A STUDY OF CORONARY ARTERY DISEASE IN TYPE 2 DIABETIC WOMEN

Dissertation submitted in partial fulfillment of regulation for the award of M.D. Degree in General Medicine (Branch I)

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

Chennai

March 2009

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certificate

*This is to certify that the dissertation entitiled "**A study of coronary artery disease in type 2 diabetic women**, herewith submitted by **Dr DIVAKARAN.M.G**, post graduate in General Medicine Coimbatore Medical College Hospital is the record of a bonafide research work carried out by him under our guidance and supervision from March 2008 to October 2008.*

Prof Dr.U.M.NATARAJAN
Professor and Chief
Medical Unit III

Prof Dr
K.Umakanthan.MD
Professor & Head
Department of Medicine

Dean
Coimbatore Medical College
Coimbatore - 641 014

Date:
Coimbatore

DECLARATION

I solemnly declare that the dissertation titled **" A STUDY OF CORONARY ARTERY DISEASE IN TYPE 2 DIABETIC WOMEN "** was done by me from March 2008 to October 2008 under the guidance and supervision of **Professor Dr.U.M.NATARAJAN.MD.**

This dissertation is submitted to the Tamilnadu Dr. MGR Medical University towards the partial fulfillment of the requirement for the award of MD Degree in General Medicine (Branch I).

Dr.DIVAKARAN.M.G

Place : Coimbatore

Date : 01.12.2008

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CONTENTS

CORONARY ARTERY DISEASE IN TYPE-2 DIABETIC WOMEN

INTRODUCTION

Diabetes is expanding in pandemic proportions worldwide.

According to the recent statistical reports from the World Health Organization, India leads the world with the largest number of diabetic subjects[1]

Classification

DM is classified on the basis of the pathogenic process that leads to hyperglycemia.

The two broad categories of DM are designated type 1 and type 2. Type 1 diabetes is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production.

Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

The pathophysiological process of atherosclerosis in diabetic subjects is accelerated by several factors such as hyperglycemia, insulin resistance,

abnormal lipid profile, oxidative modification of lipoproteins, increased blood pressure, altered rate of fibrinolysis etc.

Diabetes and coronary artery disease

Diabetes mellitus is a disorder characterized by hyperglycemia and occurs due to impaired insulin secretion and/or impaired insulin sensitivity. Though diabetes mellitus is a metabolic disease, it is also considered as a vascular disease. Affection of the medium sized blood vessels leads to coronary artery disease (CAD), peripheral vascular disease (PVD) and cerebrovascular disease (CVD). Indeed, CAD accounts for more than 50% of the mortality among type 2 diabetic subjects. All the manifestations of CAD are at least two fold more common in patients with diabetes than in non diabetic individuals [2]

Cardiovascular risk factors in diabetic subjects

Diabetes mellitus and CAD share many common risk factors. According to Reaven[3] diabetes and CAD are constituents of the metabolic syndrome in which insulin resistance plays a contributory role. The term metabolic syndrome describe the clustering of risk factors including hypertension, dyslipidemia, hyperglycemia, insulin resistance[4]and abdominal obesity[5].This cluster has been shown to

predict death in type 2 diabetic subjects [6]. In addition a number of other factors for CAD such as atherothrombotic factors, fibrinolytic factors, coagulation factors and inflammatory markers have also been described in diabetic patients.

Hyperglycemia and CAD

Increase in plasma glucose levels have long been recognized as a risk factor for CAD.

Hypertension and CAD

Studies have shown that an increase by 5 mm of Hg is associated with 34% increase in risk for cardiovascular disease [7].

Dyslipidemia and CAD

The term diabetic dyslipidemia refers to a constellation of abnormalities including high triglycerides, low HDL cholesterol and changes in LDL cholesterol qualitatively with an excess of small dense LDL. The excess risk for CAD seen among diabetes is attributed to diabetic dyslipidemia, particularly increase in small dense LDL

Hypercoagulation and Hypofibrinolysis and CAD

Diabetes is associated with various abnormalities of the haemostatic and fibrinolytic system. Indeed diabetes is considered to be a hypercoagulable

and hypofibrinolytic state. An increased level of fibrinogen and PAI-1 has been indicated by both clinical and epidemiological studies among diabetic subjects [8].Reduced fibrinolysis may predispose diabetic patients to deposit fibrin and this may exacerbate accumulation of LDL, as dyslipidemia is a common phenomenon among these subjects..

Lipoprotein(a) and CAD

Lipoprotein(a) is a complex of apolipoprotein (a) and LDL. Lp(a) has a striking homology and common genetic determinants with plasminogen and can competitively inhibit plasminogen activity leading to impaired fibrinolysis.Lipoprotein (a) has also been implicated in enhanced oxidation and foam cell formation. Lp(a) has an independent association with CAD in Type 2 diabetic patients [9]. An increase in lipoprotein (a) was associated with increase in carotid intimal medial thickening, a preclinical atherosclerotic marker[10]. This suggest that Lp(a) is associated with CAD even at an early stage of atherosclerosis and thus could play a major role in the development of CAD.

Homocysteine and CAD

Homocysteine, a sulphur containing amino acid is an atherothrombogenic moiety, which triggers platelet adhesion in cell culture and has been shown to be strongly associated with CAD in several studies[11].

There is emerging evidences that inflammatory processes and specific immune mechanisms are involved in atherogenesis[12]. Atherosclerotic lesions are heavily infiltrated by cellular components associated with inflammation like macrophages and T lymphocytes[13]. It has been shown that inflammatory markers predict future cardiovascular events. C-reactive protein (CRP) has recently gained lot of interest,[14] and studies have shown CRP to be associated with both diabetes and CAD [15] [16].

Ischemic Heart Disease

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

Unstable Angina, ST and Non-ST-Elevation Myocardial Infarction:

Patients with ischemic heart disease fall into two large groups: patients with chronic coronary artery disease (CAD) who most commonly present with stable angina and patients with acute coronary syndromes (ACSs). The latter group, in turn, is composed of patients with acute myocardial infarction (MI) with ST-segment elevation on their presenting electrocardiogram (STEMI)and those with unstable angina and non-ST-segment elevation MI (UA/NSTEMI) .The relative incidence of UA/NSTEMI compared to STEMI appears to be increasing.

