b / III a inhibitors

3..Intra-aortic balloon counter-pulsation

4.Rescue PCI

5.PCI and GP IIb / IIIa combination.

Coronary branches which are clinically important are:

1. LCA A. Anterior descending

   B. Circumflex

2. RCA A. Right main coronary artery

   B. Posterior descending artery

The biochemical changes which occur in acutely ischemic myocardium are :

1. Anaerobic glycolysis
2. Inadequate ATP production
3. Lactic acid accumulation
4. Mitochondrial glycogen depletion and swelling

These changes are early and reversible.

In Indians the CAD risk factors are :

1. Lipoprotein (a)
2. High LDL
3. Low HDL
4. Hypertension
5. Diabetes
6. Tobacco
7. Hyperhomocysteinemia

There are four mechanism of angina :

1. Primary angina : due to coronary vasospasm as in Prinzmetal angina.
2. Secondary angina : exertional angina mainly due to increased demand
3. Mixed form
4. Syndrome X : with normal coronaries, there is angina but there is a positive threadmill test.

Silent Myocardial ischemia -Prevelance :

1. In asymptomatic middle aged men 2-4 %
2. In asymptomatic post MI 20-30 %
3. Angina 80 – 90%
4. MI – 25 %

Reasons are :

1. Pain system is defective :
    a. Elderly patients with dementia or stroke
    b. Pain threshold is high
    c. Autonomic changes at receptor level
    d. Neuropathy eg. Alcohol, DM.
2. Collateral vessels protective effect.
3. There is denervation of pain pathway in the previous myocardial scar
4. Denervation surgically after CABG.

Evolution of infarction :

1. Irreversible damage of myocardium follows longer periods of ischemia
2. An advancing wave front of necrosis develops in the territory supplied by the infarct related artery.
3. Collaterals when effective / fibroinolysis endogenously can delay damage to myocardium.
4. During the early 6 hours , the myocardium is destined to die
5. Restoration of patency of coronary artery completely as early as possible is the effective way to prevent long – term damage.

Four types of MI :

I --- primary coronary event is the reason

II ---secondary to ischemia due to imbalance.

III --sudden cardiac death

IV -- iatrogenic

1. PCI
2. Verified thrombosis of stent
3. CABG.

ST elevation but no ischemia :

1. Early repolarisation
2. LVH / LBBB
3. Brugada syndrome
4. Hyperkalemia

Chest pain but no ischemia:

1. Myocarditis
2. Pericarditis
3. Acute aortic dissection
4. Pulmonary embolism
5. Costochondritis
6. Gastro-oesophageal disorders

Various thrombolytic agents:

Fibrin-non specific:

1. Streptokinase.
2. Anisolated plasminogen streptokinase activator complex
3. Urokinase
4. Arvin

Fibrin specific:

1. Staphylokinase
2. Recombinant single chain urokinase
3. rtPA / alteplase
4. Reteplase

Indications for their use are:

1. Acute myocardial infarction
2. Pulmonary thromboembolism
3. Acute ischemic stroke

4. Deep venous thrombosis

5. Acute peripheral arterial occlusion

Also used in:

1.cardiac arrest

2.Thrombosis of prosthetic heart valves

3.Sub acute and late stent related thrombosis

4. loculated pericardial effusions

5.thrombus in right atrium

6.cerebral sinus thrombus

An ideal thrombolytic should be

1. Specific to thrombus
2. Act rapidly
3. Efficacy should be high
4. Side effects low

5. Low incidence of rescue procedures, reocclusion
6. Easy administration
7. Cost effective
8. Long term effects should be good

Early thrombolytic therapy has the following advantages:

1. Patency of occluded artery is restored early
2. Infarct size is limited
3. LV fuction is preserved
4. Mortality and morbidity are decreased

Complications associated with streptokinase:

1. Hypotension
2. Reperfusion arrhythmia
3. Allergic risks
4. Major / minor bleeding.

ACS AND GIK INFUSION:

During ischemia , cardioprotection due to Glucose Insulin Potassium infusion is due to reduction in free fatty acids. High levels of free fatty acids

has been associated with higher incidence of ventricular fibrillation in early phases.

Glycolytic flux is increased and the development of contractures due to ischemia is reduced. Reperfusion injury is decreased and post infarction myocardial contractility is improved. FFA induced biochemical abnormalities are reduced by normalising intramitochondrial energy production. Final outcome is reduction in infarct size .This helps to increase myocardial salvage and thereby improve clinical outcomes.

MATERIALS AND METHODS

STUDY POPULATION:

This study was conducted among 100 patients , admitted in coronary care unit with the diagnosis of ST elevation myocardial infarction. Out of 100, 60 are diabetics and 40 are non-diabetics. 60 males and 40 females are studied. Among males, 40 are diabetics and 20 are non-diabetics; among females 20 are diabetics and 20 are non-diabetics.

INCLUSION CRITERIA:

1. Patients with STEMI coming to hospital within 12 hours of chest pain
2. Known diabetic or newly diagnosed during hospital stay
3. Non-diabetics

EXCLUSION CRITERIA:

1. Patients presenting late after 12 hours of chest pain
2. Type 1 diabetics
3. Patients with impaired glucose tolerance
4. Patients with history of previous MI.
5. Patients with only stress hyperglycemia on admission.

ANTICIPATED OUTCOME:

Successful thrombolysis with streptokinase (> 70% ST segment resolution) is significantly more in non-diabetics when compared to diabetics, whereas failed thrombolysis (< 30% ST segment resolution) is significantly more in diabetics than non-diabetics.

DATA COLLECTION:

- Detailed Clinical History ,
- Detailed Clinical Examination ,
  - Random blood sugar values are obtained on admission.
- Electrocardiogram obtained on admission and 90 min after streptokinase infusion.
- Fasting and post prandial glucose values are recorded from all patients , in the morning of day following admission, or once the patients are stable.

LABORATORY INVESTIGATIONS:

- Electrocardiogram obtained on admission and 90 min after streptokinase infusion.
- Random, fasting and post-prandial (2 hr) blood glucose are obtained.

STUDY PROTOCOL:

- Patients who are diagnosed with ST elevation myocardial infarction are included in the study.
- Random blood sugar values are obtained on admission.
- Electrocardiogram obtained on admission and 90 min after streptokinase infusion.
- Fasting and post prandial glucose values are recorded from all patients , in the morning of day following admission, or once the patients are stable.
- The results are then analysed.

DESIGN OF STUDY:

Prospective interventional study

PERIOD OF STUDY:

April 2014 to August 2014

COLLABORATING DEPARTMENTS:

Department of General Medicine,

Department of Cardiology,

Department of Biochemistry.

ETHICAL CLEARANCE:

The study was approved by the ethical committee of Govt. Rajaji Hospital, Madurai.

CONSENT:

Individual written and informed consent from patient andor attendant.

