IMPAIRED GLUCOSE TOLERANCE IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION - A PERSPECTIVE STUDY

Dissertation submitted for

DM Degree (Branch II) Cardiology
February 2006

The Tamilnadu Dr.M.G.R.Medical University
Chennai, Tamilnadu.

CERTIFICATE

This is to certify that this dissertation titled **"IMPAIRED GLUCOSE TOLERANCE IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION - A PERSPECTIVE STUDY"** submitted by **DR.G.Prathap Kumar** to the faculty of Cardiology, The Tamil Nadu Dr. M.G.R. Medical University, Chennai. in partial fulfillment of the requirement for the award of DM degree Branch II [Cardiology] is a bonafide research work carried out by him under my direct supervision and guidance .

Professor and Head,
Department of Cardiology,
Madurai Medical College and
Govt. Rajaji Hospital, Madurai.

.

DECLARATION

I, **Dr.G.Prathap Kumar**, solemnly declare that the dissertation titled **"IMPAIRED GLUCOSE TOLERANCE IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION - A PERSPECTIVE STUDY"** has been prepared by me.

This is submitted to the Tamil Nadu, Dr. M.G.R. Medical University Chennai, in partial fulfillment of the regulations for the award of DM degree Branch II [Cardiology].

Place : Madurai

Date :

DR. G. PRATHAP KUMAR

ACKNOWLEDGEMENT

My sincere thanks to **The Dean, Dr.M.Vasantha M.D,** for permitting me to use the facilities of Madurai Medical College and Govt. Rajaji Hospital to conduct this study.

My Professor and Head of the Department of Cardiology, **Prof.Dr.M.Anandhan M.D.D.M,** has always guided me, by example and valuable words of advice through out the conduct of the study and also during my postgraduate course. My sincere thanks to him.

My heartfelt thanks to my **Prof.Dr.M.Annamalai M.D.D.M,** for his valuable support and guidance through out the study and also for making my stay in the unit both informative and pleasurable.

I will ever remain in gratitude to my guide **Dr.S.Murugan, MD. DM,** not only for guiding me through this study, but also for being my mentor and source of inspiration during the period of my postgraduate training. I thankyou sir with my heart.

I express my sincere thanks to the Reader of the Department of Cardiology, **Prof.Dr.Jeyachandran M.D., D.M,** for his valuable help and guidance through out my study.

Knowledge and kindness abounds my beloved teachers, **Dr.S.Palanichamy, M.D.D.M, Dr.V.Amuthan,M.D.D.M, Dr.R.A.Janarthanan M.D.DM, Dr.S.Balasubramanian M.D.DM, Dr.S.Nainamohammed M.D.DM,** I owe them a lot and my sincere thanks to them without whose help the study would not have been a reality.

I express my immense pleasure in thanking **Prof. Dr. Ramadevi, M.D.,** the Professor and Head of the Department of Biochemistry, Madurai Medical College, Madurai, for her valuable help through out my study.

I express my sincere thanks to my co-post graduates for their immense help and enthusiasm. I also thank staff nurses and laboratory technicians who helped me to finish my dissertation without any hindrance.

I express my warm gratitude to Media Nett Internet Browsing Centre for their cooperation to complete this work in time.

I express my heartfelt thanks to all my patients without whom this study would not have been possible.

Last but not the least; I thank God almighty for this abundant blessing, the lessons which I have learned and for the strength and guidance to complete the study successfully.

CONTENTS

INTRODUCTION

Acute Myocardial Infarction is a serious and life threatening disorder. There are various risk factors for the development of Acute Myocardial Infarction. Of them, the most important and the one which is causing havoc among South Asian and Indian population is the relationship between abnormal glucose metabolism and Acute Myocardial Infarction. It is a well known fact that Diabetes Mellitus, a full blown form of abnormal glucose metabolism is associated with increased risk of cardiovascular events like AMI, unstable angina, Cerebrovascular events like stroke & also with peripheral vascular disease.

Whether the new concept of Impaired Glucose Tolerance, Impaired Fasting Glucose also have similar effects on the morbidity and mortality of the patients with AMI & their relationship is either causal or casual needs to be urgently evaluated.

Also, the incidence of Impaired Glucose Tolerance, Impaired Fasting Glucose is increasing in the population especially among the Indians and South East Asians. The Impaired Glucose Tolerance, Impaired Fasting Glucose are considered as prediabetic state, in the contemporary literature. Whether the detection of an individual in this prediabetic state & proper treatment with life style modification can bring down the risk of future cardio vascular events like Unstable Angina, AMI are questions to be answered.

With this background of Impaired Glucose Tolerance, Impaired Fasting Glucose metabolic abnormalities, their incidence in the patients with Acute Coronary Syndromes

and their influence on the outcome of the cardio vascular events with respect to mortality and morbidity is studied in this dissertation.

Also the effect of these prediabetic states on the left ventricular function in the post myocardial infarction period and on the functional capacity of the individual is studied in detail in this thesis.

AIMS OF THE STUDY

1. To compare and contrast the in-hospital outcomes of patients with Acute Myocardial infarction with normal Glucose Metabolism and Abnormal Glucose Metabolism – Impaired Glucose Tolerance.
2. To study the effect of Impaired Glucose Tolerance on the left ventricular function in these patients.
3. To assess the functional capacity of the patients with Myocardial infarction with Impaired Glucose Tolerance.

REVIEW OF LITERATURE

Whether high but non diabetic blood glucose levels are predictive of increased mortality from Coronary Artery Disease is not a new issue. This topic was discussed in International collaborative group in 1979. The conclusion from this analysis was that there was no consistent, strong and graded associated between asymptomatic hyperglycemic individuals and coronary artery disease.

Donaheu and Orchard reviewed the same question and concluded that glucose levels were related to Coronary artery disease risk, but whether the effect was linear or threshold was not clear in their study.

Jarret et al concluded that the risk did not appear to be related linearly with the glucose levels, but is apparent only in the upper percentiles of glucose distribution.

In our study we report the association of Fasting Blood Sugar and 2 hour post glucose challenge blood sugar level with the in-hospital events like arrhythmias, heart failure, recurrent angina, pericarditis and death.

We also report the association between fasting blood sugar and 2 hour glucose levels with Left ventricular function by analyzing the ventricular ejection fraction, end diastolic volume, end systolic volume, Wall motion score index and functional capacity as assessed by number of Mets in standard Bruce protocol Symptom limited Treadmill test before discharge from the hospital.

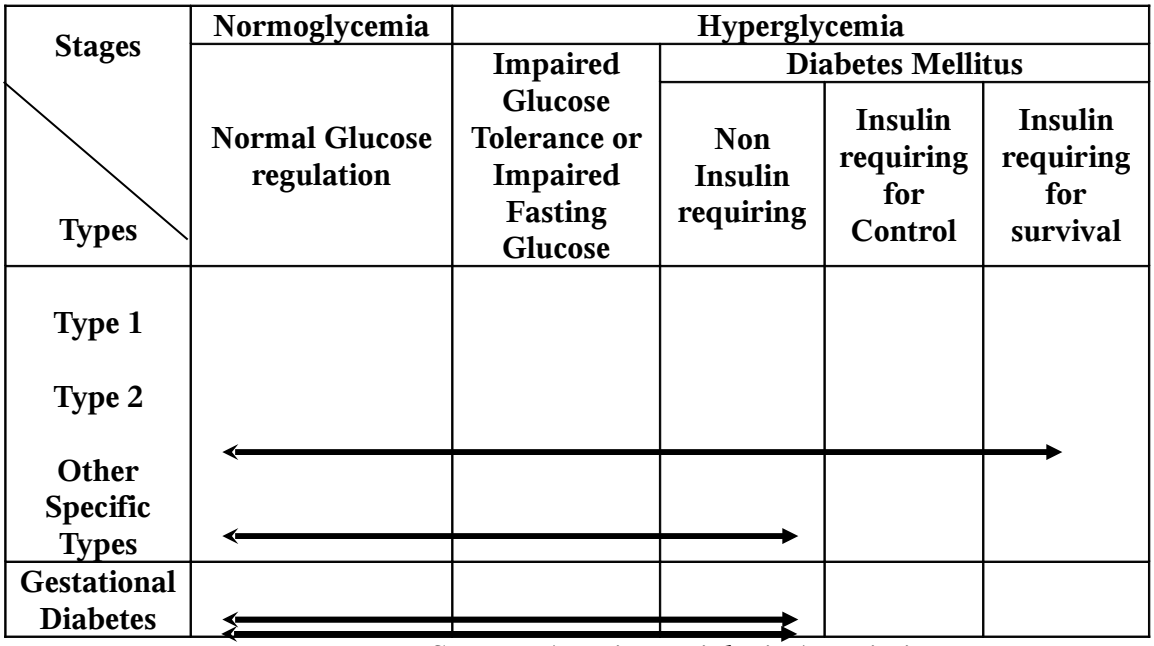
Hyperglycemia in the absence of diagnosis of diabetes (blood sugar < 200mg %) is a common phenomenon in stress related conditions like Acute Myocardial Infarction.

The cause of this hyperglycemia is primarily from excessive release of counter regulatory hormones.

Also, hyperglycemia refers to a pre-diabetic state in patients who are not diagnosed to have diabetes and whose blood sugar levels are in the abnormal range. This state is referred to as Impaired Glucose Tolerance.

Impaired Glucose Tolerance and Impaired Fasting Glucose are a continuum in the spectrum of disorder of glycemia.

Disorders of Glycemia : Etiologic Types and Stages



Source : American Diabetic Association

So, the disorder Impaired Glucose Tolerance and Impaired Fasting Glucose are considered as pre-diabetic state.

Multiple studies have shown that hyperglycemia in the diabetic range was associated with 3-4 fold increase in coronary artery disease risk and the outcome in the patients with diabetes was far more worse than that of the patients with out diabetes.

We in our study are establishing that whether this statement could be extrapolated to the patients who fall in Impaired Glucose Tolerance and Impaired Fasting Glucose range.

Recently, ACC/AHA guidelines have included the presence of Diabetes Mellitus as a major risk factor for coronary artery disease. Also, the Framingham Heart study reiterates that the patients with hyperglycemia in diabetic range have increased mortality and morbidity than the patients with normal glycemia.

A recent concept of Dysglycemia which includes Impaired Glucose Tolerance and Impaired Fasting Glucose is also under vogue. **Sahay et al** in his review has introduced the concept of Dysglycemia. The risk of coronary artery disease is high even at the time of diagnosis of Type 2 Diabetes Mellitus, hence the pre-diabetic states are also associated with increased risk of coronary artery disease.

Cardio vascular disease is leading cause of morbidity and mortality in patients with Diabetes Mellitus and the risk of Myocardial Infarction can be as high as in non diabetic individuals with history of Myocardial Infarction.

This has led to the National Cholesterol Educational Programme Adult Treatment Panel III (NCEP ATP III) to consider diabetes as Coronary Artery Disease equivalent.

It is now being recognised that revised blood glucose even below the threshold necessary to diagnose diabetes or even impaired glucose tolerance is associated with considerable increased risk of coronary artery disease. There appears to be a continuous relation between risk of coronary artery disease and raised post prandial glucose

concentration that extends from barely elevated levels right into the diabetic range.

That the glucose concentration associated with increased risk of Coronary Artery Disease are lower than those required for diagnosis of diabetes should not be surprising. Since these criteria are based on specific glucose concentration above which the individuals are at risk for development of nephropathy and retinopathy and not cardio vascular disease.