Almost one-half of patients with UA/NSTEMI are women, while more than three-fourths of patients with STEMI are men.

Cardiac biomarkers

Cardiac troponins are currently the preferred biomarkers for myocardial damage because of their high sensitivity and specificity. CK-MB is the best alternative, if cardiac troponin assays are not available.

Determinations of total CK, aspartate aminotransferase, and lactate dehydrogenase are no longer recommended.

Risk of CAD in women

The relative risk for fatal coronary heart disease associated with diabetes is 50% higher in women than it is in men. This greater excess coronary risk may be explained by more adverse

cardiovascular risk profiles among women with diabetes, combined with possible disparities in treatment that favour men.[17]

Various risk factors like diabetes, dyslipidemia, hypertension, hypercoagulation, hypofibrinolysis and inflammation are associated with CAD. Some of these factors are modifiable by therapeutic interventions. Most of these factors can be modified by life style modifications like dietary modification, regular physical activity, weight reduction and cessation of smoking. Control of CAD in diabetic patients would however require a multi-pronged approach to reduce the risk of CAD, which includes in addition to life style modifications, tight control of hyperglycemia, blood pressure and hyperlipidemia as shown in the recent Steno - 2 study [18].

AIMS AND OBJECTIVES

1.To study the incidence of coronary artery disease in women with type-2 diabetes mellitus.

2.To assess the association between glycemic control and the risk of coronary artery disease in type 2 diabetic women.

3.To evaluate the role of risk factors in the development of coronary artery disease in type 2 diabetic women.

REVIEW OF LITERATURE

Diabetes mellitus and CAD

Although diabetes may be a problem of glucose metabolism, the American Heart Association (AHA) has recently stated that "diabetes is a cardiovascular disease"[19] .

The Framingham Heart Study revealed one to five fold increase in PAD, CHF, CAD, MI, and sudden death in patients with diabetes mellitus.

Both type 1 and type 2 diabetes are powerful and independent risk factors for CAD, stroke, and peripheral arterial disease[20],[21],[22].

Type 2 diabetes patients without a prior MI have a similar risk for coronary artery–related events as nondiabetic individuals who have had a prior MI.

When patients with diabetes develop clinical events, they sustain a worse prognosis than patients without diabetes[23].

The absence of chest pain ("silent ischemia") is common in individuals with diabetes, and a thorough cardiac evaluation is indicated in individuals undergoing major surgical procedures.

CAD is more likely to involve multiple vessels in individuals with DM.

RISK FACTORS

Risk factors for macrovascular disease in diabetic individuals include dyslipidemia, hypertension, obesity, reduced physical activity, and cigarette smoking.

Additional risk factors more prevalent in the diabetic population include microalbuminuria, an elevation of serum creatinine, and abnormal platelet function.

Insulin resistance, as reflected by elevated serum insulin levels, is associated with an increased risk of cardiovascular complications in individuals with and without DM.

Individuals with insulin resistance and type 2 DM have elevated levels of plasminogen activator inhibitors (especially PAI-1) and fibrinogen, which enhances the coagulation process and impairs fibrinolysis, thus favoring the development of thrombosis.

Diabetes is also associated with endothelial, vascular smooth-muscle, and platelet dysfunction

Role of Inflammatory Markers

Increased serum levels of glycated albumin, hsCRP and TNF-alpha are associated with the presence and severity of CAD and renal impairment in patients with T2DM.[24]

A prospective study showed the relationship between cardiovascular risk factors, selected biomarkers (high-sensitivity C-reactive protein [hs-CRP], interleukin [IL]-6, and osteoprotegerin [OPG]), and the progression of coronary artery calcification (CAC) in type 2 diabetic subjects.

Coronary artery calcification is pathognomonic of coronary atherosclerosis. Osteoprotegerin is a signaling molecule involved in bone remodeling that has been implicated in the regulation of vascular calcification and atherogenesis.

In a study on Inflammatory markers, insulin resistance and carotid intima-media thickness in North-Indian type 2 diabetic subjects,

Plasma glucose and insulin (fasting and after 2 hours of 75 gm of oral glucose), lipids and serum levels of C-reactive protein (CRP), fibrinogen and Tumour Necrosis Factor (TNF)-alpha were measured. Carotid (Intima-Medial Thickness) IMT was measured using high "resolution B-Mode ultrasonography. Insulin resistance was calculated using HOMA-IR

model. Electrocardiogram (ECG) and exercise ECG were recorded for the evidence of coronary heart disease (CHD).HOMA-IR, waist hip ratio, serum triglycerides, serum cholesterol, fasting serum insulin and CRP were significant predictor of IMT. Concentrations of inflammatory markers were significantly higher in diabetic patients than in control group. Inflammatory markers are associated with type 2 diabetes but only CRP is associated with development of accelerated atherosclerosis and subsequent development of CHD. [25]

- Levels of fasting plasma glucose, body mass index, serum total lipids, serum total cholesterol, serum triglycerides and blood pressure of 177 Libyan diabetic patients were determined. The mean levels of all variables except plasma glucose were significantly higher in the female patients than their male counterparts. Correlations were present between blood pressure levels and age/body mass index/serum total lipids. There was a significant correlation between systolic pressure levels and the duration of diabetes. Serum cholesterol and serum triglyceride levels correlated with diastolic blood pressure levels only.[26]

Sub-clinical vascular disease in type 2 diabetic subjects:

A low ABI is highly prevalent in subjects with diabetes and is related to age, duration of diabetes, smoking habit, and hypertriglyceridemia. Although chronic complications are frequently

associated with a low ABI, only renal damage is independently associated with peripheral artery disease.[27]

A study of Prevalence of subclinical atherosclerosis in asymptomatic diabetic patients by 64-slice computed tomography showed that the prevalence of coronary plaques detectable by 64-slice CT in asymptomatic diabetic patients is very high.[28]

