

# The incidence and clinical profile of ischaemic heart disease in non-insulin dependent diabetes mellitus

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## Abstract

Ischaemic heart disease is defined as “Cardiac disability acute or chronic, arising from reduction or arrest of blood supply to the myocardium in association with disease process in the coronary arterial system. Ischaemic heart disease is one of the leading cause of death among adults both in developed and developing countries. In this study, prevalence of asymptomatic IHD, various presentations in non-insulin dependent Diabetes mellitus. Provocable ischaemia, effort tolerance in patients of IHD with coexisting non-insulin dependent Diabetes mellitus.

**Keywords:** Coronary artery disease; Ischaemic heart disease; Non-insulin dependent, Diabetes mellitus.

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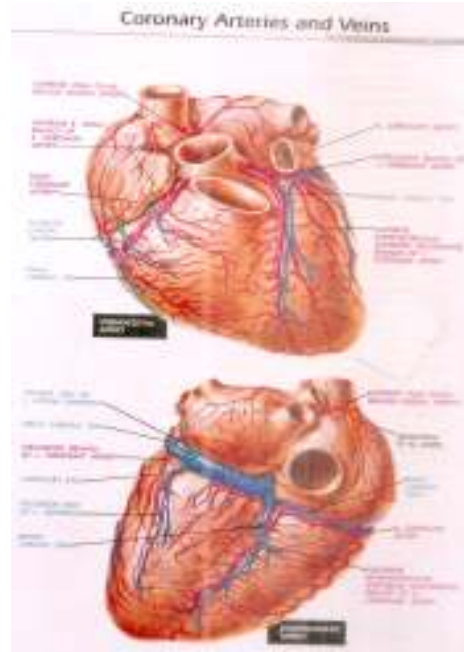
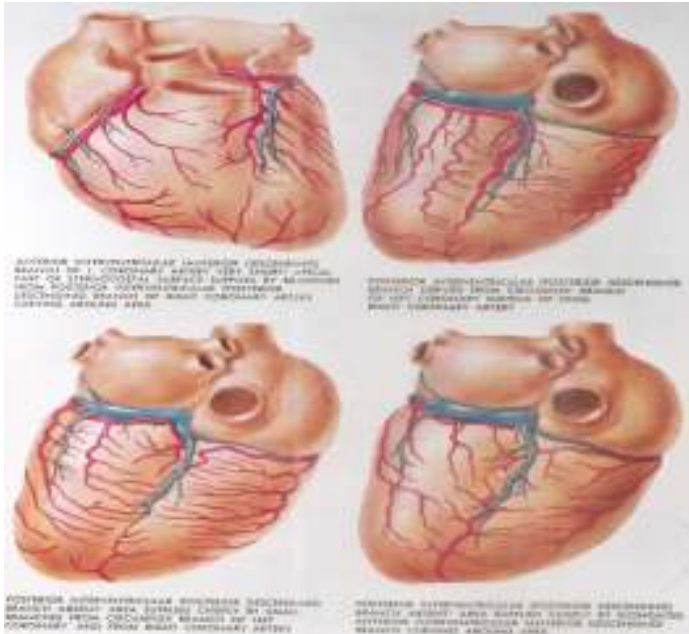
## INTRODUCTION

Ischaemic heart disease is defined as “Cardiac disability acute or chronic, arising from reduction or arrest of blood supply to the myocardium in association with disease process in the coronary arterial system (WHO)”. Ischaemic heart disease is one of the leading cause of death among adults both in developed and developing countries. Heart needs rich blood supply for oxygen and nutrition. Myocardial infarction results when there is decrease in blood supply such that it causes focal massive

of the necrosis cardiac muscle. The most observed cause is atherosclerosis. Clinical manifestation is the result of ischaemia invariably due to advanced atherosclerosis. Nevertheless for many years the cause and pathogenesis of atherosclerosis remained unsolved. A number of theories of atherogenesis were formulated. Risk of ischaemic heart disease varies to the burden of risk factors.

## OBJECTIVES

1. To know the prevalence of asymptomatic Ischaemic heart disease in non **insulin** dependent diabetes mellitus.
2. To study various presentations of Ischaemic heart disease in patients of non insulin dependent diabetes mellitus.
3. To study provocable Ischaemia, effort tolerance in patients of Ischaemic heart disease with coexisting non insulin dependent diabetes mellitus.
4. To know the influence of Diabetes as independent risk factor.



### Coronary circulation

1. Left Coronary Artery: Larger than right, arises from left sinus of Valsalva, near upper border at the level of cusp. The short stem (0.5-2 cm) bifurcates or trifurcates and forms.
  - a. Anterior inter-ventricular descending branch
  - b. Circumflex branch of the left coronary artery

Right Coronary Artery: Arises from the right anterior sinus of Valsalva of the aorta and runs along the right antero-ventricular sulcus embedded in fat.