Although post prandial glucose levels above which the patients are at an increased risk of coronary artery disease is not yet defined, it may be as low as 98 mg %. Since this value is much lower than that which would qualify for diagnostic of Impaired Glucose Tolerance. The term Dysglycemia is suggested to define the range of glucose concentration associated with risk of Coronary Artery Disease (**Gerstein et al**).

Dysglycemia therefore includes in addition to the pre-diabetic states (Impaired Glucose Tolerance and Impaired Fasting Glucose), blood glucose values much below this threshold.

Impaired Glucose Tolerance & Impaired Fasting Glucose places the individuals at risk of developing diabetes mellitus and its complications. Both Impaired Glucose Tolerance and Impaired Fasting Glucose appear well before type 2 diabetes mellitus is diagnosed and they present an opportunity for intervention to reduce the future burden of diabetes and associated coronary artery disease risk to the individual and to the community.

Diagnostic values for Oral Glucose Tolerance Test (OGTT) for Diabetes Mellitus & other categories of Hyperglycemia

	Whole Blood Glucose		Plasma Glucose	
	Venous	**Capillary**	**Venous**	**Capillary**
Diabetes Mellitus				
Fasting	≥ 6.1 (≥ 110)	≥ 6.1 (≥ 110)	≥ 7.0 (≥ 126)	≥ 7.0 (≥ 126)
2 hr after 75 gm glucose load	≥10.0 (≥ 180)	≥11.1 (> 200)	≥11.1 (≥ 200)	≥12.2 (> 220)
Impaired Glucose Tolerance				
Fasting Value	< 6.1 (< 110)	< 6.1 (<110)	< 7.0 (<126)	< 7.0(<126)
2 hr after 75 gm glucose load	6.7 – 10.0 (120-180)	7.8 – 11.1 (140-200)	7.8 – 11.1 (140-200)	8.9-12.2 (160-220)
Impaired Fasting Glucose				
Fasting Value	5.6 – 6.1 (100-110)	5.6-6.1 (100-110)	6.1-7.0 (110-126)	6.1-7.0 (110-126)
2 hr after 75 gm glucose load	<6.7 (<120)	<7.8 (<140)	<7.8 (<140)	<8.9 (<160)

Source : American Diabetic Association

Note :

1. Values are given in mmol/lt, values given in the parenthesis are mg/dl.
2. The plasma glucose is 15% higher than the whole blood glucose. In a fasting state the 'Venous and Capillary Whole blood glucose is one and the same. But varies in the postprandial state. But with plasma glucose both the venous and capillary values are and the same.

3. WHO recommends 75 gm glucose load for adults and pregnant women.
4. Fasting value alone is considered less reliable, because true fasting cannot be assured and spurious diagnosis of diabetes may readily occur.
5. 1 mmol/l x 18 = mg % (conversion formula).

Importance of Impaired Fasting Glucose and Impaired Glucose Tolerance:

There is no clear consensus with current evidence on whether Impaired Fasting Glucose and Impaired Glucose Tolerance should be classified as diseases. But they clearly represent risk factors and risk markers for diabetes and cardio vascular disease respectively. Both Impaired Fasting Glucose and Impaired Glucose Tolerance are similarly associated with increased risk of diabetes. But Impaired Glucose Tolerance is strongly associated with cardio vascular disease outcomes.

Risk of hyperglycemia

Several explanations may account for the observed increased risk between hyperglycemia and poor prognosis after myocardial ischemia. **Metha et al** in his observation has found that hyperglycemia may be directly toxic to ischemic myocardium. Increase in the lactate content and intra cellular acidosis in the cells of ischemic myocardium are seen in patients with hyperglycemia.

Hyperglycemic patients are relatively deficient in insulin and this leads to both reduced peripheral uptake of glucose and may lead to decrease in the availability of glycolytic substrate for cardiac muscle utilization and increase in free fatty acid

concentration in ischemic musculature. These changes may reduce myocardial contractility even at increased oxygen concentration. It also increases the myocardial oxygen demand for the amount of myocardial work done leading to pump failure, and promote arrhythmias. (**Sarah E.Capes et al**)

According to **Sarah E.Capes et al** in meta analysis of 15 articles hyperglycemia is not simply an epiphenomenon of stress response mediated by cortisol and nor-adrenaline. It is associated increased risk of in-hospital mortality, increased risk of congestive heart failure and cardiogenic shock.

Hyperglycemia is a reflection of relative insulin deficiency and is associated with increased lipolysis, and excess circulating Free Fatty Acids (FFA), this effect may be exaggerated in cases of acute stress like Acute Myocardial Infarction.

Free Fatty Acids (FFA), although normally the substrate of choice for healthy myocardium, are toxic to ischemic myocardial and may lead to damaged cardiac cell membrane, calcium overload, and arrhythmias.

Moreover in animal studies conducted by **Mjos et al**, high concentration of Free Fatty Acids during myocardial ischemia causes increase in myocardial oxygen demands and decreased myocardial contractility.

Beta blockers suppress this release of Free Fatty Acids in patients with myocardial infarction and lessens the harmful effects of hyperglycemia and insulin deficiency. (**Malmberg et al**)

Insulin deficiency may also limit the ability of cardiac muscle to take up glucose

for anaerobic metabolism. In animal studies by **Ebreli et al**, preservation of myocardial function during ischemia correlates with increased uptake and metabolism of glucose.

The potential importance of insulin deficiency is also highlighted by randomised controlled trials in which insulin administered to patients without diabetes who have had acute myocardial infarction have improved clinical outcomes.

A similar observation was reported in DIGAMI study in which 620 patients with diabetes who had acute myocardial infarction were randomly assigned an insulin infusion followed by multidose subcutaneous insulin treatment for at least 3 months or conventional management. In that study, insulin lowered mortality by 28% (p 0.11) after mean follow up of 3-4 yrs and high glucose concentration on admission predicted higher risk of mortality.

Acute hyperglycemia may also precipitate an osmotic diuresis. The resulting volume depletion may interfere with the Frank Starling mechanism, an important compensatory mechanism for the failing Left Ventricle in which increased end diastolic volume leads to increased stroke volume.

Hyperglycemia may be a marker of more extensive cardiac damage in acute myocardial infarction, more extensive cardiac damage may lead to a greater rise in stress hormones promoting glycogenolysis and may also increased the risk of congestive heart failure and mortality.

Hyperglycemia in Impaired Glucose Tolerance is associated with hypertension, dyslipidemia and insulin resistance, a complex situation called Metabolic Syndrome - X.

According to National Cholesterol Educational Programme Adult Treatment Panel III, metabolic syndrome is diagnosed by following criteria.

Risk factors	Defining Levels
Abdominal obesity (Waist Circumference) Men Women	 > 102cm (> 40 in) > 88 cm (> 35 in)
Triglycerides	> 150 mg%
HDL – C Men Women	 < 40 mg% < 50mg%
Blood Pressure	> 130 / 80 mm Hg
Fasting Glucose	> 110 mg %

Diagnosis is established when > 3 of these risk factors are present.

Criteria for Hypertriglyceridemic waist in men

Character	Criteria
Triglyceride	> 2.0 mmol/l
Waist	> 90cm

Pathophysiology of Hyperglycemia in causing vascular disease

Abnormalities in endothelial and vascular smooth muscle cell function as well as propensity to thrombosis, contribute to atherosclerosis and its complications. Endothelial cells are biologically active and produce substances that maintain intra vascular hemostasis. It also ensures adequate blood flow and nutrient delivery while preventing thrombosis and leukocyte diapedesis.

Most important of the substances produced by endothelium is Nitric Oxide (NO). Metabolic derangements like hyperglycemia and hyperlipidemia increase free fatty acid liberation and insulin resistances and prevent Nitric Oxide production.

Impaired Glucose Tolerance mediate the abnormalities in endothelial cell function by affecting synthesis or increased degradation of Nitric Oxide.

Experimental evidence supports that hyperglycemia decreases endothelium derived Nitric Oxide. Hyperglycemia induces a series of cellular events that increases the production of Reactive Oxygen Species like super oxide anion that inactive Nitric Oxide to form peroxynitrite.

Hyperglycemia may initiate this process by increasing super oxide anion production via mitochondrial electron transport chain. Super oxide then promotes a cascade of endothelial process that produce oxygen derived free radicals which activate second messengers like Protein Kinase C (PKC).

Mitochondrial production of super oxide anion also increases the production of Advanced Glycation End products (AGE). These glycated proteins adversely affect the cellular function by altering the protein function and by activating the Receptors for Advanced Glycation End products (RAGE). Advanced Glycation End products perse increase the production of oxygen derived free radicals. Receptors for Advanced Glycation End products activation increases intra cellular enzymatic super oxide production.

Hyperglycemia induced oxidative stress increases the levels of Asymmetric Dimethyl Arginine (ADMA), a competitive antagonist of Nitric Oxide Synthase (NOS), by impairing the activity of dimethyl arginine dimethyl aminohydrolase to metabolise Asymmetric Dimethyl Arginine (ADMA).

Hyperglycemia also increases the production of lipid second messenger Diacyl Glycerol (DAC). Diacyl Glycerol causes membrane translocation and activation of Protein Kinase C (PKC), which decreases endothelium dependent vaso relaxation.

Free Fatty Acids liberation and Endothelial function

Circulating Free Fatty Acids are increased in Impaired Glucose Tolerance, because of their excess liberation from adipose tissue and diminished uptake by skeletal muscle. Free Fatty Acids impair endothelial function by increasing the production of oxygen derived free radicals, activation of Protein Kinase C (PKC) and exacerbation of dyslipidemia. Both hypertriglyceridemia and low High Density Lipoprotein (HDL) have been associated with endothelial dysfunction.

Impaired Glucose Tolerance, Thrombosis and Coagulation

Platelet function is also abnormal in Impaired Glucose Tolerance. Expression of both glycoprotein Ib and IIb / IIIa are increased, augmenting the platelet von Willebrand Factor (vWF) and platelet fibrin interaction. Hyperglycemia further changes platelet function by impairing calcium hemostasis. It also alters many aspects of platelet activation and aggregation, including platelet confirmation and release of mediators.

Plasma coagulation factors (eg. Factor VII and Thrombin) and lesion based

coagulants (tissue factors) are increased in impaired glucose tolerance. Endogenous anticoagulation like thrombomodulin and protein C are decreased. Also the production of Plasminogen Activator Inhibitor (PAI-1), a Fibrinolytic inhibitor is increased. Thus, a propensity for platelet activation and aggregation coupled with a tendency for coagulation is relevant for an increased risk of thrombosis complicating plaque rupture and atherosclerotic coronary artery disease.

Hyperglycemia also causes increase in local and systemic inflammation during acute myocardial infarction. Studies suggest that acute "T" cell activation may play a role in plaque instability and acute clinical manifestation of coronary atherosclerosis (**Ross et al**).

According to **Raffaele Marfella et al** hyperglycemia during myocardial infarction is associated with increased levels of inflammatory markers, enhanced expression of cytotoxic 'T' cells and reduced expression of 'T' cells implicated in limitation of immune process.

Insulin is found to be a central factor in inhibiting cytokine release like IL – 8, decreased C-Reactive Protein (CRP) levels and inhibiting T cell activation. So, patients with insulin resistance like impaired glucose tolerance have increased cytokine release, increase in the levels of C-Reactive Protein (CRP) in blood and increased activation of T cells.