ANALYSIS:

Statistical analysis

CONFLICT OF INTEREST:

Nil

FINANCIAL SUPPORT:

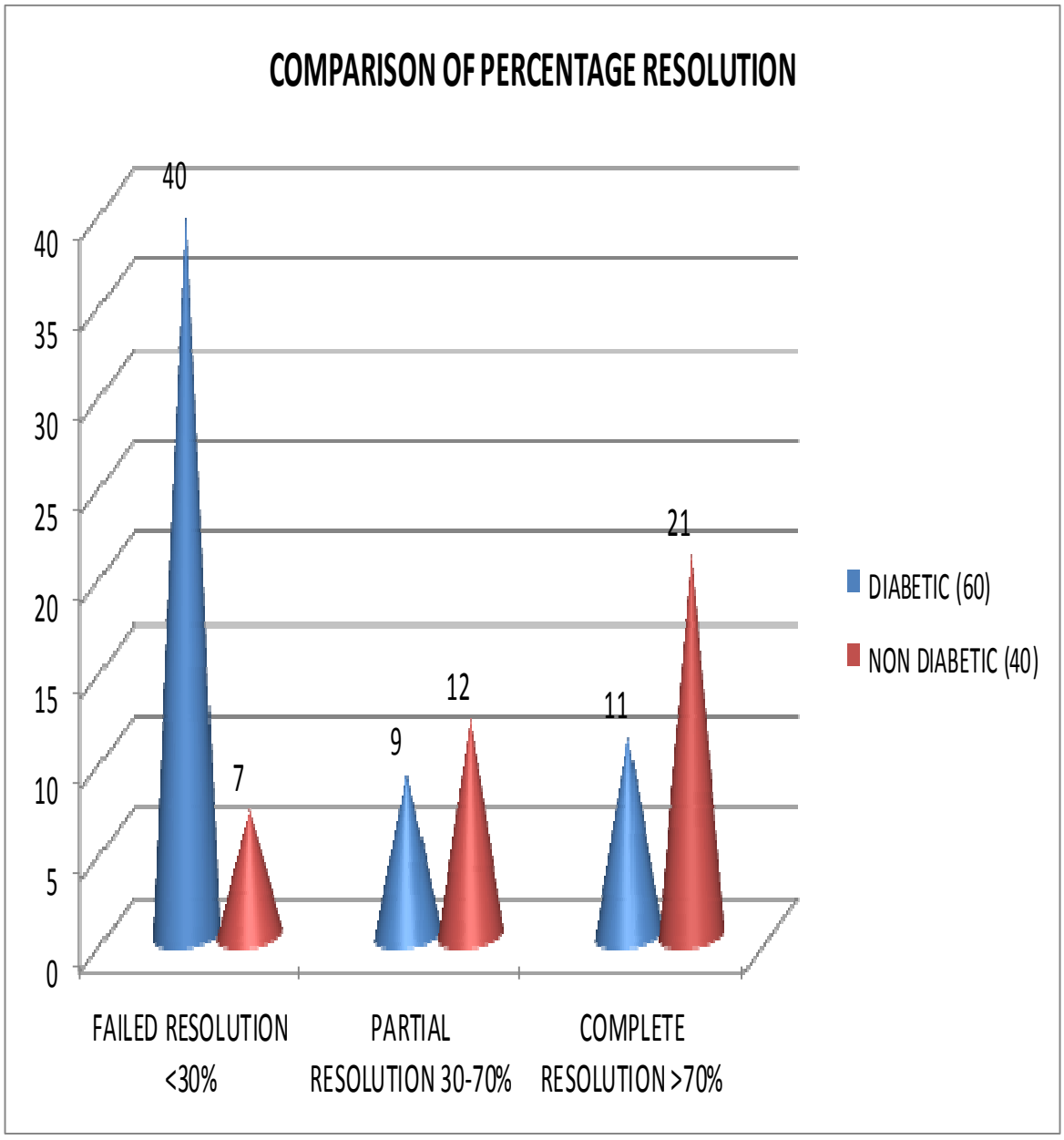
Nil

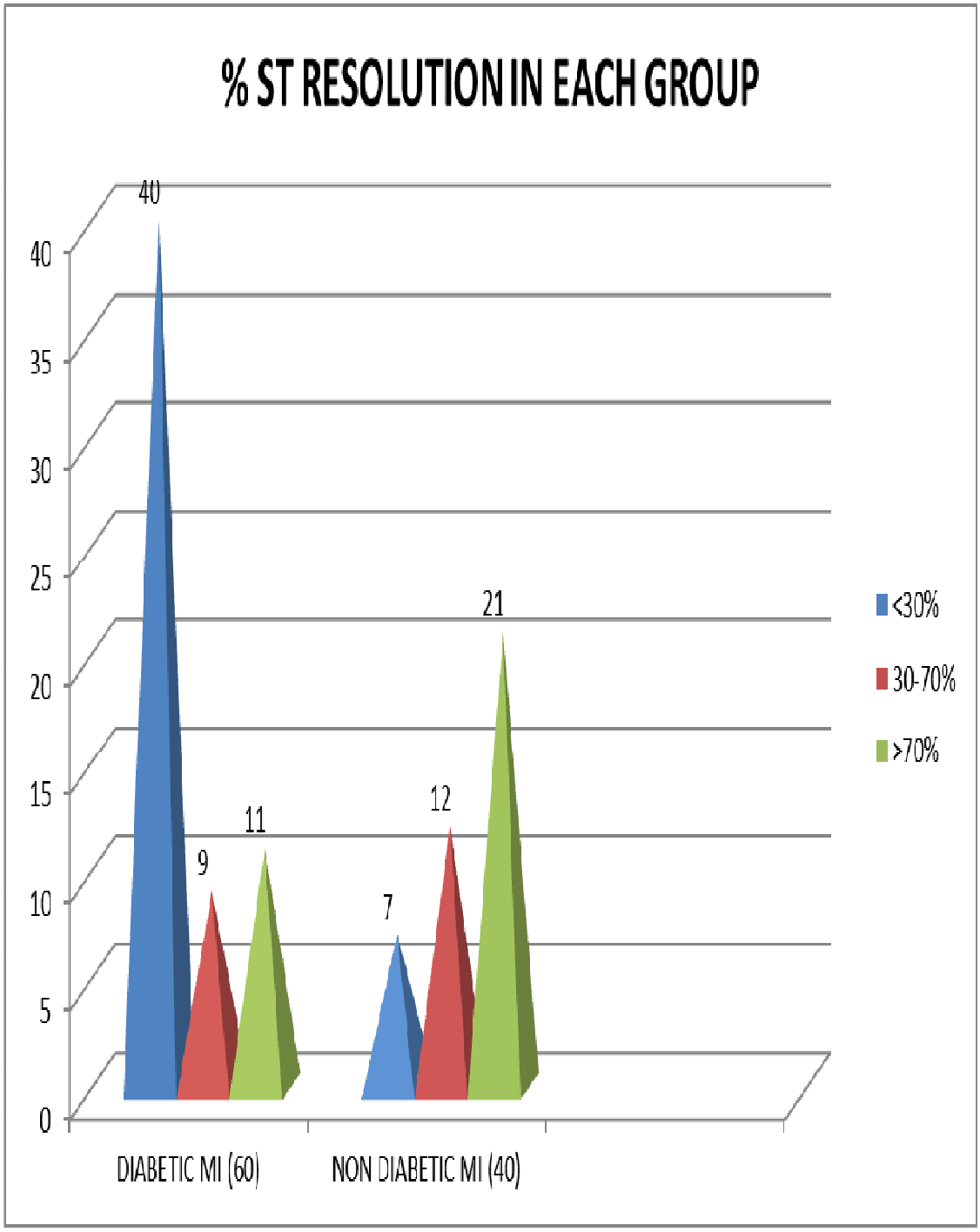
RESULTS AND INTERPRETATIONS:

TABLE 1: ST SEGMENT RESOLUTION IN STUDY POPULATION

	FAILED RESOLUTION <30%	PARTIAL RESOLUTION 30-70%	COMPLETE RESOLUTION >70%	P VALUE
DIABETIC (60)	40(67%)	9(15%)	11(18%)	0.001
NON DIABETIC (40)	7(17.5%)	12(30%)	21(52.5%)	0.038
TOTAL (100)	47	21	32	
'P' VALUE	0.004		0.020	

On comparing the ST segment resolution among Diabetic and non-diabetic myocardial infarction patients , by using Chi square test, it is found that failed thrombolysis (<30% resolution) is more in diabetics than non-diabetics (p value is 0.004) which is significant whereas successful thrombolysis (>70% resolution) is more in non-diabetics than diabetics (p value is 0.020; significant).


COMPARISON OF PERCENTAGE RESOLUTION
40
7
9
12
11
21
0
5
10
15
20
25
30
35
40
DIABETIC (60)
NON DIABETIC (40)
FAILED RESOLUTION <30%
PARTIAL RESOLUTION 30-70%
COMPLETE RESOLUTION >70%


% ST RESOLUTION IN EACH GROUP
40
35
30
25
20
15
10
5
0
40
9
11
7
12
21
<30%
30-70%
>70%
DIABETIC MI (60)
NON DIABETIC MI (40)

In diabetic MI patients(n=60), the number of people with successful thrombolysis(>70% ST resolution) is 11 (18%), whereas failed thrombolysis (< 30% ST resolution) is 40 (67%). p value is 0.001, which is significant.