The study concluded that baseline CAC severity and suboptimal glycemic control are strong risk factors for CAC progression in type 2 diabetic subjects.[29]

The Diabetes Heart Study concluded that QT duration correlates with the amount of coronary artery calcium score(CAC) in a predominantly diabetic population. The association between QT duration and CAC is driven by QRS and not JT interval duration.[30]

DM and Peripheral Vascular Disease

- Diabetic patients with diabetic foot were more likely to have a higher prevalence of cardiovascular risk factors such as hypercholesterolemia, hypertriglyceridemia, hyperuricemia, and microalbuminuria or proteinuria, a higher prevalence of a previous cardiovascular morbidity (coronary artery disease, transient ischemic attack/ischemic stroke, diabetic retinopathy), and a higher prevalence of

subclinical cardiovascular disease. Furthermore, diabetic patients with foot ulceration showed, on a 5-year follow-up, a higher incidence of new-onset vascular events (coronary artery disease, transient ischemic attack/ischemic stroke, diabetic retinopathy). At multivariate analysis, duration of diabetes, age, hemoglobin A1c, and DFS maintained a significant association with cardiovascular morbidity; but DFS presence showed the highest hazard ratio.[31]

Carotid ultrasound, blood lipids and waist determination can predict a future coronary revascularisation in the type 2 diabetic cohort.[32]

The presence of arterial hypertension, hyperlipidemia, physical inactivity, intermittent claudication, the value of systolic pressure, BMI, waist and hip measurement, glycemia and blood lipid fraction (total cholesterol, HDL, LDL, non-HDL, triglycerides) were entered in a model. Ultrasound measurements: carotid IMT, presence of carotid plaques and stenosis, and ABI were also included in the analysis. Based on the univariate and multivariate findings, the presence of internal carotid artery (ICA) stenosis (OR 4,562, 95% CI 1,327-15,687), carotid plaque (OR 1,465, 95% CI 0,829-2,591), and increased waist measurement (OR 1,371, 95% CI 0,757-2,483) were found as significant independent predictors of future PCI. LDL and non HDL cholesterol were found to be factors independently associated with the need for future CABG by univariate analysis, which was not confirmed by multivariate analysis.

Metabolic syndrome and CAD

The most prevalent metabolic syndrome component was arterial hypertension (78.3%). Low HDL was detected in 67.9%, hypertriglicerydaemia in 62.7%, and an increased waist in 49.8% of the study population.[33]

In Type 2 DM and HTN without epicardial coronary stenosis, an impairment of coronary flow reserve is demonstrable. This is partly

explained by an increased left-ventricular mass, able to condition the hyperemic stimulation of myocardial blood flow.[34]

BP Control

All people with diabetes-regardless of age, gender, and race and ethnicity-may benefit from efforts to prevent hypertension. The control of elevated blood pressure is inadequate and broad-based efforts are needed to improve blood pressure control.[35]

Stress and risk of CAD

A significant proportion of patients report 'high' levels of subjective stress in the 2-4 week period preceding acute coronary events. This study confirms the association of subjective stress and acute coronary events[36],[37]

Role of genetics

Genetic analysis of the soluble epoxide hydrolase gene, EPHX2, in subclinical cardiovascular disease in the Diabetes Heart Study:

Epoxide hydrolase is involved in metabolism of vasoactive and anti-inflammatory epoxyeicosatrienoic acids to their corresponding diols. Consequently, epoxide hydrolase 2 (EPHX2) is a candidate cardiovascular disease (CVD) gene. The R287Q polymorphism was associated with carotid artery calcified plaque (CarCP) in EAs. Other EPHX2 polymorphisms were associated with coronary

artery calcified plaque (CorCP), CarCP or carotid artery intima-media thickness (IMT).The results provide additional evidence that EPHX2 contributes to the risk of subclinical CVD, although the true trait defining polymorphisms may not be identified and the effect size could be small.[38]

Presence of T2DM significantly modulates the vascular risk conferred by the PAI-1 -675 4G/5G polymorphism in angiographied coronary patients.[39]

CAD in women

Type 2 diabetes increases relative risk of cardiovascular disease two- to fourfold compared with the risk in the general population [40414243].The increase in cardiovascular risk is particularly high in women.

The protection against atherosclerosis in premenopausal women is almost completely lost in women with diabetes [44].

Diabetic postmenopausal women develop more severe CAD compared to non-diabetic women. This association is independent of other predisposing factors and suggests an independent effect of T2DM on the atherosclerotic process, at least in women after menopause.[45]

Excess risk of fatal coronary heart disease associated with diabetes in men and women was studied in a meta-analysis of 37 prospective cohort studies.

The study concluded that the relative risk for fatal coronary heart disease associated with diabetes is 50% higher in women than it is in men. This greater excess coronary risk may be explained by more adverse cardiovascular risk profiles among women with diabetes, combined with possible disparities in treatment that favour men.[46]

Screening in Asymptomatic women

The results obtained from a study of CAD in asymptomatic women suggested a high prevalence of CAD in diabetic women. Thus, this population should be investigated from the cardiovascular point of view even without cardiac symptom. Of the noninvasive diagnostic methods used, dipyridamole MPS was the one that showed the highest discrimination power in relation to diabetic women with CAD.[47]

Gestational diabetes, pregnancy hypertension, and late vascular disease:

As a forme fruste of later type 2 diabetes, GDM-affected gravidas are identified as at risk of diabetes-related atherosclerosis, glomerular disruption, and pathogenic retinal angio-genesis. Late pregnancy preeclampsia is associated with elevated mid-

pregnancy BMI, blood pressure, fasting glucose and insulin, urate, and C-reactive protein, suggestive of metabolic and immune dysregulation..[48]

Hyperleptinemia

Hyperleptinemia as a Robust Risk Factor of Coronary Artery Disease and Metabolic Syndrome in Type 2 Diabetic Patients:

Leptin has been linked to adiposity, insulin resistance, and coronary artery disease (CAD). Other variables associated with CAD were age, sex, hypertension, low-HDL cholesterolemia, and hsCRP. Hyperleptinemia might be an independent risk factor for CAD and MS in diabetic subjects. And the simultaneous measurement of insulin resistance and leptin concentration might be helpful for screening subjects with a high-risk of CAD.[49]

Cardiac parasympathetic dysfunction in type 2 diabetes mellitus

A study on Independent predictors of cardiac parasympathetic dysfunction in type 2 diabetes mellitus concluded that parasympathetic dysfunction mainly coexists with somatic neuropathy. It may be isolated, or precede detection of other complications. Age and female gender are the other predictors of reduced heart rate response to deep breathing in type 2 diabetes mellitus.[50]

In a study of Insulin resistance as predictor of the angiographic severity and extent of coronary artery disease Patients with more severe degree of IR had a more severe, extensive, and distal type of CAD than patients with lower degree of IR[51]

Albuminuria

In diabetic patients with albuminuria, Doppler strain and SR imaging detected subclinical LV systolic and diastolic dysfunction; and albuminuria was associated with myocardial dysfunction in diabetic patients without overt heart disease.[52]

OX-LDL

Elevated levels of ox-LDL, can serve as an independent and significant predictor for future cardiac events in type 2 diabetic patients with CAD.[53]

Uncomplicated diabetes mellitus is equivalent for coronary artery disease- New support from novel angiographic myocardial perfusion-myocardial blush:

Diabetes mellitus (DM) is accepted as coronary heart disease equivalent even in the presence of normal coronary artery on coronary angiography. Evaluation of microvascular circulation with novel angiographic perfusion indexes "myocardial blush grade" (MBG) and "myocardial filling time" (MFT) in patients with

uncomplicated DM showed that microvascular function is worse in subjects with both diabetes and coronary artery disease than in non-diabetic subjects with coronary artery disease. The most impressive result of the study was diabetic patients with normal coronary angiography had similar MBG and MFT results with non-diabetic coronary artery disease patients. DM causes microvascular dysfunction even when one has normal coronary angiography and this put them in the same risk group with non-diabetic coronary artery patients.[54]

Waist-to-height Ratio and Coronary Artery Disease :

Waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHeiR), and BMI are indicators for obesity. A study examined the usefulness of these indicators for coronary artery disease (CAD) in Taiwanese type 2 diabetic patients. Only WHeiR was significant for both sexes and it also showed the greatest decrease in -2 log likelihood, the largest magnitude of odds ratio, and the smallest AIC while compared with the other indices in either sex. It concluded that WHeiR has the superiority of independent association with CAD and the highest magnitude of association than WC, WHR, and BMI in both sexes. The usefulness of WHeiR should not be neglected in clinical practice.[55]

In addition to CAD, cerebrovascular disease is increased in individuals with DM (threefold increase in stroke).

Individuals with DM have an increased incidence of CHF. The etiology of this abnormality is probably multifactorial and includes factors such as myocardial ischemia from atherosclerosis, hypertension, and myocardial cell dysfunction secondary to chronic hyperglycemia.

Endothelial dysfunction in diabetes mellitus

The vascular endothelium has been shown to be important in modulating blood cell-vessel wall interaction, regulating blood flow, angiogenesis, lipoprotein metabolism, and vasomotion. The mechanism of this increased vascular resistance is probably partly due to the increase in the intercellular signal transduction kinase, protein kinase C (PKC)[56575859] which result in an increase in endothelin-1.

An important mediator in maintaining vascular homeostasis is endothelium-derived relaxing factor (EDRF)[60] which has been found to be nitric oxide. [61]which results in relaxation of vascular smooth muscle [62636465]

Type 2 diabetes have an impairment of both endothelial-dependent and endothelial-independent (smooth muscle) vasodilator function in contrast to type 1 DM patients[66],[67].

Acute hyperglycemia impairs endothelial-dependent vasodilation in both macro- and microvessels[68] .

Insulin also may play a role. Insulin results in vasodilation due in part to nitric oxide production.

Several studies have shown that high doses of vitamin C can improve endothelial-dependent vasodilation in patients with both type 1 and type 2 diabetes [6970].

Intensive lipid lowering by statin therapy does not improve vasoreactivity in patients with type 2 diabetes, suggesting that mechanisms other than dyslipidemia are responsible for endothelial dysfunction [71].

Endogenous competitive inhibitor of nitric oxide synthase, asymmetric dimethylarginine (ADMA)[72] ADMA has been found to be elevated in subjects with diabetes [7374].

The detection of impaired fasting glucose is a strong risk factor for type 2 diabetes.

Recent evidence suggests that either lifestyle intervention or treatment with metformin also can reduce the development of diabetes in persons at high risk[75] .

MATERIALS AND METHODS

Design and data collection:

A descriptive study design was adopted and samples were collected by systematic random sampling method.

Ethics commitee approval was obtained and informed consent was taken from participants.

Inclusion critera:

All type 2 diabetic women attending diabetology clinic,medical wards and ICCU are included & 170 patients selected by systematic random sampling method.

Exclusion criteria:

Type 1 diabetic women,children,men& pregnant diabetic patients.

Measures:

Each patient was interviewed to obtain detailed history and examined thoroughly.

Height ,weight and waist circumferences were examined with standardized techniques and equipments.

BMI and Waist height ratios were computed.

BMI calculated by dividing weight in Kg by height in M^2

Blood pressure was examined in supine position in the right upper limb.

Serum total cholesterol and triglycerides measurement were done after 12hours of fasting.

ECG and Echocardiographic evaluation were done for coronary artery disease patients.

Statistical analysis:

Statistical analysis was done using SPSS software for windows.

Means compared by applying student's t-test,proportions compared by z test.

DIAGNOSTIC CRITERIA

FOR DIBETES MELLITUS:

The National Diabetes Data Group and World Health Organization diagnostic criteria was used

Criteria for the Diagnosis of Diabetes Mellitus

1.Symptoms of diabetes plus random blood glucose concentration 11.1 mmol/L (200 mg/dL)*or*

2.Fasting plasma glucose 7.0 mmol/L (126 mg/dL)*or*

3.Two-hour plasma glucose 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test

In our study 1,2 criteria were used.