Also hyperglycemia is associated with increased Troponin levels probably as a consequence of more extensive myocardial damage.

Raffaele Marfella et al in a study further found out that, hyperglycemia positively correlated with both infarct segment length and Wall Motion Score Index. With increasing blood sugar levels wall motion score index increased and with increasing wall motion score index patient had poor prognosis. Wall motion score index positively correlated with extent of myocardial infarction. A wall motion score index of greater than 1.7 correlated approximately with 20% myocardial infarction by perfusion scan studies.

The increase in Myocardial Performance Index (MPI) which measures both systolic and dialostic parameters of ventricular function indicates worst functional outcome after myocardial infarction in hyperglycemic patients. The diminished diastolic filling time, prolongation of mitral regurgitation and decreased ejection time in hyperglycemic patients suggest, hyperglycemia may influence cardiac synchronisation after acute myocardial infarction.

Dyssynchrony between right ventricular and left ventricular contraction are independent predictors of heart failure and cardiac mortality in patients with congestive cardiac failure.

MATERIALS AND METHODS

The study was carried out with the aim of comparing the in-hospital events like Arrhythmias, congestive heart failure, recurrent angina, Pericarditis & death among patients with acute ST elevation myocardial infarction eligible for thrombolysis with normal glucose metabolism and Impaired Glucose Tolerance.

Patients admitted in our Intensive coronary care unit with acute ST elevation Myocardial infarction were divided into two groups based on their glucose metabolism as patients with normal glucose metabolism and those with Impaired Glucose Tolerance.

Acute ST elevation myocardial infarction was defined as typical chest pain of ischemic origin lasting for > 20 minutes with ECG evidence of ST elevation of atleast 1mm in 2 contiguous limb leads and atleast 2mm in 2 contiguous chest leads, with typical rise and fall of biochemical markers of myocardial necrosis.

If the patients have any of the 2 above criteria, he/she was included as a patient with acute ST elevation Myocardial Infarction. Eligibility criteria for thrombolysis was scrutinized as per ACC/AHA guidelines for management of ST elevation myocardial infarction. All patients with pre-existing Diabetes Mellitus or blood sugar level in the diabetic range were excluded from the study.

All the study and control patients were treated with thrombolysis with Injection Streptokinase 1.5 million units in 100ml of normal saline to be run over 1 hour. Other medications were given as per the need of the patients and at the discretion of the treating physician.

At admission all patients were drawn blood for random blood glucose estimation. On the next morning after overnight fasting of 10-16 hours an Oral Glucose Tolerance Test was performed as per American Diabetic Association Recommendation.

A fasting blood sample was taken before giving glucose load. The subject was made to drink 75gms of glucose dissolved in 250-300ml of water. The glucose load was consumed over a period of 5 minutes. Blood samples are collected in fluoride – oxalate test tubes to prevent Red Blood corpuscles from metabolizing glucose.

Venous plasma collected from the patients were estimated for glucose by glucose oxidase method in our biochemistry laboratory. The values were expressed in mg %.

Lipid Profile

Blood for lipid estimation was collected after an overnight fast within 24-48 hours of admission. Cholesterol and Triglycerides were measured by enzymatic calorimetric assays. High Density Lipoprotein and Low Density Lipoprotein cholesterol measures were done enzymatically using selective solubilisation method.

Glycosylated Hemoglobin

Glycosylated Hemoglobin was estimated by cation-exchange resin method using Monozyme's Glycohemin kit. It is a rapid 10 minutes assay with conversion chart from Glycosylated Hemoglobin A_1% to Glycosylated Hemoglobin A_1c%. The normal value for Glycosylated Hemoglobin A_1 were between 6.0 to 8.7% which corresponded to 4.48 to 6.44 for Glycosylated Hemoglobin A_1C.

A good clinical history with documentation of duration of chest pain and previous

history of Myocardial Infarction, Angina, Hypertension was taken. Detailed clinical examination at admission was done as per our intensive coronary care protocol. Systolic and diastolic Blood Pressure were measured using mercury sphygmomanometer. Phase I of korotkoff's sound was taken as Systolic Blood Pressure and phase V as Diastolic Blood Pressure. Killip's class was ascertained for every single subject at admission.

After thrombolysis and during hospital stay other parameters like successful thrombolysis, defined as greater than 50% resolution of the ST segment elevation at 90 minutes after Injection Streptokinase, complications like Arrhythmias, Congestive heart failure, Recurrent angina, development of pericarditis and death were monitored.

Complications were treated as per standard treatment protocol like cardioversion for hemodynamically unstable ventricular tachycardia and ventricular fibrillation. Complete heart block was treated with transvenous temporary pacing. Congestive heart failure was treated with diuretics, inotropes, and vasodilators. Recurrent Angina was treated with nitroglycerin infusion, intravenous heparin and beta blockers.

An day 3 of admission all patients underwent two dimensional echo cardiography and Doppler evaluation. Left Ventricular function was assessed using End Diastolic Volume, End Systolic Volume and Ejection Fraction. Ejection Fraction was calculated by Modified Simpson's method.

All the 16 segments as per American society of echocardiography classification were carefully investigated for wall motion abnormalities with naked eye and M – mode examination. Wall motion score was ascertained as 1 if the segment was normally

contracting. A score of 2 was given for hypo kinetic segment, 3 for akinetic segment. Dyskinetic segment was given a score of 4, and aneurysm was scored at 5.

Wall motion score index was calculated using the formula ,

Wall motion score index = Sum of wall motion scores ÷ number of segments visualized.

Presence or absence of Left Ventricular clot was assessed using two dimensional echo cardiography.

All the subjects with out Left Ventricular clot underwent symptom limited Treadmill Test by Bruce protocol and their functional capacity was assessed an day 5-7 before discharge from the hospital. The functional capacity was calculated as number of Mets of exercise the patients was able to perform before achieving either the target heart rate or development of symptoms necessitating stopping of the procedure.

Body mass index was calculated for all patients using the formula

$$\text{Body Mass Index} = \frac{\text{Weight in kg}}{(\text{Height})^2 \text{ in metre}}$$

To ensure correct reading, for height, the patients were made to stand on a flat surface against a wall bare footed and measurement were taken in cms. Weight was measured in kilograms by using the same weighing scale for all the patients.

Measurement of waist circumference

Waist circumference was measured at mid point between the ribcage and 2 cm above the top of the iliac crest. Two measurement of waist circumference were made and the average was taken.

Waist circumference of > 103 cm in male and > 88 cm in female were considered abnormal.

All the parameters and variables were tabulated in a master chart and were analysed by computer analysis. Data were analysed utilizing the software – Epidemiological information package – 2002 (EPI Info 2002) developed by the center for disease control and prevention, Atlanta for World Health Organisation.

Mean, Standard deviation and 'p' values were calculated using this package. Chi-square test was used to find out the significance of relationship between the groups and other variables.

RESULTS AND OBSERVATIONS

The relationship of parameters in study group i.e., patients with Impaired Glucose Tolerance and control group i.e., normal glucose metabolism revealed the following,

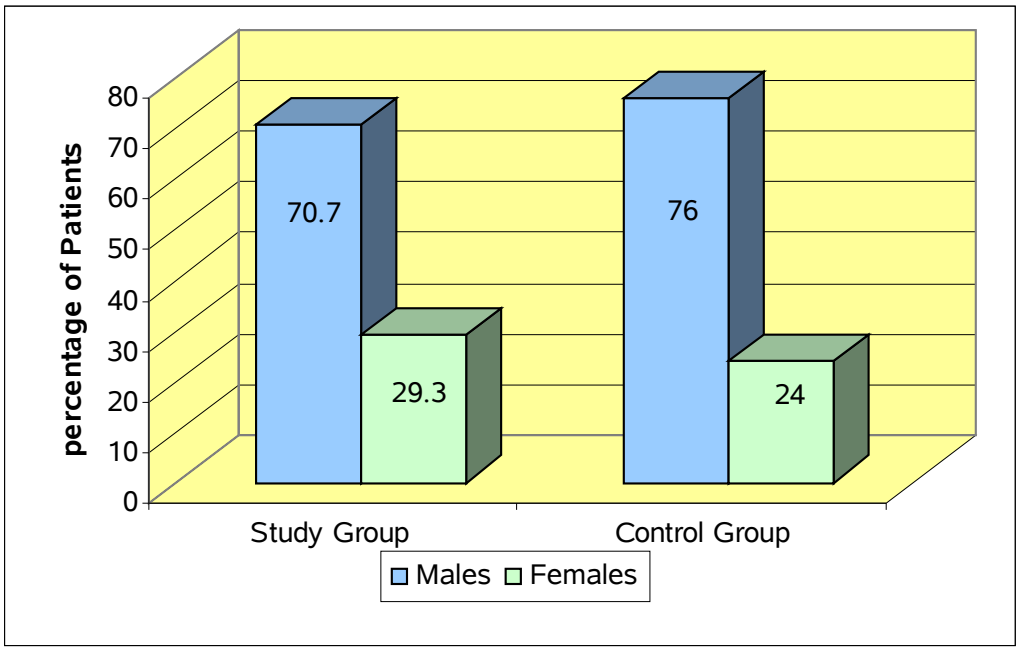
Sex distribution between the study group n=75 and control group n=25 were similar.

53 patients (70.7%) in the study group and 19 patients (76%) in the control group were males. The ‘p’ value was not significant showing there was no selection bias.

Table - 1

Sex Distribution

Sex	**Study group (n=75)**		**Control Group (n=25)**		**‘p’**
	No.	**%**	**No.**	**%**	
Males	53	70.7	19	76	0.797
Females	22	29.3	6	24	

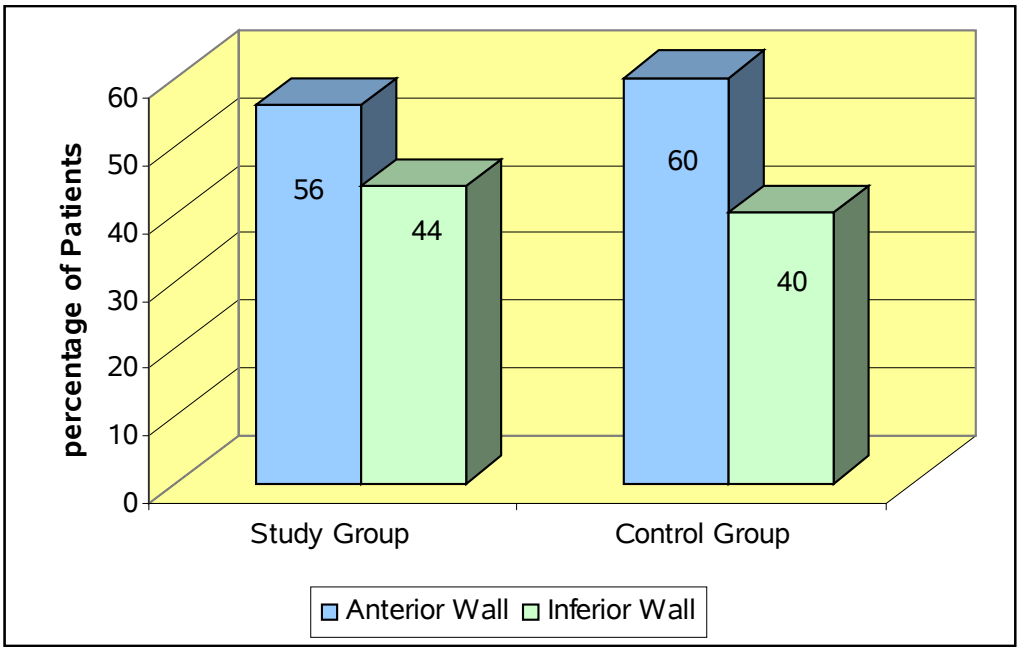


Similarly the distribution of myocardial infarction also did not slow any significant 'p' value. 42 patients (56%) in study group and 15 patients (60%) in control group had Anterior Wall Myocardial Infarction.