In non-diabetic MI patients (n=40), the number of people with successful thrombolysis (>70% ST resolution) is 21 (52%), whereas failed thrombolysis (<30% ST resolution) is 7 (17.5%) . p value is 0.038 which is also significant.

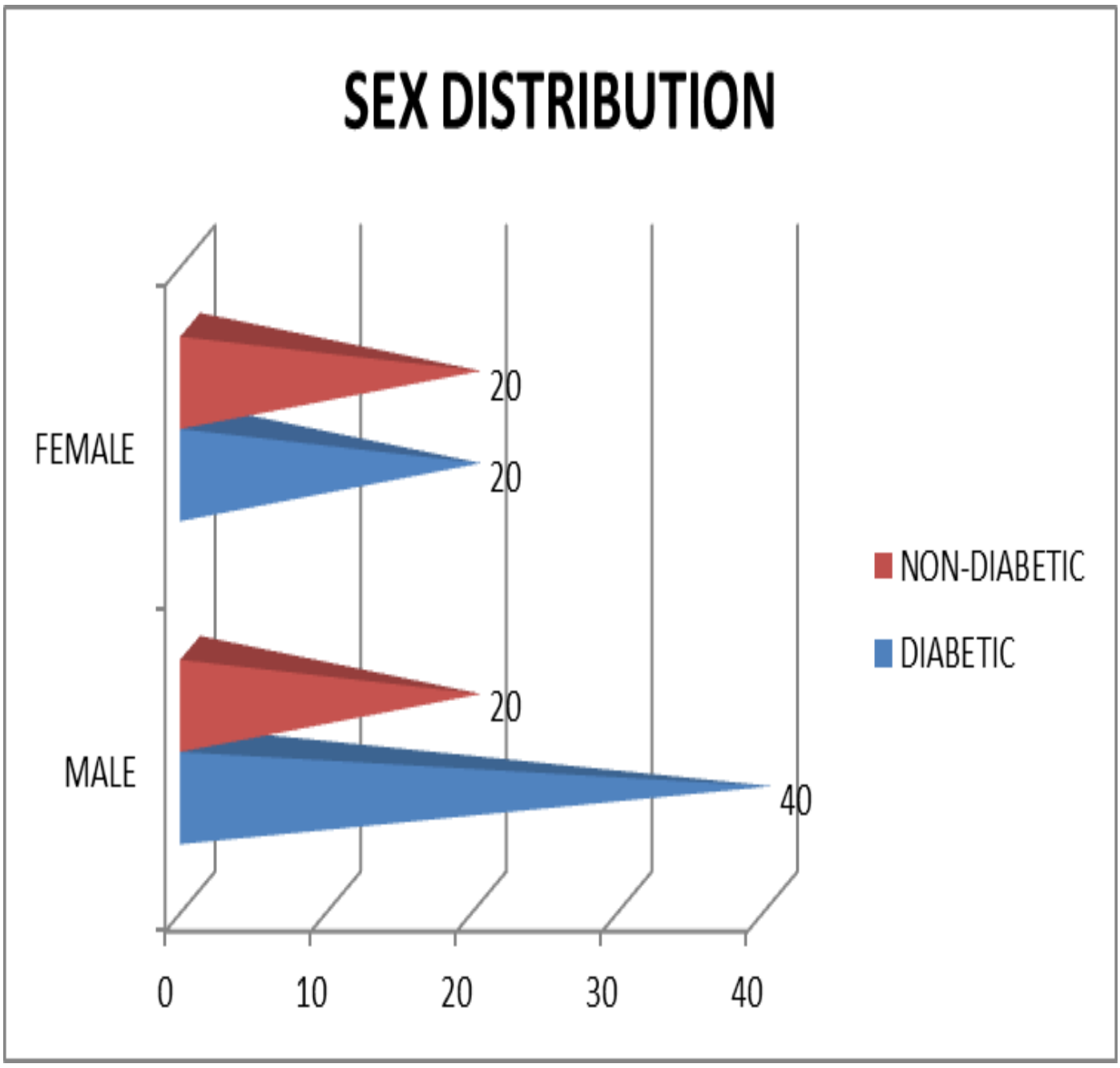
TABLE 2 : AGE CHART

AGE GROUP (IN YEARS)	% OF STUDY POPULATION
31-40	1
41-50	19
51-60	44
61-70	32
71-80	4

TABLE 3 : GENDER CHART

	MALE	FEMALE
DIABETIC	40	20
NON-DIABETIC	20	20

In the study population, (n=100), number of diabetics is 60, in which males 40 ; females 20. Number of non diabetics is 40 in which males 20 and females 20.


SEX DISTRIBUTION
FEMALE
MALE
20
20
20
40
0
10
20
30
40
NON-DIABETIC
DIABETIC

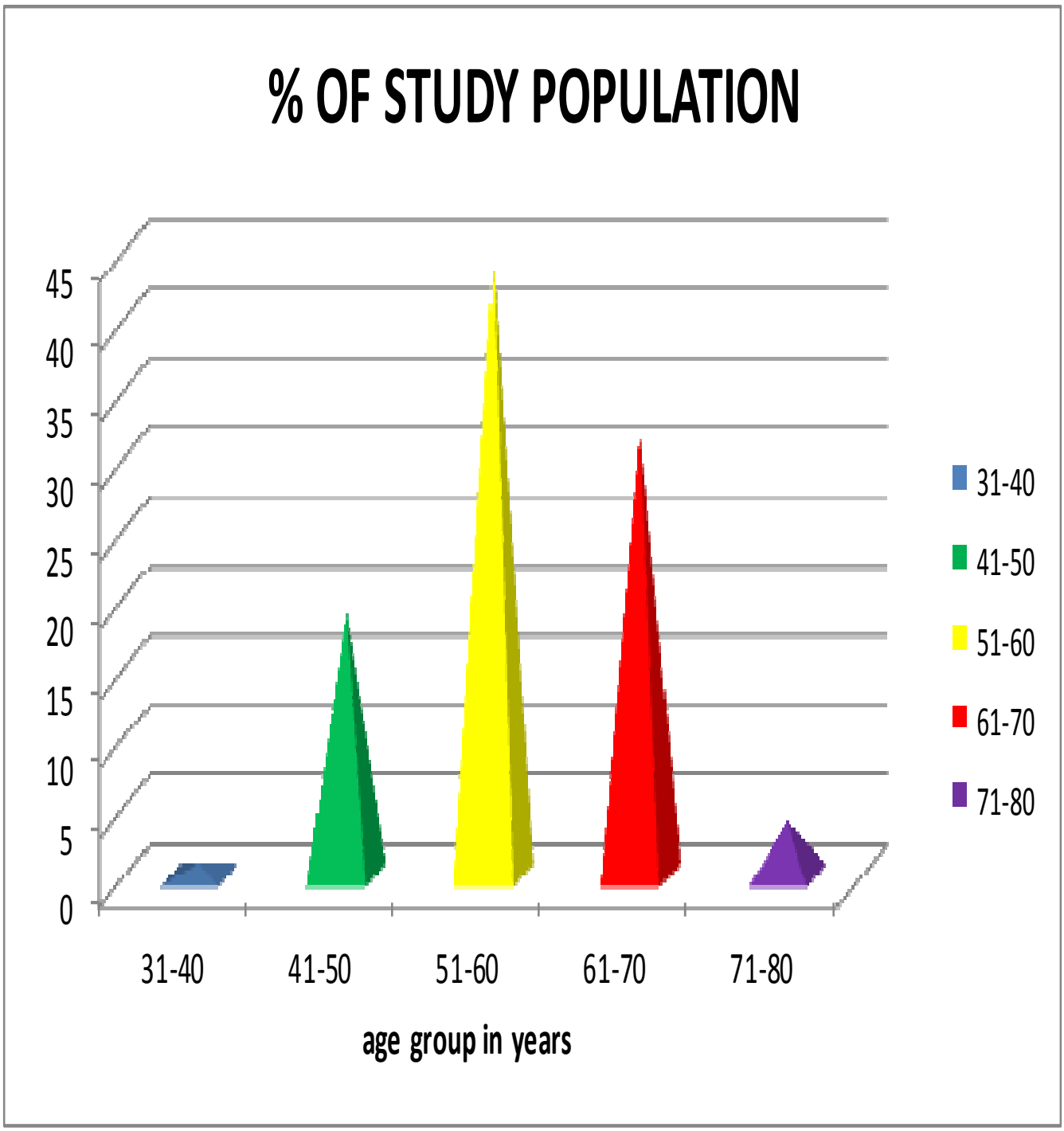

% OF STUDY POPULATION
45
40
35
30
25
20
15
10
5
0
31-40
41-50
51-60
61-70
71-80
age group in years
31-40
41-50
51-60
61-70
71-80