FOR HYPERTENSION:

Joint National Conference –VII criteria followed

Category	Systolic(mm Hg)	Diastolic(mm Hg)
Optimal	<120	<80
Prehypertenson	120-139	80-89
Stage-1	140-159	90-99
Stage-2	>/=160	>/=100

FOR CORONARY ARTERY DISEASE:

History, ECG changes and echocardiographic criteria were used.

HISTORY

chest discomfort, usually described as heaviness, pressure, squeezing, smothering, or choking, and only rarely as frank pain. Angina is usually crescendo-decrescendo in nature, typically lasts 2–5 min, and can radiate to either shoulder and to both arms, especially the ulnar surfaces of the forearm and hand. It can also arise in or radiate to the back, interscapular region, root of the neck, jaw, teeth, and epigastrium.

Stable angina pectoris is characterized by chest or arm discomfort that may not be described as pain but is reproducibly associated with physical exertion or stress and is relieved within 5–10 min by rest and/or sublingual nitroglycerin.

UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features: (1) it occurs at rest (or with minimal exertion), usually lasting >10 min; (2) it is severe and of new onset (i.e., within the prior 4–6 weeks); and/or (3) it occurs with a crescendo pattern (i.e., distinctly more severe, prolonged, or frequent than previously).

Symptoms of AMI

The classic symptom of AMI is precordial or retrosternal discomfort that is commonly described as a pressure, crushing, aching, or burning sensation. Radiation of the discomfort to the neck, back, or arms frequently occurs, and the pain is usually persistent. The discomfort

typically achieves maximum intensity over several minutes and can be associated with nausea, diaphoresis, generalized weakness, and a fear of impending death. Some patients, particular the elderly, may also present with syncope, unexplained nausea and vomiting, acute confusion, agitation, or palpitations.

ELECTROCARDIOGRAM[76],[77]

ISCHEMIA

a)Sub endocardial ischemia:

A combination of two diagnostic criteria is required in at least one ECG lead for the diagnosis.

1)At least1.0 mm(0.10mv)depression at the J point.

2)Either a horizontal or downward slope towards the end of the ST segment at its junction with the T wave.

b)Transmural ischemia

presence of one of the following criteria is required for the diagnosis.

1)elevation of the origin of the ST segment at its junction(Jpoint)with the QRS of (a)>=1.0 mm(0.10mv)in two or more limb leads(b)>=2.0mm(0.2mv)in two or more precordial leads,OR

2)Depression of the origin of the ST segment at the J point of >=2.0 mm(0.20mv)in at least two of the three leads V1-V3.

MYOCARDIAL INFARCTION

a)convex ST segment elevation in corresponding leads(early).

b)QS complexes or abnormal Q waves ie. Q waves of 0.04 seconds or more in width or

25% or more of the voltage of the R wave in the same lead or

Both in the corresponding leads(late)

c)T wave inversion (typically deep,symmetric) in the corresponding leads(late)

ANATOMICALZONE	ECG ZONE
INFERIOR WALL	LII,III,Avf
ANTERO SEPTALWALL	V1-V4
EXTENSIVE ANTERIOR WALL	LI,AVL,V1-V6
ANTERO LATERAL WALL	LI,AVL,V5-V6
INFERO LATERAL WALL	LII,LIII,AVF,AVL,V5-V6

ECHOCARDIOGRAPHY

Abnormalities of wall motion on two-dimensional echocardiography ,estimation of left ventricular (LV) function,presence of right ventricular (RV) infarction, ventricular aneurysm, pericardial effusion, and LV thrombus.

Doppler echocardiography for the detection and quantitation of a ventricular septal defect and mitral regurgitation, two serious complications of STEMI.

ECG showing acute inferior wall myocardial infarction

Chest x-ray showing cardiomegaly

ANALYSIS OF RESULTS

ANALYSIS OF VARIOUS SYMPTOMS OF DIABETES

In our study of the 170 diabetic women the following symptom frequencies were observed in relation with the level of post prandial blood sugar(PPBS).

SYMPTOMS OF DIABETES	PPBS<140	140-200	PPBS>200
POLYDIPSIA	1	21	21
POLYPHAGIA	0	18	7
POLYURIA	2	33	35
WEIGHTLOSS	0	2	0
FATIGUE	1	36	22
PRURITUS	0	3	4
INFECTIONS	0	0	2
ANGINAL PAIN	0	24	24
NONANGINAL PAIN	1	10	5
DIMVISION	0	5	3

ANALYSIS OF VARIOUS SYMPTOMS OF CORONARY ARTERY DISEASE

Out of the 170 patients analysed 64 patients developed various forms of coronary artery disease(CAD).The symptom frequencies observed in those patients are given below.

SYMPTOMS	CAD IN ECG	ECG NORMAL	P value
CHESTPAIN	47	1	<0.05
	16	0	NS
DYSPNOEA	5	5	
DIAPHORESIS	2	0	
PALPITATION	12	6	<0.05
EDEMA	6	5	
GIDDINESS	20	11	<0.05
DYSPEPSIA	21	20	<0.05
VOMITING	2	0	

AGE DISTRIBUTION

Among the 64 patients who developed coronary artery disease 26 patients belonged to the 50-60 years age group(40.6%),19 patients in the 40-50 years age group(29.7%),13 patients in the 60-70 years age group(20.3%),4.7% both in 30-40 and 70-80 years age groups.

AGE GROUP	NO:OF CAD PATIENTS	PERCENTAGE OF CAD PATIENTS
30-40	3	4.7%

40-50	19	29.7%
50-60	26	40.6%
60-70	13	20.3%
70-80	3	4.7%
>80	0	.0%

OCCUPATION AND CAD

In our study the following results were obtained regarding the correlation of occupation and CAD.Among the 64 CAD patients 26 had sedentary jobs(40.6%),14 were manual labourers(21.9%).