Table - 2

Distribution of Myocardial Infarction Location

Myocardial Infarction Location	Study group (n=75)		Control Group (n=25)		'p'
	No.	%	No.	%	
Anterior Wall	42	56	15	60	0.9071
Inferior Wall	33	44	10	40	

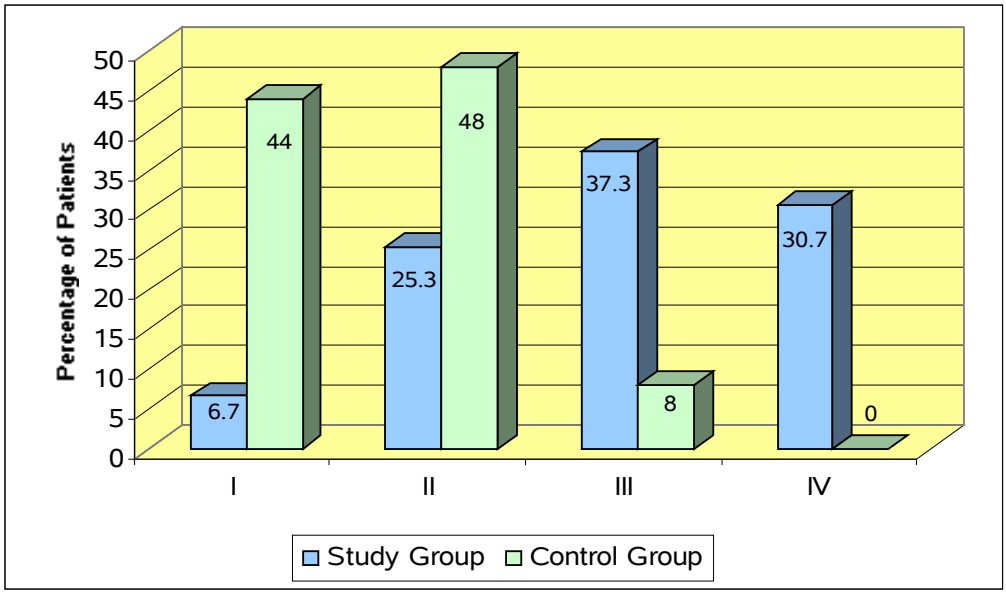


On analyzing the Killip Class, 5 patients (6.7%) were in Killip Class I, 19 patients (25.3%) in Class II, 28 patients (37.3%) in class III and 23 patients (30.7%) in class IV, in the study group and 11 patients (44%) in class I, 12 patients (48%) in class II and 2 patients (8%) in class III in the control group.

Table - 3

Killip's Class Distribution

Killip's Class	Study group (n=75)		Control Group (n=25)		'p'
	No.	%	No.	%	
I	5	6.7	11	44	0.0001(Sig.)
II	19	25.3	12	48	
III	28	37.3	2	8	
IV	23	30.7	-	-	



The mean Killip class was 2.92 ± 0.91 in the study group and 1.64 ± 0.63 in control group with significant 'p' value of 0.0001.

Previous history of hypertension also correlated well with in the study group with 41.3% of patients (31) were taking treatment for hypertension.

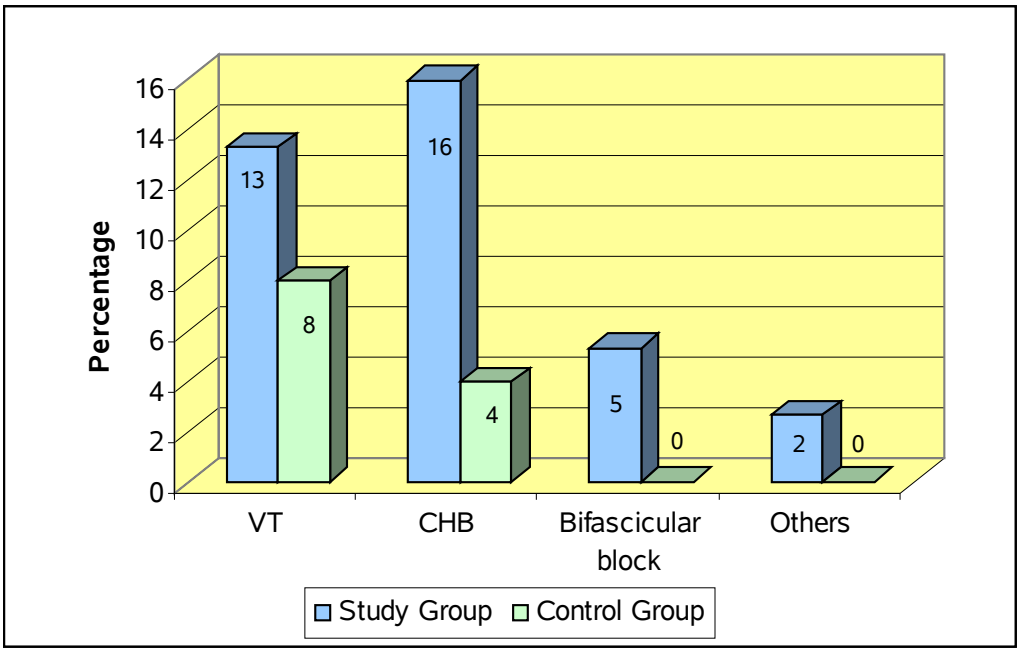
On analyzing the complications, Arrhythmias were more common in the study group. A total of 28 patients (37.3%) had some form of Arrhythmias Ventricular Tachycardia / Ventricular Fibrillation or Complete Heart Block in the study group. Only 3 patients (12%) had Arrhythmias in the control group. The incidence of Arrhythmias was more in the study group with significant 'p' value of 0.0338.

Ventricular Tachycardia was seen in 10 patients (13.33%), Complete Heart Block in 12 patients (16%), Bifascicular Block in 4 patients (5.33%) and Others in 2 patients (2.67%).

Table - 4

Spectrum of Arrhythmias

Arrhythmias	Study group (n=75)		Control Group (n=25)	
	No.	%	No.	%
VT / VF	10	13.33	2	8
CHB	12	16	1	4
Bifascicular block	4	5.33	0	0
Others	2	2.67	0	0

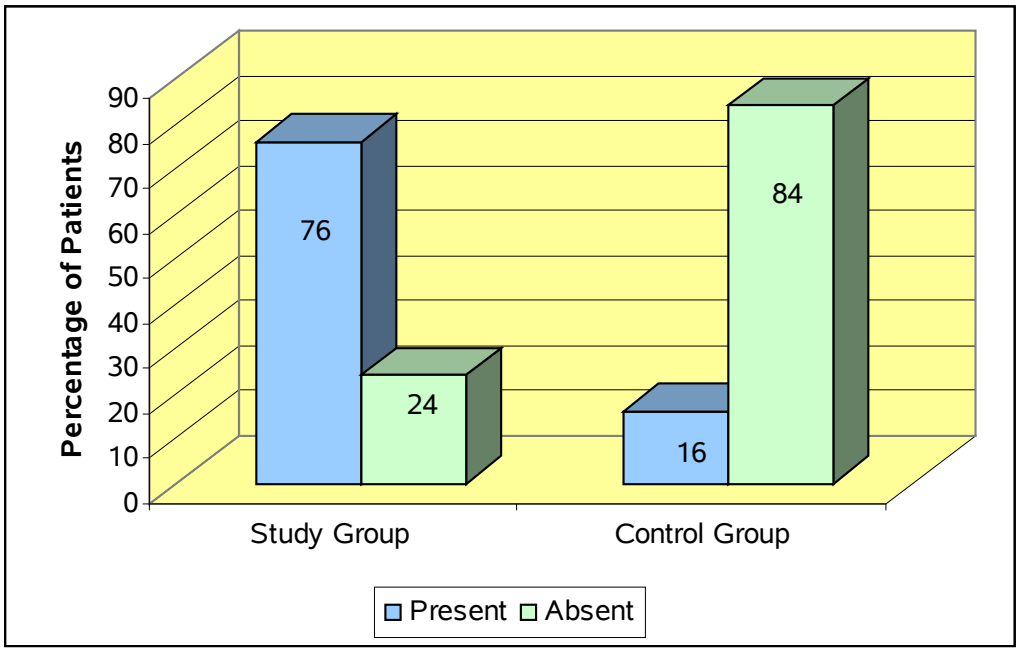


Congestive heart failure was present in 57 patients (76%) in the study group and 4 patients (16%) in the control group. Congestive heart failure was associated with poor outcome in our study. This also had a significant 'p' value of 0.0001.

Table - 5

Comparison of Congestive Heart Failure between the two groups

Congestive Heart Failure	Study group (n=75)		Control Group (n=25)		'p'
	No.	%	No.	%	
Present	57	76	4	16	**0.0001**
Absent	18	24	21	84	



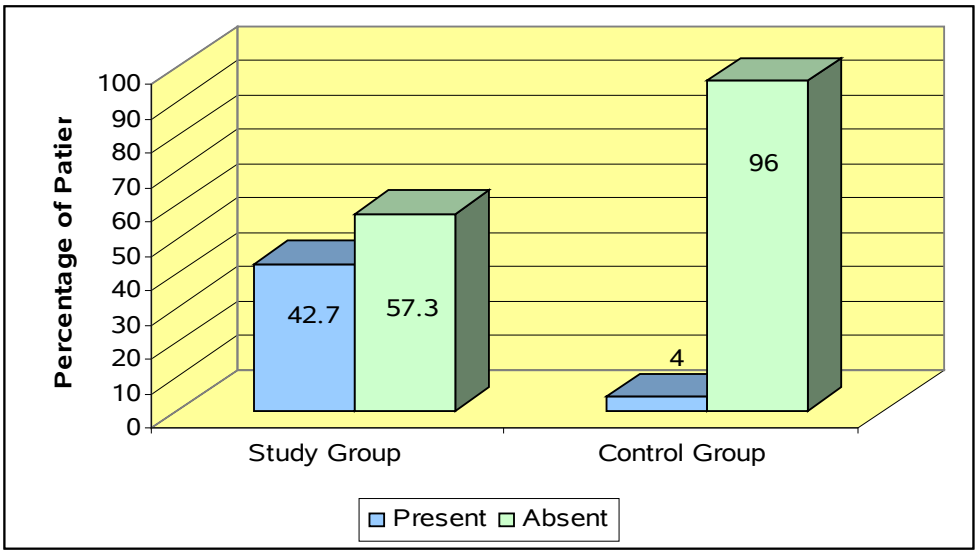
The relative incidence of recurrent angina needing nitroglycerine and heparin therapy were seen in 28 patients (37.3%) in the study group and only 3 patients (12%) in the control group. (p=0.0338).

Similarly there were 32 patients (42.7%) with Left Ventricular clot in the study group and only 1 patient (4%) in the control group. (p=0.0009).