TABLE 4: LOCATION OF MI

DIABETIC STATUS/ LOCATION OF MI	DIABETIC	NON-DIABETIC
ANTEROSEPTAL	7	9
ANTERIOR WALL	35	17
INFERIOR WALL	18	14

Among the location of MI, anterior wall constitutes majority in both diabetic and non diabetic groups. Inferior wall comes second and anteroseptal constitutes the least

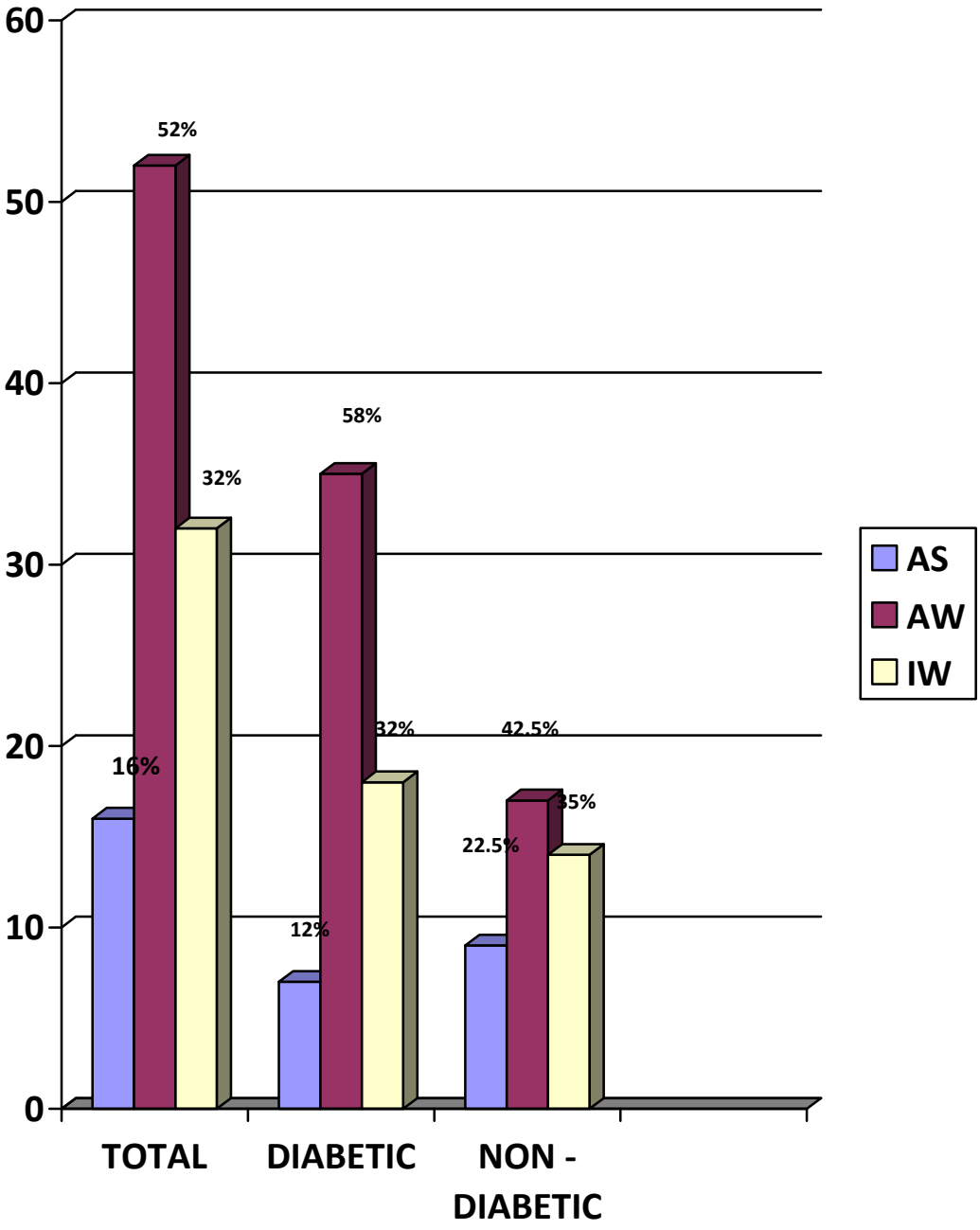
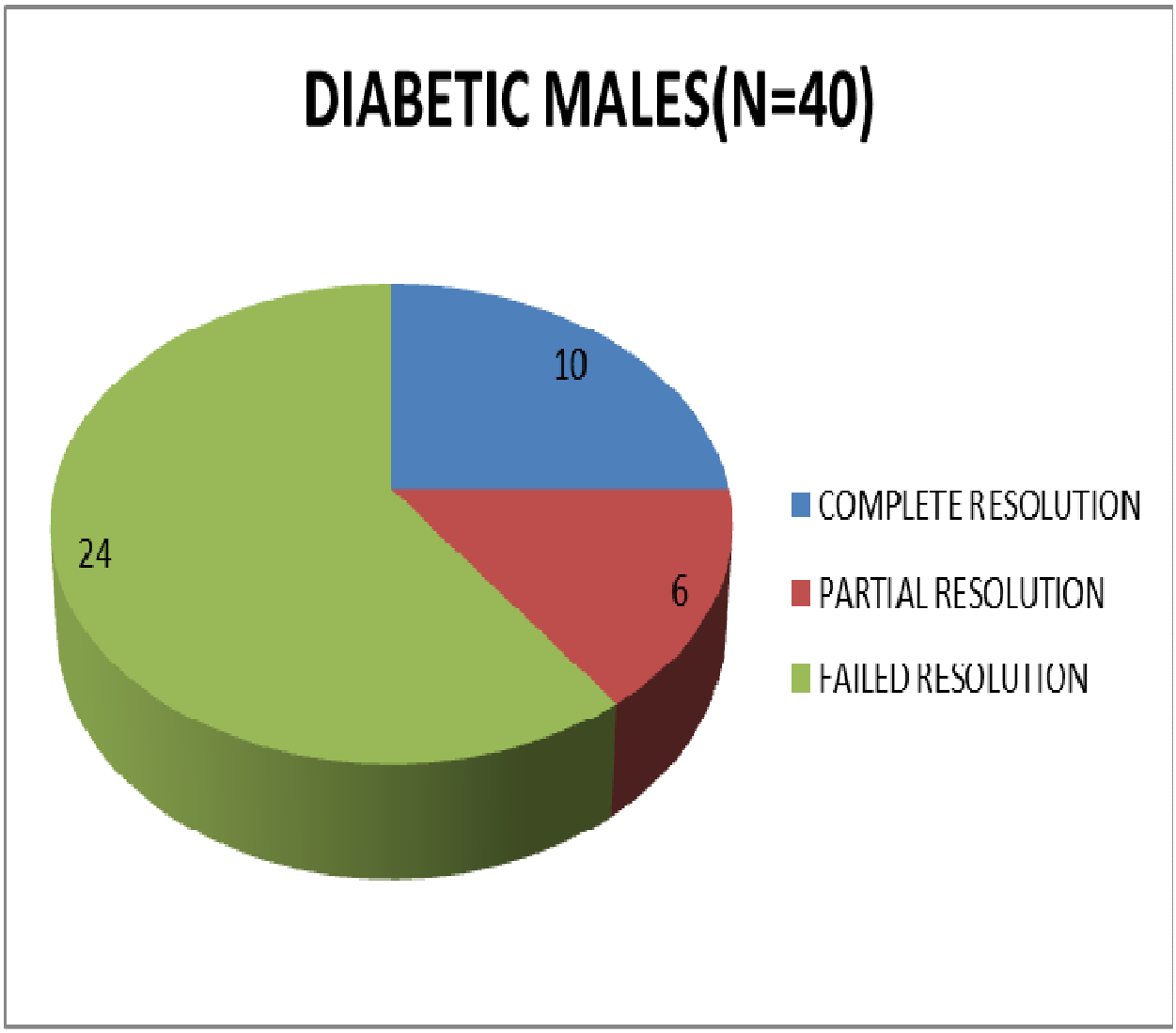