OCCUPATION	NO: OF CAD PATIENTS	PERCENTAGE
Manual labourer	14	21.9%
Moderate exertion	24	37.5%
Sedentary Job	26	40.6%

INCIDENCE IN PREMENOPAUSAL V/S POSTMENOPAUSAL WOMEN

Among the 170 patients studied 34(20%)were premenopausal and136(80%) were postmenopausal. Out of the 64 CAD patents 51 (79.7%)were postmenopausal women and 13(20.3%) were premenopausal.

MENSTRUAL H/O	COUNT	PERCENTAGE
Premenopausal	34	20.0%
Postmenopausal	136	80.0%

MENSTRUAL H/O	CAD IN ECG	PERCENTAGE
PREMENOPAUSAL	13	20.3%
POSTMENOPAUSAL	51	79.7%

STRESS AND CAD

In the study a significant proportion (28 out of the 64 patients) reported 'high' levels of subjective stress in the 2-4 week period preceding acute coronary events.

STRESS	CAD IN ECG	NORMAL ECG	P VALUE
ABSENT	36	104	<0.05
PRESENT	28	2	<0.05

BODY MASS INDEX AND CAD

BMI of 18-25 is considerd to be normal,25.1-29.9 as overweight,>30 as obese,<18 as underweight.In the study out of 64 CAD patients 38 (59.4%)were overweight,16(25%) had normal weight,10(15.6%) were obese and none of them were underweight.

BMI	CAD	CAD%	TOTAL	TOTAL%
BMI<18	0	.0%	0	.0%
BMI 18.10-25	16	25.0%	41	24.1%
25-29.99	38	59.4%	106	62.4%
BMI>30	10	15.6%	23	13.5%

ANALYSIS OF WAIST CIRCUMFERENCE

In our study, 43 out of the 64 CAD patients (67.2%) had waist circumference >88 cm,21(32.8%) had waist circumference <88 cm.

WAIST CIRCUMFERENCE	NO: OF CAD PATIENTS	PERCENTAGE
>88CM	43	67.2%
<88CM	21	32.8%

ANALYSIS OF WAIST- HEIGHT RATIO

This study examined the, usefulness of waist-to-height ratio (WHeiR)as an indicator for coronary artery disease (CAD).36(56.3%) CAD patients had WHeiR<0.56 and 28(43.8%) had WHeiR>0.56.

WAIST- HEIGHT RATIO	NO:OF CAD PATIENTS	PERCENTAGE
<0.56	36	56.3%
>0.56	28	43.8%

ANALYSIS OF HYPERTENSION

Among the 170 patients studied 36(21.1%)had hypertension

SBP WITHOUT CAD	COUNT	PERCENTAGE
140-160	23	13.5%
>160	13	7.6%

Age group of the hypertensive patients were as shown below. Largest number of hypertensives (39.3%) were in the 50-60 years age group.

AGE	SBP	PERCENTAGE
30-40	1	2.13
40-50	11	30.60
50-60	15	39.30
60-70	6	19.75
70-80	2	6.00
>80	1	2.13

A significant percentage of CAD 23.4% with p value <0.05 were observed among patients with systolic BP in the range of 140-160 mm of Hg.

SBP	CAD	PERCENTAGE	P VALUE
<120	12	18.8%	NS
120-140	24	37.5%	NS
140-160	15	23.4%	<0.05
>160	13	20.3%	NS

DBP	COUNT	PERCENTAGE
90-100	10	5.9%
>100	1	.6%

GLYCEMIC CONTROL

In the study of PPBS and the incidence of CAD,maximum incidence is found in 200-250 mg% range(34.4%);26% in 140-200mg% range,20.3% in 250-300mg% range and 0 % in<140 mg % range.

PPBS&GLYCEMIC CONTROL	NO:OF CAD PATIENTS	PERCENTAGE
<140	0	0%
140-200	17	26.6%
200-250	22	34.4%
250-300	13	20.3%
300-350	9	14.1%
>350	3	4.7%

In study of FBS and incidence of coronary artery disease significant number of patients had FBS >125 mg%.

FBS	CAD	PERCENTAGE
<110	8	12.5%
110-125	6	9.4%
>125	50	78.1%

SERUM CHOLESTEROL

In the study significant correlation was found between hypercholesterolemia and the incidence of coronary artery disease.67.2% of coronary artery disease patients had moderate hypercholesterolemia.

TOTAL CHOLESTEROL	NO: OF CAD PATIENTS	PERCENTAGE	P VALUE
DESIRABLE	15	23.4%	NS
MODERATE HYPERCHOL	43	67.2%	NS
HYPERCHOL	6	9.4%	<0.05

SERUM TRIGLYCERIDES

In the study of correlation between serum triglycerides and the incidence of coronary artery disease,60.9% of the CAD patients had triglycerides >150mg%.

TRIGLYCERIDES	NO: OF CAD PATIENTS	PERCENTAGE
<150	25	39.1%
>150	39	60.9%

ECG ANALYSIS

Among the 170 type 2 diabetic women studied,64(37.6%)had evidence of coronary artery disease.

No of patients with ischaemic heart disease excluding myocardial infarction = 48

No of patients with myocardial infarction=16

NSTEMI=10

STEMI=6

Various conduction defects in CAD patients=7

Various arrhythmias in CAD patients=3

ECG	COUNT	PERCENTAGE
CAHD	64	37.6%
NORMAL	106	62.4%

ECG	COUNT	PERCENTAGE
ARRHYTHMIAS	0	.0%
CONDUCTION DEFECTS	0	.0%
IHD	42	24.7%
IHD&ARRHYTHMIAS	1	.6%
IHD&CD	5	2.9%
NORMAL	106	62.4%
NSTEMI&ARRHYTHMIAS	1	.6%
NSTEMI&CD	1	.6%
NSTEMI	8	4.7%
STEMI	3	1.8%
STEMI&ARRHYTHMIAS	2	1.2%
STEMI&CD	1	.6%

ECHOCARDIOGRAPHY

In the echocardiographic evaluation of CAD patients,all patients with myocardial infarction had regional wall motion abnormalities,one patient had papillary muscle dysfunction and four had left ventricular dysfuncyion.