Table - 6

Incidence of Left Ventricular Clot

Left Ventricular Clot	Study group (n=75)		Control Group (n=25)		'p'
	No.	%	No.	%	
Present	32	42.7	1	4	**0.0009**
Absent	43	57.3	24	96	



Death was seen a 11 patients in the study group (14.3%) and one patients (4%) in the control group. The percentage of patients was 3.5 times higher in the study group than in the control group. There was a statistically significant difference. (p=0.0414).

Table - 7

Percentage of Death

Death	Study group (n=75)		Control Group (n=25)		'p'
	No.	%	No.	%	
Yes	11	14.7	1	4	0.1414
No	64	85.3	24	96	

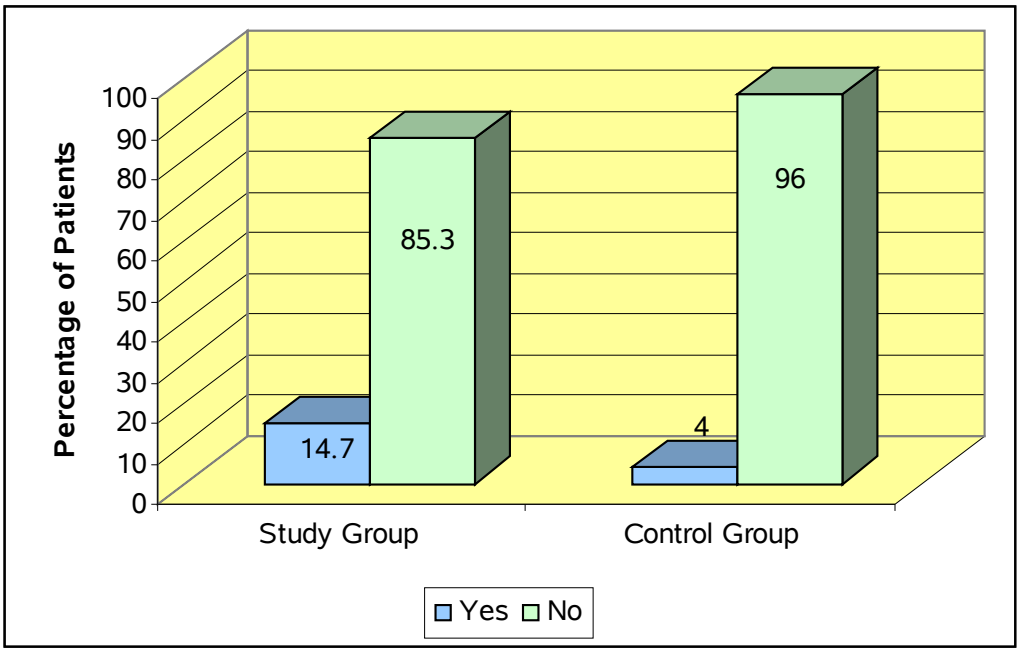


Table - 8

Mean Values of the Parameters in the Study and Control Groups

Parameters	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
Age	54.9	9.9	52.2	11.5	0.3671
Chest pain duration	6.4	2.3	6.5	1.9	0.9692
SBP	112.4	33.1	101.7	6.4	0.4722
DBP	74.5	15.9	73.2	5.7	0.9246
PR	83.4	23.5	83.4	13.3	0.7829
Hb A_1C	5.5	0.27	5.4	0.26	0.1954
RBS	176.7	16.6	123.5	11.7	0.0001
FBS	110.7	9.7	84.7	12.3	0.0001
BS 1 hour	182.2	12.6	119	15.3	0.0001
BS 2 hour	163.9	11	102	11.9	0.0001
TC	193	46	168.7	33.2	0.0131

TGL	157.4	51.9	132.8	33.2	0.0406
HDL	39.9	3.8	39.9	3.5	0.8678
LDL	112.9	39.3	99.4	31.6	0.075
VLDL	33	12.5	27.3	6.7	0.038
BMI	28.2	1.6	20.7	0.9	0.0001
Waist	103.9	5.4	89.5	4.1	0.0001
EF	40.8	4.6	49.6	3.7	0.0001
EDV	117.2	15.2	102	9.9	0.0001
ESV	69.2	14.1	51.8	7.7	0.0001
WMSI	1.98	0.27	1.45	0.18	0.0001
METS	5.02	0.5	6.47	0.96	0.0001

When the biochemical markers of Impaired Glucose Tolerance were analysed all the variables, Random blood sugar, Fasting blood sugar and 2 hour post glucose challenge blood sugar were showing high statistical significance between the study and the control group.

When analyzing the lipid profile of both the groups Total Cholesterol, Triglycerides, Very Low Density Lipoproteins showed positive correlation in the Impaired Glucose Tolerance group.

The Body Mass Index and the Waist Circumference were also found to be abnormal in the study group when compared to the control group.

The age of the study group and the control group were similar without any statistical difference. Also the duration of chest pain i.e., the door to needle time did not show any statistically significant difference between the two groups. These points were reiterated here to show that there was no selection bias among the two groups.

The systolic blood pressures, the diastolic blood pressure and the pulse rate at admission also did not show any significant difference between the two population of patients.

The mean Hemoglobin A_1C was 5.5 ± 0.27 in the study group and 5.4 ± 0.26 in the control group suggesting that all these patients have not been known diabetics over the previous 120 days.

Random Blood Sugar showed a significant p value when compared with control patients. Study patients had a random blood sugar of 176.7 ± 16.6 mg% and control patients had 123.5 ± 11.7 mg % (p=0.0001).

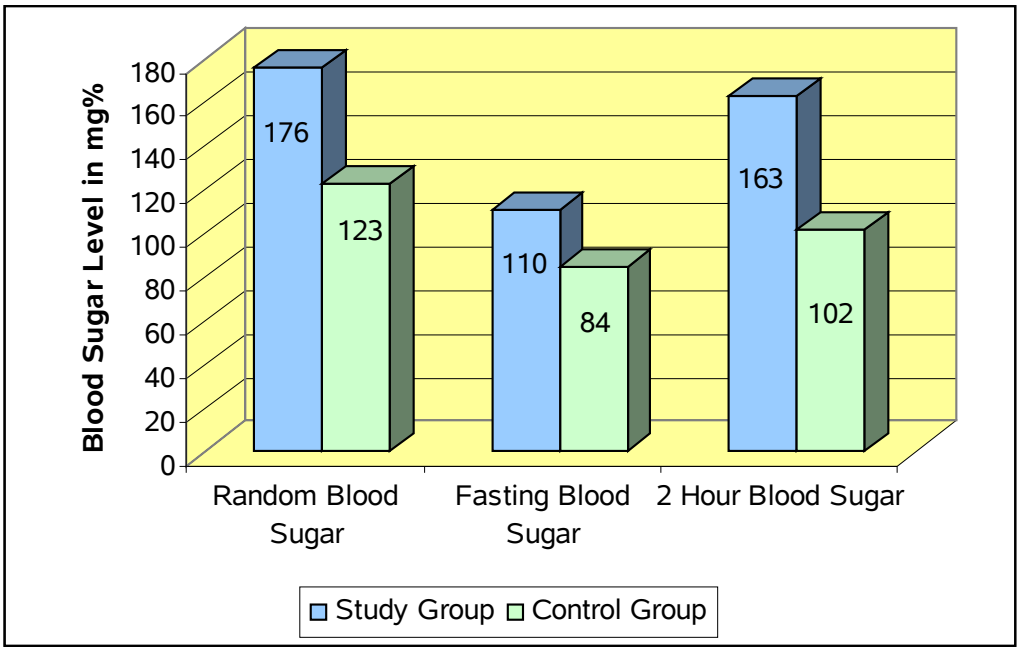
Fasting Blood Sugar also showed a significant 'p' value with study patient having a mean of 110.7 ± 9.7 mg % and controls 84.7 ± 12.3 mg% (p=0.0001).

The mean 2 hour blood sugar was 163.9 ± 11.0 mg% in the study group and 102 ± 11.9 mg% in the control group with a significant 'p' of 0.0001.

Table - 9

Comparison of Blood Sugar Levels

Blood Sugar Level	**Study**		**Control**		**'p'**
	Mean	**S.D.**	**Mean**	**S.D.**	
Random	176.7	16.6	123.5	11.7	**0.0001**
Fasting	110.7	9.7	84.7	12.3	**0.0001**
2 hour	163.9	11	102	11.9	**0.0001**



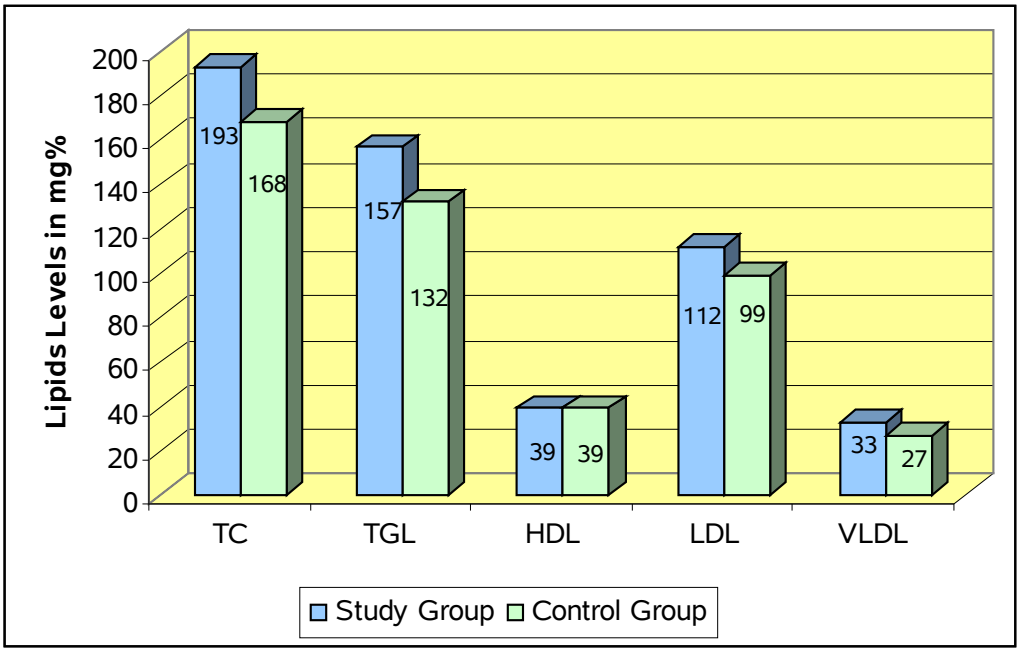
Similarly Total Cholesterol and Triglycerides were significantly different among patients between study group and control group. Total Cholesterol was 193 ± 46 mg% in the study group and Triglycerides was 157.4 ± 51.9 mg% in the study group as against 168.7 ± 33.2 mg% and 132.8 ± 33.2 mg% in the control group ($p<0.05$).

Even though the mean Low Density Lipoproteins was 112.9 ± 39.3 mg% in the study group as against 99.4 ± 31.6 mg% in the control group, the p value was not significant ($p=0.075$).

Table - 10

Comparison of Lipid Profile

Lipids	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
TC	193	46	168.7	33.2	0.0131
TGL	157.4	51.9	132.8	33.2	0.0406
HDL	39.9	3.8	39.9	3.5	0.8678
LDL	112.9	39.3	99.4	31.6	0.075
VLDL	33	12.5	27.3	6.7	0.038



The Body Mass Index in the study group was 28.2 ± 1.6 as against 20.7 ± 0.9 in the control group which was statistically significant (p=0.0001).