Blood supply of the special areas of heart

Sinus node - R.C.A.	55%
L.C.A.	45%
A.V. node - R.C.A.	90%
L.C.A.	10%

### Physiology of coronary circulation

The normal coronary circulation is able to provide oxygen to the heart under a wide range of conditions and is able to increase its flow 5 or 6 times the value at rest. At rest the coronary blood flow is approximately 70 to 90 ml per 100 gm per minute (5% of cardiac output). The oxygen consumption of the heart is about 8-10 ml/100 gm/min. At rest the heart extracts 70-80% of oxygen from each unit of blood delivered to it. So oxygen consumption can be increased significantly only by increasing blood flow. The chemical factors influencing coronary blood flow include lack of oxygen, increased local concentration of carbon dioxide, PH+, K +, lactate, prostaglandins, adenosine and adenine nucleotide all of

which cause coronary vaso dilatation. Neural factors influencing coronary blood flow are sympathetic and para sympathetic nerves. Stimulation of cardiac sympathetic nerves produces a direct vasoconstriction of the coronary arteries. This vasoconstriction is however normally overwhelmed by vasodilatation secondary to the increase in myocardial metabolism produced by the sympathetic stimulation of heart rate and myocardial contractility. Vagal stimulation produces bradycardia and may decrease myocardial contractility, both of which decrease myocardial oxygen requirements and this results in secondary coronary vasoconstriction.

### Clinical features of coronary artery disease

Coronary artery disease both in diabetics and non diabetics becomes clinically manifest as angina pectoris, myocardial infarction, congestive heart failure, Arrhythmia or sudden death. It may also go undetected and remain asymptomatic in a few the risk for cardiovascular disease is about same for diabetic men and women double that of non-diabetic population.

When a patient gives a history of typical angina pectoris, anatomically severe coronary atherosclerosis will be confirmed in more than 90% of instances. The diabetic may present with vague and atypical chest, neck or upper extremity pain or epigastric discomfort. A wide variety of symptoms may be anginal equivalents. Fatigue, particularly when produced abruptly by exercise and relieved promptly with rest may signal ischaemic heart disease. Unexplained nausea, vomiting, hypoglycemia or stroke may precede unstable coronary disease or myocardial infarction. The young patient with juvenile

onset diabetes is particularly likely to have atypical features.

**Coronary risk factors:** Coronary risk factors play a major role in the development of coronary atherosclerosis and mortality.

### Diabetes mellitus

Diabetes mellitus is a strong risk factor for cardiovascular disease. This risk is markedly increased in younger diabetics and diabetic women are even more prone to Ischaemic Heart Disease than are diabetic men. Diabetes carries an equal, strong risk for both men and women. Diabetes mellitus is associated with an increase in atherosclerosis observed at autopsy in a variety of populations worldwide. The mechanism by which diabetes predisposes to Coronary artery disease is poorly understood. There does appear to be some evidence suggesting a decreased concentration of HDL cholesterol in diabetics and high prevalence of hypertension associated with hyperglycemia. Recent research into the association of NIDDM and Ischaemic heart disease has concentrated on the interactions among various metabolic abnormalities in diabetes.

- a. Insulin has been shown to act like a growth factor on the arterial wall, promoting the infiltration of smooth-muscle cells into the intima and their replication there.
- b. It may also affect the activity of LDL receptor and the binding and degradation of LDL, in fibroblast and other cells.
- c. Hyperinsulinaemia and insulin resistance are associated with hypertension and atherogenic lipoproteins profile.
- d. Triglyceride rich lipoproteins are more atherogenic in diabetics than in non diabetics.
- e. The formation of lipid peroxides is increased in diabetics. Oxidised LDL accelerates the accumulation of cholesterol within endothelial macrophage. It may also promote atherogenesis by its cytotoxic properties and its stimulation of monocyte chemotaxis.

The association between NIDDM and IHD may be linked to genetic predisposition. Both diseases may be linked through a third factor such as obesity or low HDL cholesterol concentration.

### Pathologic changes in coronary artery disease

The earliest recognizable atheromatous changes seem to be the accumulation of aggregates of lipid-laden macrophages in the intima. In addition to atheromatous and thrombotic blockade of the coronary arteries, emboli of all types can lodge within an otherwise normal coronary artery. Such emboli can consist of bits of thrombi, valvular calcification, bits of tumour, and even

on occasion, small foreign bodies. Various kinds of inflammatory aortitis can involve the vessels; syphilis of the aortic wall can occlude the ostia and surgeons can inadvertently disturb the blood flow. All these events can result in severe myocardial difficulties. Diabetes mellitus is a potent independent risk factor for cardiovascular disease. Diabetes affects the heart in diverse ways, specifically: (1) earlier and more severe CAD; (2) autonomic neuropathy; (3) cardiomyopathy; and (4) microvascular disease.