ECHO	COUNT	PERCENTAGE
CHAMBER ENLARGEMENT	0	0%
PMD	0	0%
RWMA	14	8.2%
RWMA&LVD	4	2.4%
R,P	1	0.6%

DISCUSSION

ANALYSIS OF CORONARY ARTERY DISEASE

Incidence of coronary artey disease in diabetes mellitus varies from 11% to 77% as reported by various authors.

The present study showed an incidence of 37.6%. The study conducted by Banerjee j.c et [78]al found out an incidence of 35%,Pathania and sachar et al 21.8% ,Stearns et al 37%,Shah [79] et al 36%,Pathak et al 32.5%,Lundback et al 63%,Liebow et al 42%,Bradley&Bryfogle et al 40%,Anderson et al 77%,Ahuja et al 11%.

Incidence of coronary artery disease varies from 11to77 % in western literatures.Indian studies showed an incidence of 10 to 36%.The variation in the incidence of coronary artery disease may be explained by

1.The difference in diagnostic criteria adopted by different authors,

2.The presence and absence of various risk factors in the selected study populations,

3.Phenotypic,genotypic and environmental variations,

4.Various bias.

Incidence of coronary artery disease in general population varies from 1 to 6% as reported by Padmavathy Mathur et al and different authors.

The incidence of myocardial infarction is 9.5% in the present study.

Vaishnava et al [80]reported an incidence of 8% whereas Bryfogle and Bradley reported 8.6%.

ANALYSIS OF HYPERTENSION

In the present study the incidence of hypertension was 21.1% . A significant percentage of CAD (23.4%)with p value <0.05 were observed among patients with systolic BP in the range of 140-160 mm of Hg.

In the Framingham study blood pressure of diabetic patients were significantly higher than in matched nondiabetic controls.

Incidence of hypertension in diabetes mellitus varies from 21.1% to 68% as reported by various authors.Our study showed an incidence of 21.1%.The Framingham study[81] showed an incidence of 54%,Balme and cole 60%,Banerjee et al [82]43.4%,Lundback et al 68%,Liebow et al 34.8%,Pathania et al 27.8%.

Hypertension independently influences the incidence of coronary artery disease as reported by the Framingham study.Both systolic and diastolic hypertension influences the incidence.In diabetic patients hypertension accelerates coronary atherosclerosis.

INCIDENCE OF CAD IN DIFFERENT AGE GROUPS

Atherosclerotic heart disease complicates the course of diabetes mellitus with increasing frequency in older age groups.

Our study showed an incidence of 40.6% in 50-60 years age group.Vaishnava et al [81]reported an incidence of 37.3% in 50-60 years age group.Banerjee et al [79]reported 87.7% in 70-80 years,Bradley Bryfogle 89%,Pathania sachar 51.3%,Shah et al [80]75%, Urset al 25% ,all in 70-80 years.

Both Indian and western studies report that the incidence of CAD is negligible in less than 40 years.In the present study incidence in fourth decade is 4.7%.

In the Framingham study patients who developed CAD belonged to 45-64 years age group.

INCIDENCE IN PREMENOPAUSAL V/S POSTMENOPAUSAL WOMEN

Premenopausal women are relatively free of CAD.Oliver et al reported a male female ratio of 16:1 below 40 years of age,7:1 in the fifth decade,1:1 above 70 years of age.

The protection against atherosclerosis in premenopausal women is almost completely lost in women with diabetes. [38]

Among the Indian studies Pathania and Sachar,Vaishnava et al[81] reported equal sex incidence where as Pathak et al ,Banerjee et al,Urs and Shah observed a 2:1male:female ratio.Incidence of coronary artery disease is more in diabetic women than non diabetics.

In Our study CAD incidence was 79.7% in the postmenopausal and 20.3% in the premenopausal age group.

Framingham study and a recent meta analysis of 37 propective cohort studies revealed excess mortality from CAD in diabetic women[18].

OBESITY AND CAD

Obesity increases the CAD risk independently and through the associated metabolic syndrome components.Obesity has influence on the insulin secretion,insulin sensitivity and the lipoprotein metabolism.

Waist circumference (WC), waist-to-height ratio (WHeiR), and BMI are indicators for obesity. Our study examined the usefulness of

these indicators for coronary artery disease (CAD) type 2 diabetic women patients

BODY MASS INDEX AND CAD[83],[84]

In our study CAD incidence was significantly higher in overweight patients with BMI 25-29.9(59.4%),15.6% in obese patients(BMI>30)and 25% in patients with normal weight.

ANALYSIS OF WAIST CIRCUMFERENCE[85],[86]

Several studies have reported that waist circumference >88cm in women increases the risk of CAD.

In our study 67.2% had waist circumference >88 cm, 32.8% had waist circumference <88 cm.

ANALYSIS OF WAIST- HEIGHT RATIO

A study in Taiwanese type 2 diabetic patients had concluded that WHeiR has the superiority of independent association with CAD and the highest magnitude of association than WC, WHR, and BMI in both sexes[54].

Our study examined the usefulness of waist-to-height ratio (WHeiR)as an indicator for (CAD). 56.3% of CAD patients had WHeiR<0.56 and 43.8% had WHeiR>0.56.No significant correlation can be made from WHeiR and incidence of CAD from our study.

GLYCEMIC CONTROL AND INCIDENCE OF CAD

The importance of glycemic control in preventing the development and progression of long term complications of diabetes mellitus was proven by different studies.[87]

Diabetes control and complications trial and UKPDS were among the few important studies.[88],[89],[90] In the DCCT there was 41% risk reduction for macrovascular complications in tightly controlled type 1 diabetic patients.

In our study of PPBS and the incidence of CAD,maximum incidence is found in 200-250 mg% range(34.4%);26% in 140-200mg% range,20.3% in 250-300mg% range and 0 % in<140 mg % range.