Similarly Waist circumference was 103.9 ± 5.4 cm in the study group and 89.5 ± 4.1 in the control group (p=0.0001).

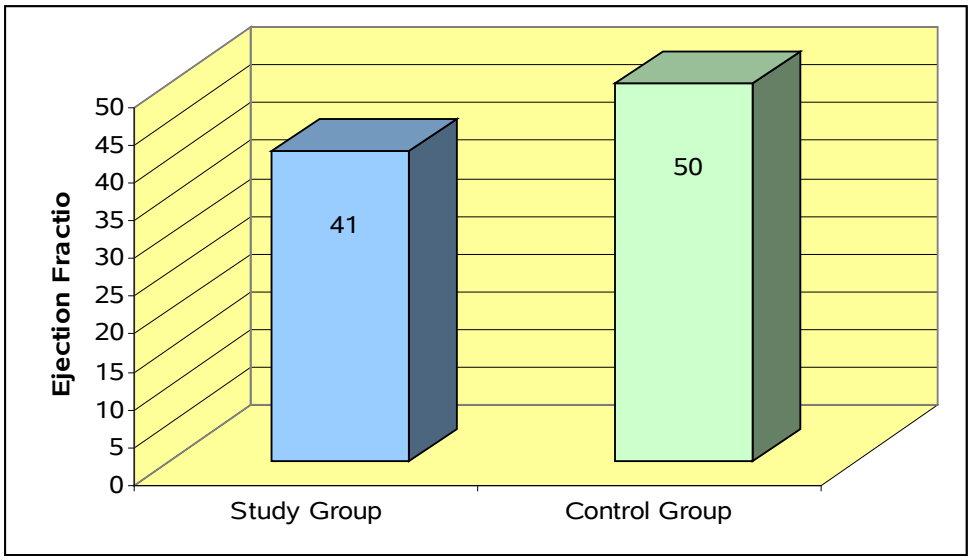
When the indices of left ventricular function were analysed, ejection fraction, end

diastolic volume, end systolic volume were significantly different between the study and the control groups. The mean ejection fraction was 40.8 ± 4.6 in the study group and 49.6 ± 3.7 in the control group which was statistically significant (p=0.0001).

Table - 11

Comparison of Ejection Fraction

LV function	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
Ejection Fraction	40.8	4.6	49.6	3.7	0.0001

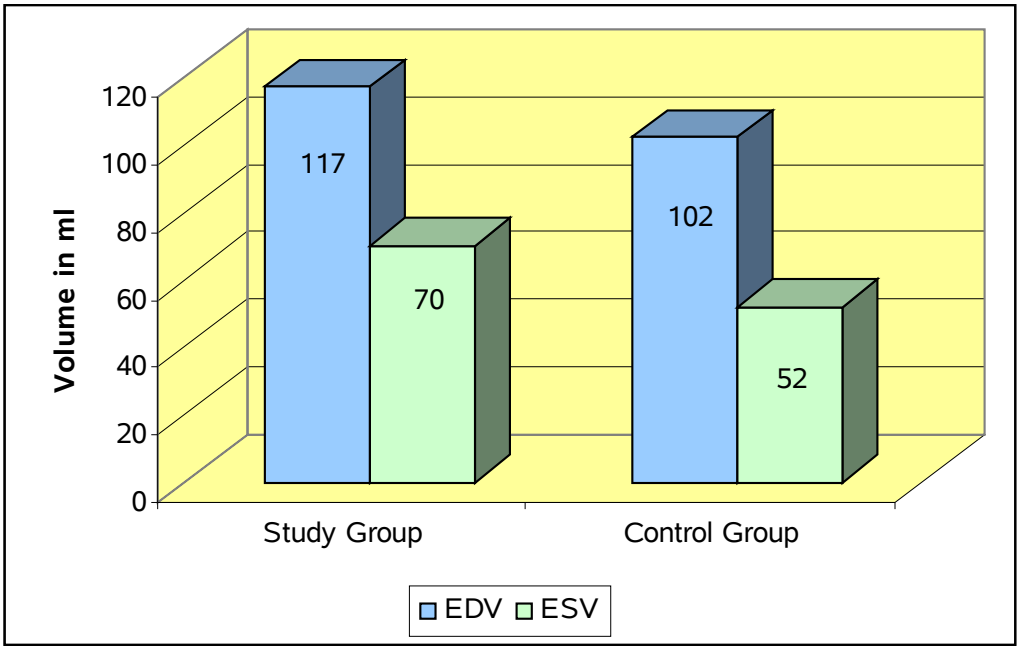


When end diastolic volume and end systolic volume were compared the mean were 117.2 ± 15.2 ml and 69.2 ± 14.1 ml in the study group and 102 ± 9.9 ml and 51.8 ± 7.7 ml in the control group respectively which were statistically very significant (p=0.0001).

Table - 12

Comparison of Ventricular Volumes

Ventricular Volume	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
End Diastolic	117.2	15.2	102	9.9	0.0001
End Systolic	69.2	14.1	51.8	7.7	0.0001

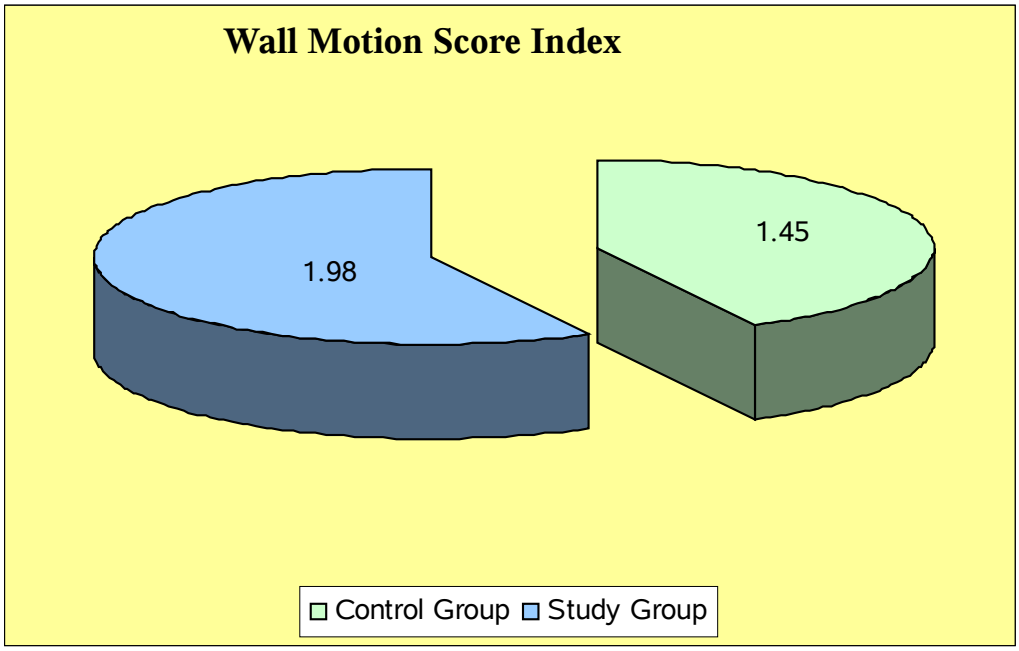


When Wall Motion Score index was compared between the two groups, the mean score was 1.98 ± 0.27 in the study group which showed larger segmental loss of contractility as against 1.45 ± 0.18 in the control group. The p value was again significant (p=0.0001).

Table - 13

Comparison of Wall Motion Score Index

Regional Wall Motion	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
WMSI	1.98	0.27	1.45	0.18	0.0001(Sig.)

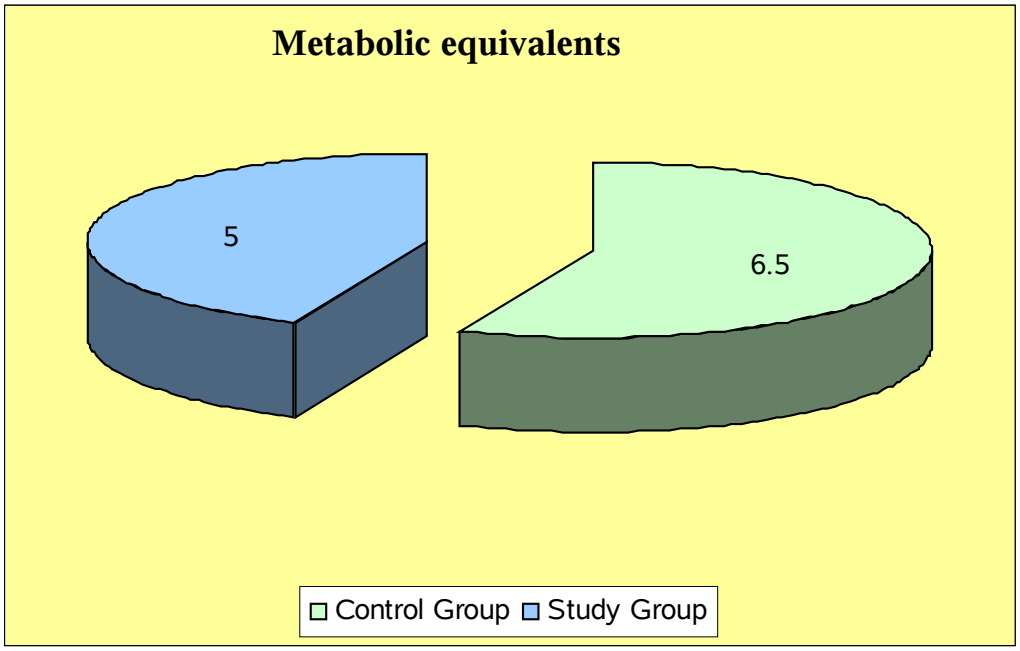


Similarly functional capacity as assessed by pre-discharge Symptom limited Treadmill test using Bruce protocol the mean Mets achieved before stopping the test was 5.02 ± 0.5 in the study group and 6.47 ± 0.96 in the control group (p=0.0001).

Table - 14

Comparison of Functional Capacity

Functional Capacity	Study		Control		'p'
	Mean	S.D.	Mean	S.D.	
Mets	5.02	0.5	6.47	0.96	0.0001



Fasting Blood Sugar ≤ 110 mg% was taken as cut of points and analysis was done to find out the distribution in the study and the control group, 41 patients (54.7%) had abnormal Fasting Blood Sugar in the study group and non in the control group (p=0.0001).

Similarly 2 hour blood sugar of > 140 mg % showed statistically significant association in the study group.

27 patients (36%) had abnormal total cholesterol values as against 3 patients

(12%) in the control group. 35 patients (46.7%) had abnormal Triglycerides levels against 5 (20%) patients in the control group.

Similarly, 43 patients (52.3%) had Low Density Lipoproteins levels of >100mg% in the study group and only 7 patients (28%) had such values in the control group.

Abnormal Waist circumference (>103 cm in males and > 88cm in females) were present in 49 (65.3%) of the study patients as against none in the control group.

Thus the percentage of patients with abnormal values of Fasting Blood Sugar, 2 hour Blood Sugar, Total Cholesterol, Triglycerides, Low Density Lipoproteins, Waist Circumference and Body Mass Index were significantly different from those of the control cases.