60
50
40
30
20
10
0
52%
32%
58%
16%
12%
42.5%
22.5%
AS
AW
IW
TOTAL
DIABETIC
NON - DIABETIC

TABLE 5: ST RESOLUTION IN SUB CATEGORIES- SEX AND DIABETIC STATUS

	COMPLETE RESOLUTION	PARTIAL RESOLUTION	FAILED RESOLUTION
DIABETIC MALES(N=40)	10(25%)	6(15%)	24(60%)
DIABETIC FEMALES(N=20)	3(15%)	2(10%)	15(75%)

Among diabetics subjects (n=60), 40 are males and 20 are females. Among diabetic males, 60% had failed resolution, 15 % had partial resolution and 25% had successful resolution. Among diabetic females, 75% had failed resolution, 10% had partial resolution, 15 % had successful resolution.

DIABETICS:


DIABETIC MALES(N=40)
10
6
24
COMPLETE RESOLUTION
PARTIAL RESOLUTION
FAILED RESOLUTION

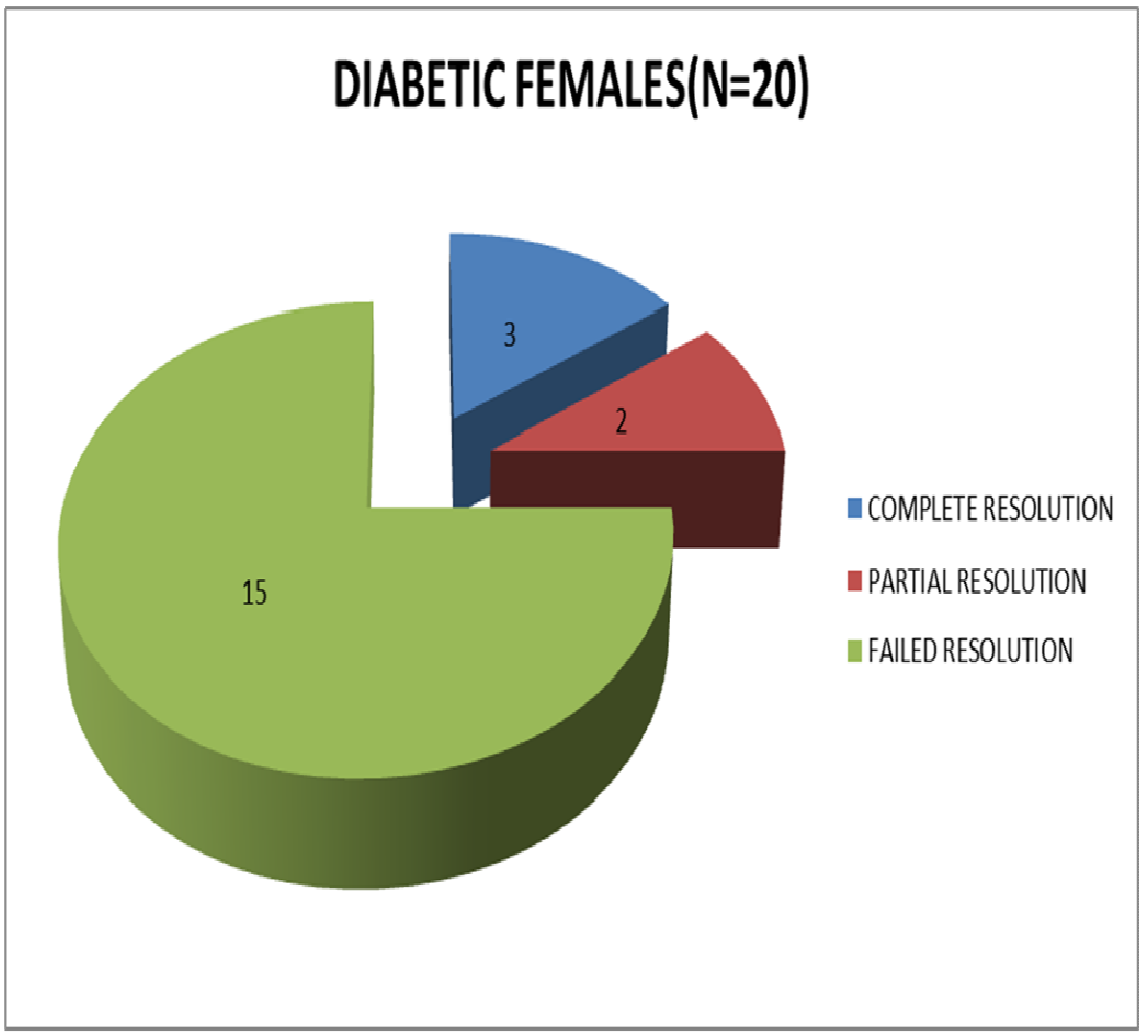
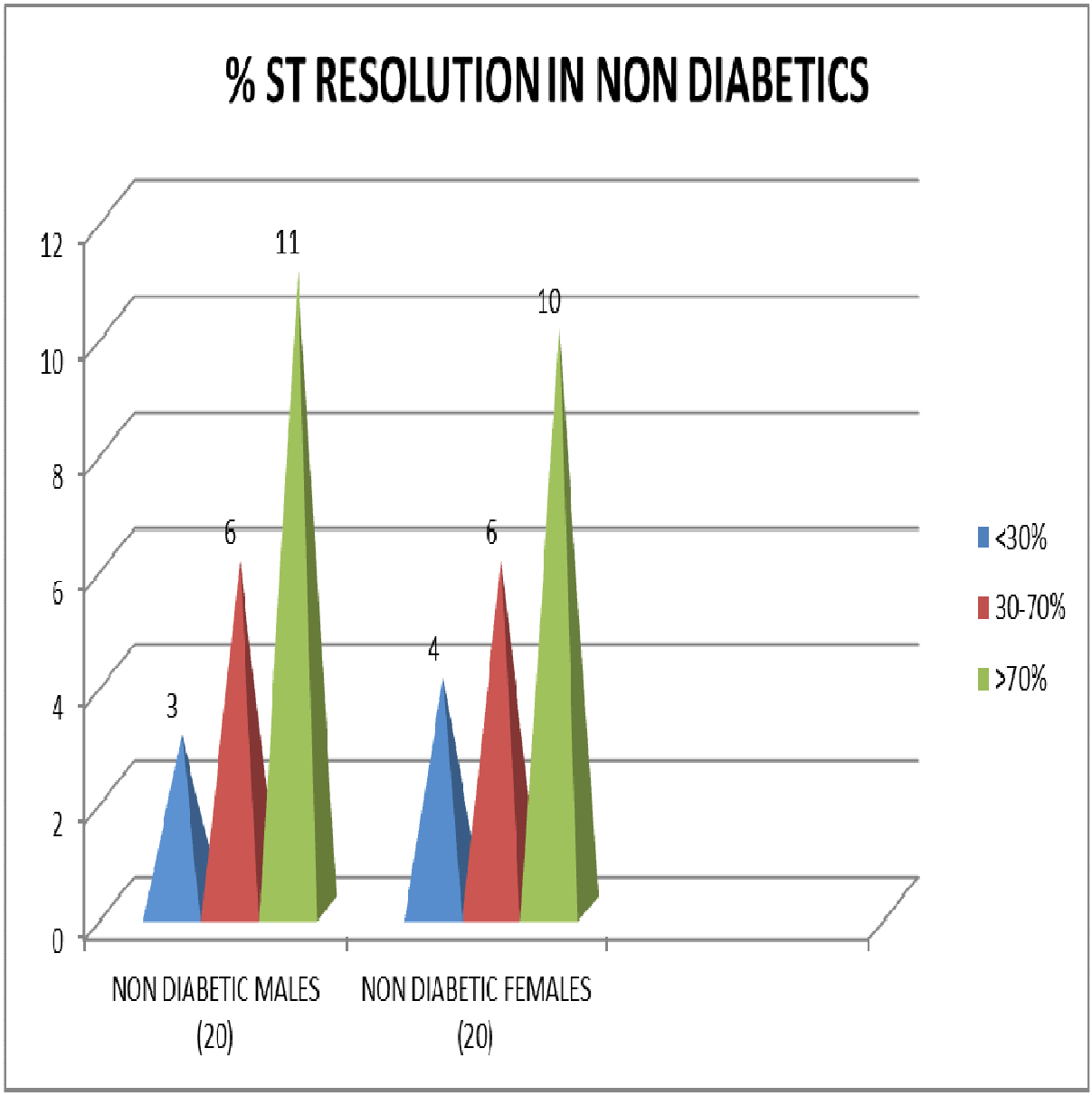