In our study of FBS and incidence of coronary artery disease significant number of patients had FBS >125 mg%(78.1%).

LIPIDS AND INCIDENCE OF CAD

Lipoprotein abnormalities are common in diabetes and contribute significantly to its complications .[91] several studies of the Lipid Profile Pattern in Diabetics from India[92] have been demonstrated a significant relationship between hypercholesterolemia and CAD.[93],[94] However, in Madras, India, 75% of people with myocardial infarction (MI) had plasma cholesterol levels less than 200 mg/dl .In another study from India, even lower level of plasma cholesterol (<150 mg/dl) in patients with CAD has been reported

In our study ,significant correlation was found between hypercholesterolemia and the incidence of coronary artery disease.67.2% of coronary artery disease patients had moderate hypercholesterolemia(210-250mg%) and 9.4% had hypercholesterolemia(>250mg%).

Studies done by Sunil Gupta Diabetes Care Center, Nagpur India [95],[96]in patients with established acute myocardial infarction (AMI) with or without diabetes and a publication from Bangalore on diabetics with CAD showed serum triglycerides levels to be higher in the diabetic group whereas other lipid fractions were nearly similar and not significantly elevated as would have been expected.

In our study of correlation between serum triglycerides and the incidence of coronary artery disease,60.9% of the CAD patients had triglycerides >150mg%.

OCCUPATION AND CAD

Vaishnava et al [81]reported an incidence of 44.7% of CAD in sedentary group,34.8% in moderatively active and 21.5% in manual labourers.

In our study the following results were obtained .Among the 64 CAD patients 26 had sedentary jobs(40.6%),14 were manual labourers(21.9%).There was a significant correlation between sedentary occupation and increased incidence of CAD.

Several studies including the one by Vaishnava et al[81] have reported the role of mental stress and the increased risk of CAD.[31,32]

In our study a significant proportion (28 out of the 64) of patients reported 'high' levels of subjective stress in the 2-4 week period preceding acute coronary events.

CONCLUSION

1)Incidence of CAD,including myocardial infarction,in type 2 diabetic women was 37.6%.

2)Incidence of myocardial infarction was 9.5%.

3)Incidence of CAD in post menopausal type 2 diabetic women was 79.7%.Incidence in pre menopausal women was 20.3%.

4)Incidence of CAD was maximum in age group 50-60 years(40.6%).

5)Incidence of hypertension was maximum in age group 50-60 years(39.3%)

6) A significant percentage of CAD (23.4%) with p value <0.05 were observed among patients with systolic BP in the range of 140-160 mm of Hg.

7) Incidence of CAD among patients with sedentary occupations was (40.6%).

8) In the study a significant proportion (28 out of the 64 patients) reported 'high' levels of subjective stress in the 2-4 week period preceding acute coronary events.

9) In the study of 64 CAD patients 59.4% were overweight and 15.6% were obese .

10)67.2% of the CAD patients had waist circumference >88 cm.

11) In the study of PPBS and the incidence of CAD,maximum incidence was found in 200-250 mg% range(34.4%)and 20.3% in 250-300mg% range.

12)Maximum incidence of CAD was found in patients with FBS>125 mg % (78.1%).

13)Moderate hypercholesterolemia (210-250 mg%) was observed in 67.2% of coronary artery disease patients and hypercholesterolemia(>250 mg%) in9.4%.

14)In the study 60.9% of the CAD patients had triglycerides >150mg%.

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APPENDIX-1

MASTERCHART

APPENDIX-2

PROFORMA

PATIENT PARTICULARS:

NAME

I.PNUMBER

AGE

OCCUPATION

SYMPTOMS OF DM:
POLYURIA
POLYPHAGIA
POLYDIPSIA
WEIGHTLOSS
FATIGUE
PRURITUS
INFECTIONS
DIMVISION

SYMPTOMS OF CAD:

CHESTPAIN
DYSPNOEA
DIAPHORESIS
PALPITATION
EDEMA
GIDDINESS
DYSPEPSIA
VOMITING

PERSONAL H/O:

SMOKING
ALCOHOLISM
STRESS

MENSTRUAL H/O:

PASTILLNESS:

HEIGHT
WEIGHT
BMI
WAIST CIRCUMFERENCE
WAIST HEIGHT RATIO

VITAL SIGNS

PULSE
SBP

DBP
GENERAL EXAMINATION:

PALLOR
CYANOSIS
XANTHELASMA
XANTHOMAS
THYROID DIS

SYSTEMIC EXAMINATION:
CVS
RS
ABD
CNS
PNS
FUNDUS

INVESTIGATIONS:

URINEALB
URINESUGAR
URINEACETONE
HEMOGLOBIN
RBS

FBS

PPBS

UREA
SERCREATININE
SODIUM
POTTASSIUM
S.CHOLESTEROL
S.TRIGLYCERIDES

CXR-PA VIEW
ECG

ECHO

APPENDIX-3
ABBREVIATIONS

CAD=CORONARY ARTERY DISEASE

BMI=BODY MASS INDEX

SBP=SYSTOLIC BP

DBP=DIASTOLIC BP

TG=TRIGLYCERIDES

WHEiR=WAIST TO HEIGHT RATIO

OCCUPATION: 1=SEDENTARY,2=MODERATE EXERTION,3=MANUAL LABOURER

ALL SYMPTOMS- 0=ABSENT,1=PRESENT

MENSTRUAL H/O-PM=POST MENOPAUSAL,M=MENSTRUATING

PAST ILLNESS-NA= NO ABNORMALITIES,HT=HYPERTENSION

FAMILY H/O-NA= NO ABNORMALITIES,D=DIABETES MELLITUS,C=CAD,H=HYPERTENSION

PALLONC=NON STEMI&CD,SA=STEMI&ARRYTHMIAS

ECHO-N=NORMAL,R=REGIONAL WALL MOTION ABNORMALITIES(RWMA),RL=RWMA&LEFT VENTRICULAR

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25 **h-Indian type 2 diabetic subjects.**

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