DISCUSSION

Impaired Glucose Tolerance as per the creiteria is associated with increased in-hospital events like arrhythmia, Congestive Heart Failure and mortality according to large number of studies quoted in the bibliography.

The basis of our study was a meta analysis from the ***Lancet 2000***; ***355: 773-78*** by **Sarah E. Capes et al**.

Sarah E. Capes et al analysed about 15 studies in which patients without diabetes but increased glucose concentration above the normal level with Acute Myocardial Infarction were observed for in-hospital events. The study conclusion was that hyperglycemia with myocardial infarction was associated with increased risk of in-hospital mortality in patients without diabetes. The risk of Congestive Heart Failure and cardiogenic shock were also increased in those patients without diabetes but with hyperglycemia of non diabetic range.

Similar results were obtained in our study, where we analysed about 75 patients with Impaired Glucose Tolerance and compared them with patients with normal glucose tolerance with both these groups had Acute ST elevation Myocardial Infarction.

There was a significant difference in various killip classes between the 2 groups with a mean of 2.92 ± 0.9 in Impaired Glucose Tolerance Group and 1.64 ± 0.63 in the control group. ($p < 0.0001$).

The incidence of in-hospital events like arrhythmias, Ventricular Tachycardia, Ventricular Fibrillation, Non-sustained ventricular Tachycardia, Complete Heart Block,

Bifascicular block were increased in the study group as compared to the control group.

Significant difference is the incidence of Congestive Heart Failure was also seen in the study group with about 76% of patients had clinically significant Congestive Heart Failure requiring treatment, unlike only 16% of patients in the control group with a statistically significant p of 0.0001.

Similarly, the incidence of recurrent angina was also significantly more in the study group than in the control group.

The relative incidence of death was 14.7% is the study group and only 4% in the control groups and most of the deaths were either due to Congestive Heart Failure or Arrhythmias or Recurrent angina or a combination of these complications.

All the patients who died had Congestive Heart Failure with Arrhythmias contributing in about 45% patients along with Congestive Heart Failure and Recurrent Angina contributing 45% among all the death. About 2 patients (18%) had only Congestive Heart Failure as major cause of their death.

When other traditional risk factor like smoking was considered, about 42 patients (56%) were smokers in the study group and 18 patients (72%) were in the control group. Still, death was about 3-4 times higher in the Impaired Glucose Tolerance as compared to that of the normoglycemic group.

Hyperglycemia was the basic culprit causing the increased incidence of all in-hospital event rates in the Impaired Glucose Tolerance group.

Hyperglycemia also contributed for the decreased Left Ventricular function in the

study group when compared to that of the control group. The ejection fraction which is the traditional index of Left Ventricular function was statistically significantly different in both the groups.

In the study group ejection fraction was around 40.8 ± 4.6 and in the control group 49.6 ± 3.2, which was statistically significant.

Similarly, the end diastolic volume and end systolic volume were also significantly different in both the groups.

The Wall Motion Score Index, a novel index for calculating the amount of myocardial jeoparadised by the ischemic insult, also was significantly higher in the study group at 1.98 ± 0.27 versus 1.45 ± 0.18 in the control group, suggesting that patients with Impaired Glucose Tolerance had larger area of Left Ventricular myocardium affected by the ischemia and infarction.

This increase in Wall Motion Score Index positively correlated with the decreased ejection fraction and the increase in the incidence of deaths among the study group when compared to the control group.

All patients who died had a Wall Motion Score Index of atleast 1.75 or greater with about 8 out of 11 patients (72%) had a Wall Motion Score Index of ≥ 2. Even in the control group, where only one death was recorded the patient had a Wall Motion Score Index of 1.75.

Thus Wall Motion Score Index had a greater prognostic influence on predicting the deaths not only among the patients with Impaired Glucose Tolerance and Acute ST

elevation Myocardial Infarction, but also in patients with normal blood glucose and Acute ST elevation Myocardial Infarction.

Functional capacity was much lower in patients with Impaired Glucose Tolerance and Acute ST elevation Myocardial Infarction than in patients with normal glycemia. It was 5.02 ± 0.5 Mets in the Impaired Glucose Tolerance group and 6.47 ± 0.96 in the control group with a significant 'p' value of 0.0001.

Thus, patient with Impaired Glucose Tolerance and Acute ST elevation Myocardial Infarction when all other criteria were equally considered had increased in-hospital event rates like Arrhythmias, both tachyarrhythmias and bradyarrhythmias (37.3% versus 12%), increased incidence of Congestive Heart Failure (76% versus 16%).

There was also increased incidence of the Recurrent Angina (37.3% versus 12%), increased incidence of Left Ventricular Clot (42.7% versus 4%) and increased incidence of death (14.7% versus 4%).

This group also had lesser ejection fraction 40.8 ± 4.6% versus 49.6 ± 3.7%, higher Wall Motion Score Index 1.98 ± 0.27 versus 1.45 ± 0.18. There was decrease in the functional capacity from 6.47 ± 0.96 in the normoglycemic groups as against 5.02 ± 0.5 in the Impaired Glucose Tolerance group.

CONCLUSION

- Impaired Glucose Tolerance in patients with Acute ST elevation Myocardial Infarction is associated with
  - increased incidence of arrhythmias
  - increased incidence of Congestive Heart Failure
  - increased incidence of recurrent angina
  - increased incidence of Left Ventricular Clot
  - increased incidence of in-hospital death
- Impaired Glucose Tolerance is also associated with decrease in the left ventricular function as suggested by decrease in the ejection fraction in this group of patients and increase in the Wall Motion Score Index.
- Impaired Glucose Tolerance is associated with decrease in the functional capacity during the Pre discharge Treadmill Test.

BIBLIOGRAPHY

1. Bannerjee AK Blood sugar and prognosis of acute myocardial infarction in the elderly : Br J.Clin Pract 1986:40:516-17
2. Bellodi G, Manicardi V, Malavasi V, et al. Hyperglycemia and prognosis of acute myocardial infarction in patients without diabetes mellitus. Am J Cardiol 1989; 64: 885-8.
3. Bolk J, van der Ploeg T, Cornel JH, Arnoia AE, Sepers J, Umans VA. Impaired glucose metabolism predict mortality after myocardial infarction. Int J Cardiol 2001; 79: 207-14.
4. Capes SE, Hunt D, Malmberg K, Gerstein HC: Stress hyperglycemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 355; 773-778, 2000.
5. Casiglia E, Oauletto P, Mazza A, Ginocchio G, di Menza G, Pavan L, Tramontin P, Capuani M, Pessina AC: Impaired glucose tolerance and its covariates among 2079 non-diabetic elderly subjects. Acta Diabetol 33: 284-290. 1996.
6. Coutinho M, Gerstein H, Wang Y, Yusuf S. The Relationship between glucose and incident cardiovascular events. Diabetes care 1999,233-40.
7. Cruikshank N.Coronary thrombosis and myocardial infarction , with glycosuria BMJ 1931 : 1: 618-19
8. Das UN: Is insulin an endogenous cardio-protector? Crit Care 6: 389-393, 2002.
9. Datey KK, Nanda NC, Hyperglycaemia after acute myocardial infarction. N Engl J Med 1969; 276: 262-65.

10. Decode study group. Glucose tolerance and mortality Comparative WHO and ADA diagnostic criteria. Lancer 1999;354:617-21.
11. Donahue RP, Abbott RD, Read DM, Yano K: Postchallenge glucose concentration and coronary heart disease in men of Japanese ancestry: Honolulu Heart Program. Diabetes 36:689-692,1987.
12. Donahue RP, Orchard TJ : Diabetes mellitus and macrovascular complications: an epidemiological perspective . Diabetes care 15: 1141-1155,1992
13. Esposito K, Nappo F, Merfella R, Giugliano G, Giugliano F, Ciotola M, Quagliaro L, Ceriello A, Giugliano D: Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans. Circulation 106: 2067-2072, 2002.
14. Fava S, Aquilina O, Azzopardi J, Agius Muscat H, Fenech FF; The prognostic value of blood glucose in diabetic patients with acute myocardial infarction Diabetes Med 1996:13:80-83
15. Feskens EJM, Kromhout D: Glucose tolerance and the risk of cardiovascular diseases: The Zutphen study. J Clin Epidemiol 45: 1327-1334, 1992.
16. Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H: Coronary –heart –disease risk and impaired glucose tolerance : The Whitehall Study , Lancet I 1373-1376-1980
17. Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H: Mortality from coronary heart disease and stroke in relation to degree of glycemia: the Whitehall Study. Br Med J 287:867-870, 1983.
18. Gerstein HC, Yusuf S: Dysglycaemia and risk of cardiovascular disease. Lancet 347: 949-950, 1996.
19. Gupta MS, Gulati JK, Malhotra KC. Insulin response and glucose tolerance in survivors

of myocardial infarction. JAPI 37:255-257, 1989.

20. Gwilt DJ, Petri M, Lamb P, Nattrass M, Pentecost BL. Effect of intravenous insulin infusion on mortality among diabetic patients after myocardial infarction. Br Heart J 1984; 51: 626-30.
21. Haffner SM, Stem MP, Hazuda HP, Mitchell BD, Patterson JK: Cardio vascular risk factors in confirmed pre-diabetic individuals : Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? JAMA 263:2893-2898,1990
22. Haffner SM. The importance of hyperglycemia in the nonfasting state to the development of cardiovascular disease. Endocr Revs 1998; 19: 583-92.
23. Herlitz J, Bang A, Karlson BW. Mortality, place and mode of death and reinfarction during a period of 5 years after acute myocardial infarction in diabetic and non-diabetic patients. Cardiology 1996; 87: 423-8.
24. Holubarsch C, Ruf T.Goldstein DJ , et al Existence of the Frank- Starling mechanism in the failing human heart : investigations on the organ , tissue and sarcomere levels , Circulation 1996:94”683-89
25. Husband DJ, Alberrti KG, Julian DG. “Stress” hyperglycaemia during acute myocardial infarction: an indicator of pre-existing diabetes? Lancet 1983; 2: 179-81.
26. International Collaborative Group : Asymptomatic hyperglycemia and coronary heart disease : a series of papers by the international Collaborative Group based on stuies in fifteen populations . J Chronic Dis 32: 829-837,1979
27. Jarrett RJ: The cardiovascular risk associated with impaired glucose tolerance. Diabetic Medl 3 (Suppl. 2): S15-S19, 1996.
28. Katherine Esposito et al., Stress Hyperglycemia and increased risk of death after

myocardial infarction in patients with and without diabetes: a systematic overview, Stroke 2004; 35: 1886.