DIABETIC FEMALES(N=20)
3
2
15
COMPLETE RESOLUTION
PARTIAL RESOLUTION
FAILED RESOLUTION

TABLE 6 : ST RESOLUTION IN SUB CATEGORIES- SEX AND DIABETIC STATUS

	COMPLETE RESOLUTION	PARTIAL RESOLUTION	FAILED RESOLUTION
NON DIABETIC MALES(N=20)	11(55%)	6(30%)	3(15%)
NON DIABETIC FEMALES(N=20)	10(50%)	6(30%)	4(20%)

Among non-diabetics subjects (n=40), 20 are males and 20 are females. Among non -diabetic males, 55% had complete resolution, 30% had partial resolution and only 15% had failed resolution. Among non-diabetic females, 50% had complete resolution, 30 % had partial resolution and only 20 % had failed resolution.

NON-DIABETICS:



DISCUSSION:

A well recognized ,effective treatment during acute myocadial infarction is I.V. Streptokinase. For cardiovascular mortality , it has beneficial effect. Early and successful reperfusion is the aim of thrombolysis. When the reperfusion is incomplete, left ventricular disfunction occurs and the risk of mortality is increased.

The ongoing process of infarction as well as the metabolic derangement (due to ischemia) of the remaining viable cells must be reversed .

Serial monitoring of the reperfusion status , using ECG is an ideal method and is also cost effective. It tells much about the myocardial perfusion than epicardial perfusion . in fact, myocardial perfusion is a better factor which should be established at an earliest time, so that myocardial death can be prevented.

Various risk factors contribute to coronary heart disease. Hyperglycemia is an important major contributor for accentuation of coronary atherosclerosis.

As assessed by previous studies, the efficacy of thrombolytic therapy is established beyond doubt, both angiographically as well as electrocardiographically.

The main purpose of this study is to showthat diabetes as an independent factor affects the thrombolytic outcome after STEMI . this assessed with the help of ECG as a simple tool. The thrombolytic efficacy of streptokinase is also assessed by this study.

In patients without diabetes , efficacy is good ; it means that success rate of thrombolysis is more; failure rate is only less. But, in a diabetic patient presenting with STEMI , who are thrombolysed with streptokinase , because of presence of unfavourable , as well as extensive plaque pathology, the efficacy is poor ; that is , failure rate is more. So , PCI may be a better option for diabetes presenting with Myocardial Infarction.

Since there is an extensive disease involving vessels at multiple levels or involving multiple vessels, it is also found in many studies that CABG would be a better option finally for diabetic myocardial infarction patients.

In diagnosing diabetes for the first time after presentation, stress hyperglycemia should be excluded. Most patients have elevated blood sugar levels at initial presentation with myocardial infarction because of stress induced factors. Once the patients’s condition has stabilised or at a time before discharge, the diagnosis of diabetes mellitus should be made.

Initially , this stress induced hyperglycemia has deterimental effect to the patient. Various studies have confirmed the efficacy of GIK (glucose insulin with potassium) infusion for treatment of stress hyperglycemia.

Over the past decades, because of aggressive control of risk factors, cardiovascular events have reduced. Life style modifications, diet plan are important aspects in management of risk factors. Finally , a multi-factorial approach is needed to reduce chronic cardiovascular complications.

CONCLUSION:

1. On comparing the thrombolytic effect of Streptokinase , it is observed that failed thrombolysis (< 30% ST resolution) is more in diabetic STEMI patients when compared to non-diabetic STEMI patients.

2. Successful thrombolysis (>70% ST resolution) is more in non-diabetic than diabetic STEMI patients.

3. Among diabetics, failed thrombolysis (67%) is more than successful thrombolysis (18%).

4. Among non-diabetics, successful thrombolysis (52.5%) is more than failed thrombolysis (17.5%).

So, the outcome of thrombolysis of acute ST elevation myocardial infarction patients is affected by type 2 diabetes mellitus . In diabetic ST elevation myocardial infarction patients , Percutaneous coronary intervention can be a better option than thrombolysis. (Arch Intern Med 2007; 167(13)).

LIMITATIONS:

1. The time period from the onset of chest pain to the time of thrombolysis , that is the total ischemic time, is not take into account.

2. The efficacy of other newer thrombolytic agents needed to be tested.

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Rolf Schröder, MD

PROFORMA

Name : Age/Sex: Occupation:

I.P. no :

Address :

Date of admission :

Date of discharge :

Presenting complaints:

H/o chest pain, breathlessness, sweating, palpitation, giddiness, etc

Past history:

History of Diabetes mellitus, previous MI.

Clinical examination:

General examination:

Consciousness, dyspnoea, diaphoresis, Pallor, cyanosis

Vitals:

Pulse Rate, Blood pressure, Respiratory Rate, SpO2, temperature.

Systemic examination:

CVS, RS, abdomen and CNS

Laboratory investigations:

Random, fasting and post-prandial glucose

Electrocardiogram

ABBREVIATIONS:

MI- myocardial infarction

ACS- acute coronary syndrome

ECG- electrocardiogram

HDL-C- high density lipoprotein cholesterol

LDL-C- low density lipoprotein cholesterol

IGT- impaired glucose tolerance

CVD- cardiovascular disease

PCI- percutaneous coronary intervention

CABG- coronary artery bypass graft

vWF- von willebrand factor

PAI-1-plasminogen activator inhibitor-1

CRP- c-reactive protein

CVA- cerebrovascular accident

CAD- coronary artery disease

PCOD- polycystic ovarian disease

OGTT- oral glucose tolerance test

HbA1C- hemoglobin A1C

LBBB- left bundle branch block

LMCA- left main coronary artery

LCX- left circumflex

RCA- right coronary artery

LAD- left anterior descending

UA- unstable angina

STEMI- ST elevation myocardial infarction

DR- diabetic retinopathy

CPR- cardiopulmonary resuscitation

AV- atrioventricular

RVMI- right ventricular myocardial infarction

MASTER CHART

S.No	NAME	AGE/ SEX	MI	DM DURATION (IN YRS)	RBS	FBS	PPBS	INITIAL STE	90 MIN	% RESOLUTION	RESULT
1	Balakrishnan	50/M	IW	2	218	183	312	4	3.5	12.5	F
2	Natarajan	61/M	AW	2	208	135	203	26.5	20	24	F
3	Murugan	60/M	AW	1	180	102	152	17	5	71	S
4	Masanam	74/M	AW	1	198	115	260	10.5	5	52	P
5	Murugesan	60/M	AW	4	156	104	160	17	7.5	16	F
6	Jeevagan	34/M	AW	0	202	180	246	7	4	42	P
7	Paulraj	60/M	IW	2	212	92	236	7	2	71	S
8	Ravi	48/M	IW	3	192	126	220	15	5	66	P
9	Mookan	49/M	AS	4	148	105	188	21	3	85	S
10	Thangaraj	45/M	AW	7	219	150	242	24	2	12.5	F
11	Lakshmanan	51/M	IW	5	189	162	248	22.5	17.5	22	F
12	Ponnaiah	53/M	AW	3.5	232	198	270	26	16	23	F
13	Kannan	44/M	IW	2	162	130	206	25	6	76	S
14	Ravikumar	48/M	IW	8	191	152	289	20.5	15	26	F
15	Ramu	56/M	IW	0	204	130	219	28	20.5	27	F
16	Arumugam	51/M	AW	6	179	118	252	14	3	78	S
17	Munusamy	55/M	AW	10	210	190	280	13	10	23	F
18	Chandran	70/M	AS	20	194	126	241	27	20	25	F
19	Saravanan	65/M	AW	8	168	108	211	16	6	62	P
20	Saleem	62/M	AW	3	169	128	258	12	10	17	F
21	Satheesh	59/M	IW	4	212	176	235	16.5	12	27	F
22	Gurusamy	75/M	AW	11	200	155	218	20	5	75	S
23	Palani	51/M	AW	0	230	192	270	14	10	28	F
24	Rajan	56/M	AW	2.5	206	175	225	23	18	22	F
25	Kannan	60/M	IW	9	186	162	210	15	12	20	F
26	Karuppaiah	48/M	AW	6.5	224	140	260	28	23.5	16	F
27	Mani	54/M	AS	7	245	135	282	7	4	42	P
28	Jeevan	64/M	AW	3	216	150	248	16	12.5	22	F
29	Karuppan	65/M	IW	5	149	102	202	22	6	72	S
30	Palpandi	71/M	AW	8	196	146	213	17	12	29	F
31	Ibrahim	47/M	AW	0	225	165	246	27	24	11	F
32	Muthupandi	54/M	IW	4	260	190	289	13	11	15	F
33	Velmani	42/M	AW	3	182	100	205	12	7	41	P
34	Mari	57/M	IW	3	198	169	240	28	8	71	S
35	Muniappan	44/M	AW	5	221	159	210	19	16.5	13	F
36	Sheik	50/M	AW	5.5	209	121	269	22	18	18	F
37	Joseph	63/M	AS	7	252	153	288	18	15	71	F
38	Gowtham	55/M	AW	1	193	140	211	7	5	28	F
39	Senthil	66/M	AW	3	215	180	260	26	22	15	F

S.No	NAME	AGE/ SEX	MI	DM DURATION (IN YRS)	RBS	FBS	PPBS	INITIAL STE	90 MIN	% RESOLUTION	RESULT
40	Marimuthu	60/M	AW	6	232	163	249	15	12	20	F
41	Padma	53/F	AS	0	205	104	210	14	7	50	P
42	Muniammal	58/F	IW	6.5	189	135	214	18.5	15.5	16	F
43	Panchu	56/F	AW	9	242	172	251	12	8.5	29	F
44	Revathi	68/F	AW	18	202	149	213	19.5	17	12	F
45	Chandra	62/F	IW	4	198	132	216	26	7	73	S
46	Karuppayee	60/F	AW	5.5	276	195	290	14	10.5	25	F
47	Rakku	70/F	AW	12	212	156	249	9	7	22	F
48	Vasantha	54/F	IW	0	195	160	269	15	13	13	F
49	Princemary	56/F	AW	7	182	159	270	15	12	20	F
50	Subetha	59/F	AW	8	250	149	285	18	11	38	P
51	Kala	72/F	IW	11.5	280	192	302	28	25	10	F
52	Petchi	66/F	AS	14	195	139	252	14	4	71	S
53	Palaniammal	61/F	IW	5	280	179	310	25.5	21	18	F
54	Ramayee	59/F	AW	0	196	155	240	18	15	17	F
55	Kalaivani	64/F	AW	9	260	170	298	10	7.5	25	F
56	Lurthubegam	61/F	IW	7	212	160	240	21	5	76	S
57	Rani	57/F	AW	3	230	149	220	30	27	10	F
58	Lakshmi	69/F	AW	9	186	130	205	14.5	11.5	21	F
59	Allirani	57/F	AS	5	259	282	314	7.5	5.5	26	F
60	Ramathilagam	52/F	AW	6	257	220	399	17	10.5	40	P
61	Elango	54/M	IW	0	135	70	1322	25	7	72	S
62	Murugaiyan	48/M	AW	0	112	85	136	13.5	7.5	44	P
63	Alagarsamy	50/M	AW	0	105	89	120	19	9	53	P
64	Balu	70/M	IW	0	140	97	109	15	3.5	77	S
65	Arokiadoss	66/M	AS	0	129	79	113	21	18	14	F
66	Chellaiya	65/M	AW	0	109	89	119	12	3	75	S
67	Muthu	61/M	AW	0	131	93	124	23	15	35	P
68	Sundar	64/M	IW	0	123	73	115	16.5	4.5	72	S
69	Murugapandi	48/M	AW	0	109	79	102	16.5	4	76	S
70	Kannan	50/M	AW	0	96	89	109	22.5	3	87	S
71	Rafeeq	56/M	IW	0	150	83	105	14	10.5	25	F
72	Velu	63/M	AS	0	119	74	112	12.5	3.5	72	S
73	Prabhakaran	54/M	AW	0	106	79	115	26	14.5	44	P
74	Mookan	51/M	AW	0	115	93	108	23	6.5	72	S
75	Thangam	46/M	IW	0	139	90	105	15	12	20	F
76	Kumar	57/M	AS	0	145	86	111	29	4	86	S
77	Muniyandi	55/M	AW	0	121	75	119	12.5	3.5	72	S
78	Ramani	52/M	IW	0	116	71	136	13	6.5	50	P
79	Selvam	67/M	IW	0	102	74	129	11.5	3.5	70	S
80	Mahalingam	65/M	AS	0	98	86	□09	19	10.5	45	P
81	Muthupechi	59/F	AS	0	98	78	121	18	5.5	69	P
82	Vadivu	55/F	AW	0	103	69	105	27	5	81	S
83	Amutha	60/F	IW	0	133	73	111	16	13	19	F
84	Pavithra	63/F	AW	0	129	89	125	27.5	24	13	F

S.No	NAME	AGE/ SEX	MI	DM DURATION (IN YRS)	RBS	FBS	PPBS	INITIAL STE	90 MIN	% RESOLUTION	RESULT
85	Rajammal	49/F	IW	0	116	67	115	23.5	3.5	85	S
86	Chellammal	54/F	AS	0	109	73	113	12.5	6	52	P
87	Priya	58/F	IW	0	131	79	119	18.5	9	51	P
88	Rasiyabegam	68/F	AW	0	145	84	124	22	6	73	S
89	Jansi	48/F	AW	0	107	89	124	9	2.5	72	S
90	Christy	54/F	AS	0	111	81	119	14	10	28	F
91	Jamela	62/F	IW	0	123	94	117	19.5	5	74	S
92	Tamilselvi	69/F	IW	0	130	74	129	26	13	50	P
93	Mookammal	64/F	AW	0	125	77	136	25	3.5	86	S
94	Muneeswari	52/F	AS	0	115	70	120	7	5	28	F
95	Rajathi	61/F	AW	0	107	92	133	13	3.5	73	S
96	Shanthi	47/F	IW	0	118	94	129	15.5	8	48	P
97	Vasantha	58/F	IW	0	128	84	130	20	4	80	S
98	Lalitha	63/F	AW	0	124	88	129	13.5	3	78	S
99	Leela	56/F	AS	0	129	79	130	22	9.5	57	P
100	Gandhimathi	70/F	AW	0	140	80	116	11.5	2.5	78	S

Ref.No.3372/E1/5/2014

Madurai Medical College,
Maduai -20. Dated: 04.2014.