29. Katherine Esposito, Raffaele Marfella, and Dario Giugliano. Stress hyperglycemia, inflammation, and cardiovascular events. Diabetes Care 2003; 26: 1650-1651.
30. Lakhdar A, Stromberg P, Yudkin JS, Prevalence importance of hyperglycaemia induced by stress after myocardial infarction , BMJ 1984:288:288
31. Leor J, Goldbourt U, Reicher-Reiss H, Kaplinski E, Behar S, and the SPRINT Study Group. Cardiogenic shock complicating acute myocardial infarction in patients without heart failure on admission: incidence, risk factors, and outcome. Am J Med 1993; 94: 265-73.
32. Lynch M, Gammage MD, Lamb P, Nattrass M, Pentecost BL, Acute myocardial infarction in diabetic patients in the thrombolytic era. Diabet Med 1994; 11: 162-5.
33. Lyons TJ: Glycation and oxidation: a role in the pathogenesis of atherosclerosis. Am J Cardiol 71: 26B-31B, 1993.
34. Madsen JK, Haunsoe S, Helquit S, Hommel E, Malthe I, Pedersen NT, Sengelov H, Jessen DR, Telmer S, Parving HH. Prevalence of hyperglycaemia and undiagnosed diabetes mellitus in patients with acute myocardial infarction. Acta Med Scand 220: 329 – 332, 1986.
35. Mak KH, Mah Pk, Tey BH, Sin FL, Chia G. Fasting blood sugar level: a determinant for in-hospital outcome in patients with first myocardial infarction and without glucose intolerance. Annals of the Academy of Medicine 22:291-295, 1993.
36. Malmberg K, Norhammer A, Wedel H, Ryden L. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes

mellitus and acute myocardial infarction. Circularion 1999; 99: 2626-32.

37. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organisation to assess Strategies for Ischemic Syndromes) Registry. Circulation 2000; 102: 1014-9.
38. Modan B, Schor S, Shani M.Acute myocardial infarction : prognosic value of blood cell count and blood glucose level JAMA 1975:233:266-67
39. Mulvihill NT, Foley JB: Inflammation in acute coronary syndromes, Heart 87: 201-204, 2002.
40. Nakajima T, Schulte S, Warrington KJ, Kopecky SL, Frye RL, Goronzy JJ, Wey and CM: T-Cell mediated lysis of endothelial cells in acute coronary syndromes. Circulation 105: 570-575, 2002.
41. National Cholesterol Education Program, Adult Treatment Panel III 2001. JAMA 2001:285;2486-2497.
42. Norhammer AM , Ryden L, Malmberg K. Admission plasma glucose. Independent risk factor for long-term prognosis after myocardial infarction even in nondiabetic patients. Diabetes Care 1999; 22: 1827-31.
43. O'Sullivan JJ, Conroy RM, Robinson K, Hickey N, Mulcahy R. In hospital prognosis of patients with fasting hyperglycemia after first myocardial infarction. Diabetes Care 1991; 14: 58-60.
44. Ohlson LO, Svardsudd K, Welin L, Erikson H, Wilhelmsen L, Tibblin G, Larsson B: Fasting blood glucose and risk of coronary heart disease, stroke, and all-cause mortality: a 17 year follow-up study of men born in 1913. Diabetic Med 3:33-37, 1986.

45. Oliver MF, Opie LH. Effects of glucose and fatty acids on myocardial ischemia and arrythmias , Lancet 1994:343:155-58
46. Opie LH, Stubbs WA.Carbohydrate metabolism in cardiovascular disease. Clin.Endocrinol Metab 1976; 5: 703-29.
47. Opie LH. Metabolism of free fatty acids, glucose and catecholamines in acute myocardial infarction. Am J Cardiol 1975; 36: 938-53.
48. Oswald GA, Cocoran S, Yudkin JS. Prevalence and risks of hyperglycemia and undiagnosed diabetes in patients with acute myocardial infarction. Lancet 1984; 1264-7.
49. Oswald GA, Smith CCT, Betteridge DJ, Yudkin JS. Determinants and importance of stress hyperglycaemia in non-diabetic patients with myocardial infarction. Br J Med 1986; 293: 917-22.
50. Pais P, Pogue J, Gerstein H,, Zachariah E, Savitha D, Jayaprakash S, Nayak PR, Yusuf S: Risk factors for acute myocardial infarcion in Indians: a case-control study. Lancet 348: 358-363, 1996.
51. Pan W, Cedres LB, Liu K, Dyer A, Schoen-berger JA, Shekelle RB, Stamler R, Smith D, Collette P, Stamler J: Relationship of clinical diabetes and asymptomatic hyperglycemia to risk of coronary heart disease mortality in men and women. Am J Epidemiol 123: 504-516, 1986.
52. Perry IJ, Wannamethee SG, Whincup PH, Shaper AG: Asymptomatic hyperglycaemia and major ischemic heart desease events in Britain. J Epidemiol Community Health 48:538-543,1994
53. Pyorala K, Savolainen E, Lehtovirta E, Punsar S, Siltanen P: Glucose tolerance and coronary heart disease: Helsinki Policemen Study. J Chron Dis 32:729-745, 1979.

54. Raffaele Marfella, et al. Effects of stress hyperglycemia on acute myocardial infarction: role of inflammatory immune process in functional cardiac outcome – Pathophysiology / Complications. Diabetes Care Nov 2003.
55. Ravid M, Berkowicz M, Sohar E. Hyperglycemia during acute myocardial infarction: a six year followup study. JAMA 1975; 233: 807-9.
56. Reunanen A, Pyorala K, Aromaa A, Maatela J, Knekt P: Glucose tolerance and coronary disease in middle aged Finnish men: Social Insurance Institutions Coronary Heart Disease Study. J Chron Dis 32: 747-758, 1979.
57. Ross R: Atherosclerosis : an inflammatory disease. N Engl J Med 340: 115-126, 1999.
58. Scheidt – Nave C, Barrett – Cornor E, Wingard DL, Cohn BA Edelstein Sl: Sex differences in fasting glycemia as a risk factor for ischemic heart disease death . Am J Epidemiol 133:565-576-1991
59. Sewardsen M, Vythilingum S, Jialal I, Becker PJ. Prognostic importance of admission plasma glucose in diabetic and non-diabetic patients with acute myocardial infarction. QJ Med 1989; 265: 461-6.
60. Sewdarson M,Jialal I, Vythilingum S, Govender G, Rajput MC stress hyperglycaemia is a predictor of abnormal glucose tolerance in Indian patients with acute myocardial infarction . Diabetes Res 1987 :6:47-49
61. Soler NG, Frank S. Value of glycosylated haemoglobin measurements after acute myocardial infarction. JAMA 1981; 246:1690 – 93
62. Sowton E. Cardiac infarction and the glucose tolerance test. Br Med J 1962; i: 84-86.
63. Tansey MJ, Opie LH. Plasma glucose on admission to hospital as a metabolic index of the severity of acute myocardial infarction. Can J Cardiol 1986; 2: 326-31.

64. The Expert Committee on the diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnostic classification of diabetes Mellitus. Diabetes Care 1997; 20:1123-27.
65. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Follow – up report on the Diagnosis of Diabetes Mellitus Diabetes Care 2003;26:3160-67.
66. Tuomilehto J, Lindstrom J, Erikkson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344: 1343-50.
67. Tuomilehto J, Schranz A, Aldana D, Pitkaniemi J: The effect of diabetes and impaired glucose tolerance on mortality in Malta. Diabet Med 11: 170-176, 1994.
68. Vaccro O, Ruth KJ, Stamler J: Relationship of postload plasma glucose to mortality with 19-year follow-up. Diabetes Care 15: 1328-1334, 1992.
69. Wilson PWF , Cupples LA, Kannel WB : Is hyperglycemia associated with cardiovascular disease?. The Framingham study . Am Heart Journal 121 :85-590,1991
70. Yarnell JWG, Pickering JE, Elwood Pc, Baker IA, Bainton D, Dawkins C. Philips DIW: Does nondiabetic hyperglycemia predict future IHD? Evidence from the Caerphilly and Speedwell Studies. J Clin Epidemio 47: 383-388, 1994.
71. Yudkin JS , Oswald GA Hyperglycaemia , diabetes and myocardial infarction Diabetes Med 1987:4:13-18.

IMPAIRED GLUCOSE TOLERANCE IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION - A PERSPECTIVE

PROFORMA

NAME : AGE : SEX : ADDRESS:

DOA : CDNO. IPNO. BMI WAIST :

CHEST PAIN :

BREATHLESSNESS : DURATION : NYHA CLASS :

PALPITATION : SYNCOPE : OTHERS :

TYPE OF AMI : STEMI NSTEMI

LOCATION OF INFARCT :

KILLIP'S CLASS :

PREVIOUS DISORDERS : MI ANGINA CHF HTN DM
DYSLIPIDEMIA

SMOKER ALCOHOLIC

DIET : VEG / NON VEG

ECG

ADMISSION

90 MINUTES AFTER SK

THROMBOLYSIS SUCCESSFUL / UNSUCCESSFUL

COURSE IN HOSPITAL ;

DRUGS : SK ASA NITR. ACEI BB STATINS DIG HEP CLOP AB

COMPLICATIONS :

ARRHYTHMIAS

CONGESTIVE HEART FAILURE

RECC. ANGINA

PERICARDITIS

DEATH

OTHERS

INVESTIGATIONS : URINE : SUGAR KETONE

RBS : BLD UREA SR.CREATININE

75GMS OGTT: FBS : 1HR : 2 HRS ;

TOTAL CHOL : HDL-C LDL-C VLDL-C TGL

ECHO : LVID(d) LVID(s) LVEF MR TR

RWMA :

WALL MOTION SCORE INDEX

STRESS TEST :

THR ACHIEVED HEART RATE BP RESPONSE

DOUBLE PRODUCT SYMPTOMS

METS ACHIEVED DURATION OF EXERCISE

ANNEXURE 1

Conversion Table of GHb A1 and GHb A1c

A_1	A_{1c}	A_1	A_{1c}	A_1	A_{1c}
5.1	3.78	7.7	5.70	10.3	7.63
5.2	3.85	7.8	5.78	10.4	7.70
5.3	3.92	7.9	5.85	10.5	7.78
5.4	4.00	8.0	5.92	10.6	7.85
5.5	4.07	8.1	6.00	10.7	7.92
5.6	4.15	8.2	6.07	10.8	8.00
5.7	4.22	8.3	6.15	10.9	8.07
5.8	4.29	8.4	6.22	11.0	8.15
5.9	4.40	8.5	6.29	11.1	8.22
6.0	4.44	8.6	s6.37	11.2	8.30
6.1	4.48	8.7	6.44	11.3	8.37
6.2	4.59	8.8	6.52	11.4	8.44
6.3	4.70	8.9	6.59	11.5	8.52
6.4	4.74	9.0	6.67	11.6	8.59
6.5	4.81	9.1	6.74		
6.6	4.89	9.2	6.81		
6.7	4.96	9.3	6.89		
6.8	5.04	9.4	6.96		
6.9	5.11	9.5	7.04		
7.0	5.18	9.6	7.11		
7.1	5.26	9.7	7.18		
7.2	5.33	9.8	7.26		
7.3	5.40	9.9	7.33		
7.4	5.48	10.0	7.41		
7.5	5.55	10.1	7.48		
7.6	5.65	10.2	7.55		

ANNEXURE 2

Abbreviations

Cpdur	- Chest pain duration
MI	- Myocardial Infarction
Pre. MI	- Previous Myocardial Infarction
HTN	- Hypertension
Succ. Thrombo	- Successful Thrombolysis
CHF	- Congestive Heart Failure
Rec. Angina	- Recurrent Angina
SBP	- Systolic Blood Pressure
DBP	- Diastolic Blood Pressure
PR	- Pulse Rate
RBS	- Random Blood Sugar
FBS	- Fasting Blood Sugar
TC	- Total Cholesterol
TGL	- Triglycerides
LDL	- Low Density Lipoprotein
VLDL	- Very Low Density Lipoprotein
BMI	- Body Mass Index
EF	- Ejection Fraction
EDV	- End Diastolic Volume
ESV	- End Systolic Volume
WMSI	- Wall Motion Score Index