Institutional Review Board/Independent Ethics Committee
Capt.Dr.B.Santhakumar,MD (FM). deanmdu@gmail.com
Dean, Madurai Medical College &
Government Rajaji Hospital, Madurai 625 020 . **Convenor**

Sub: Establishment – Madurai Medical College, Madurai-20 –
Ethics Committee Meeting – Meeting Minutes - for April 2014 –
Approved list – reg.

The Ethics Committee meeting of the Madurai Medical College, Madurai was held on 25th April 2014 at 10.00 Am to 12.00 Noon at Auditorium Hall at Govt. Rajaji Hospital, Madurai . The following members of the Ethical Committee have attended the meeting.

1.**Dr.V.Nagarajan,M.D.,D.M(Neuro)** Ph: 0452-2629629 Cell No.9843052029 nag9999@gmail.com.	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	**Chairman**
2.**Dr.Mohan Prasad, MS.M.Ch.** Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology (Retired) D.No.32, West Avani Moola Street, Madurai.-1	**Member Secretary**
3.Dr.K.Parameswari, MD(Pharmacology) Cell No.9994026056 drparameswari@yahoo.com.	Director of Pharmacology Madurai Medical College.	**Member**
4.Dr.S.Vadivel Murugan, MD., (Gen.Medicine) Cell No.9566543048 svadivelmurugan_2007@rediffmail.com.	Professor & H.O.D of Medicine Madurai Medical College	**Member**
5. Dr.L.Santhanalakshmi, MD (Physiology) Cell No.9842593412 dr.l.santhanalakshmi@gmail.com.	Vice Principal, Prof. & H.O.D. Institute of Physiology Madurai Medical College	**Member**
6.Dr.A.Sankaramahalingam, MS., (Gen. Surgery) Cell.No.9443367312 chandrahospitalmdu@gmail.com	Professor & H.O.D. Surgery Madurai Medical College, Madurai	**Member**
7.Mrs.Mercy Immaculate Rubalatha, M.A., Med., Cell.No.9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's Quarters, Gandhi Museum Road, Thamukam, Madurai-20.	**Member**
8.Thiru.Pala.Ramasamy, B.A.,B.L., Cell.No.9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72,Palam Station Road, Sellur, Madurai-20.	**Member**
9.Thiru.P.K.M.Chelliah, B.A., Cell No.9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20.	**Member**

The following project was approved

Name of the PG Student	Course	Name of the project	Remarks
Dr.R.Ramkumar ramkumar.mmc@gmail .com	**PG in MD (General Medicine) Govt. Rajaji Hospital & Madurai Medical College, Madurai**	**A study on Thrombolytic effect of streptokinase infusion between Diabetic and Non-Diabetic myocardial infarction Patients with ECG as a Tool.**	**Approved. Post study evaluation to be done.**

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.

2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the E thical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

chairman

12.5.14

Member Secretary
Ethical Committee

Ethical committee

DEAN/Convenor
Madurai Medical College &
Govt. Rajaji Hospital, Madurai- 20.

To
The above Applicant
-thro. Head of the Department concerned

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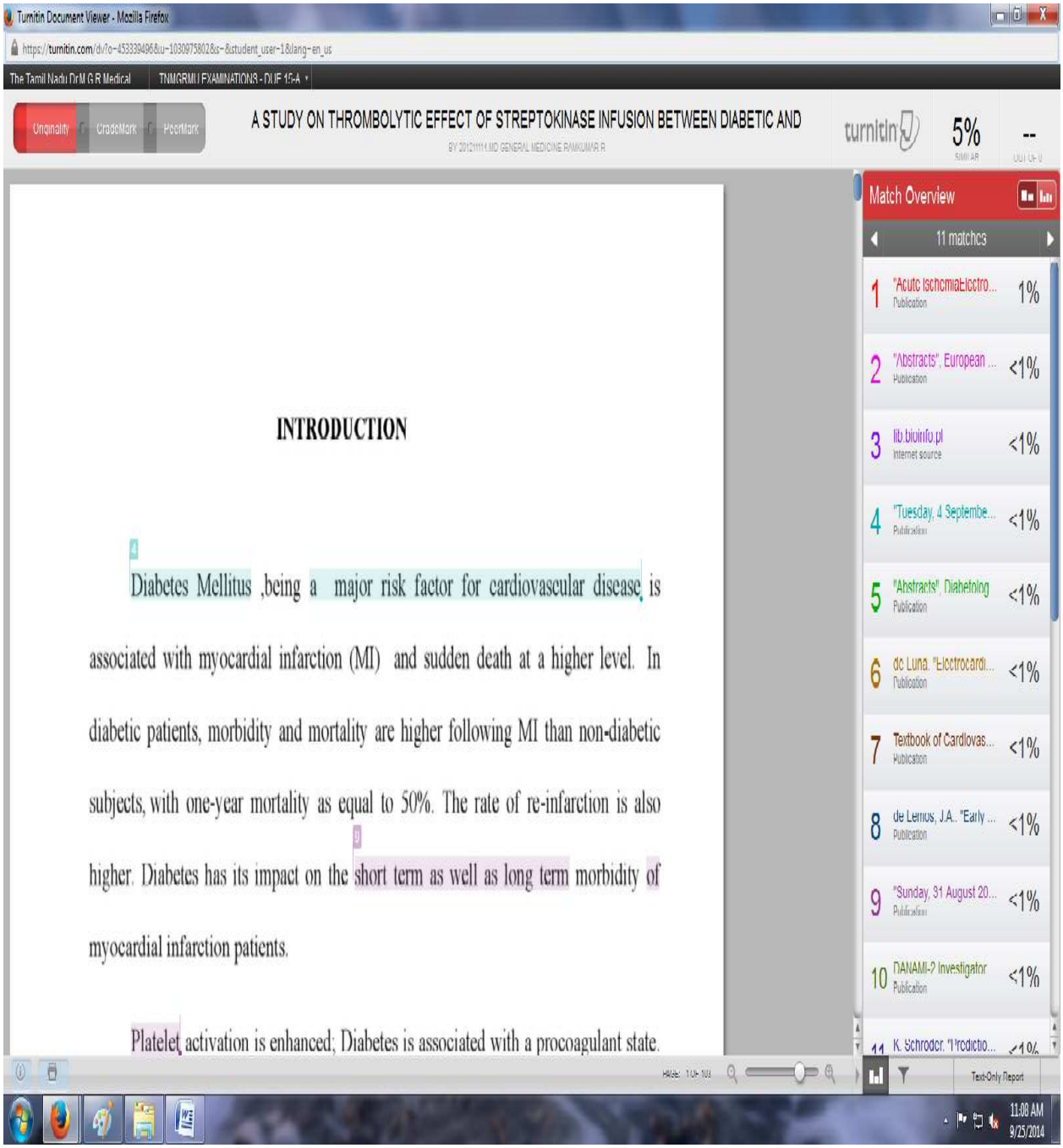
INTRODUCTION



INTRODUCTION

Diabetes Mellitus ,being a major risk factor for cardiovascular disease, is associated with myocardial infarction (MI) and sudden death at a higher level. In diabetic patients, morbidity and mortality are higher following MI than non-diabetic subjects, with one-year mortality as equal to 50%. The rate of re-infarction is also higher. Diabetes has its impact on the short term as well as long term morbidity of myocardial infarction patients.

Platelet activation is enhanced; Diabetes is associated with a procoagulant state.