### What is the natural history of coronary artery disease in diabetes?

Diabetes places a huge burden on health care resources because of the accelerated rate of CAD in diabetic individuals. The incidence of all manifestations of CAD (myocardial infarction, angina, and sudden death) is greatly increased in the patient with non-insulin dependent diabetes mellitus (NIDDM). Metabolic decompensation, especially ketoacidosis, at the time of acute infarction significantly worsens the prognosis. Normally, fatty acids provide the metabolic fuel for the heart, but as oxygen concentration falls the heart becomes more reliant on glucose. The ability of insulin to enhance glucose supply to the myocardium is antagonized by the release of stress hormones, adrenal steroids and catecholamines. Diabetes mellitus is associated with loss of both sympathetic and parasympathetic innervation to the heart. Perhaps, the most important clinical implication of this neuropathy is the increased incidence of silent myocardial ischaemia and infarction. Patients with diabetes have been reported to have silent or less painful infarcts in 32-42% of cases compared with 6-15% in non-diabetics. Although the mechanism is not entirely clear, the clinical implication of the loss of pain perception in the angina can be a poor discriminating symptom in the diabetic patient with ischaemic heart disease. On exercise and thallium scanning there is a higher incidence of silent ischaemia in diabetic subjects compared with controls, further suggesting that a significant number of ischaemic episodes are missed.

### Profile of ischaemic heart disease in diabetics

Even today frequency and severity of atherosclerotic vascular disease of the heart in diabetics continues to pose a formidable challenge to the clinician. Atherosclerosis, neither specific for diabetes nor its inevitable consequences, remains the single most important cause of heart disease and death in the diabetics. Risk factors: Hypertension, hyperlipidemia, obesity and smoking are among the widely accepted risk factors which increase atherogenesis. These factors are often operative in diabetics, particularly those with Type II diabetes, many of whom are overweight, hypertensive and have elevated levels of serum cholesterol and Triglycerides. The

generally higher mortality rate from coronary artery disease in diabetics can in part be explained by interplay of multiple risk factors. lipids: Close link between glucose intolerance and blood triglyceride levels has long been observed. Gross hyperlipidemia, mainly hypertriglyceridemia, frequently accompanies uncontrolled insulin dependent diabetes. Insulin deficiency is associated with under activity of the enzyme lipoprotein lipase responsible for hydrolysis of circulating triglycerides. Many investigators reported elevated levels of Triglyceride, cholesterol or both in diabetics with atherosclerosis. A casual determination of the serum cholesterol reflects the risk of coronary artery disease. Obesity **Cigarettes:** Heavy smoking almost doubles the cardiovascular mortality. Proportion of deaths are sudden increases progressively. Among those with hypertension and elevated cholesterol cigarette smoking increased the risk of death four-fold.

### Pathophysiology of ihd in diabetic

#### Pathologic changes in the diabetic heart

The cardiac changes which have been related to diabetes involve both the vascular systems and the myocardial interstitium. The microvasculature and the macrovasculature may involve similar pathways of endothelial damage followed by platelet adherence and aggregation. Changes are not uniform throughout the vascular tree, but rather predominantly involve either larger or smaller vessels. Atherosclerosis in the larger vessels is most frequent. Microangiopathy may encompass a sequence of changes beginning with functional abnormalities and proceeding to endothelial damage, basement membrane thickening, and hematological disturbances such as increased plasma viscosity, red cell and platelet aggregation and microthrombi. Diabetics have lesions consisting of endothelial proliferation and swelling of subendothelial histiocytes to form mounds, capillary projections, bridges and eccentric masses of cells progressing to marked narrowing or complete obliteration of small arteries and venules. Alterations in cardiac myofibrils occur as the result of these vascular changes. Atherosclerosis remains the most important cause of morbidity and mortality in long standing diabetes. Hyperglycemia is known to affect aortic wall metabolism. Sorbitol, a product of the insulin independent Aldose reductase pathway of glucose metabolism, accumulates in the arterial wall in the presence of high glucose concentration, resulting in osmotic effects including increased cell water content and decreased oxygenation. Increased glucose also appear to stimulate proliferation of cultured arterial smooth muscle cells. Insulin has important effects on key steps in the metabolism of lipids and lipoproteins and altered lipid metabolism is common in the diabetic population. Lipid

and lipoprotein levels will depend on the extent of the insulin deficiency or insulin resistance, hyperglycemia, obesity and diet. In addition to alteration in absolute levels of lipids the composition of lipoproteins may be changed by the diabetic state. LDL (Low density lipoprotein):-Levels of this highly atherogenic particle vary according to glycemic control and in general tend to be raised in poorly controlled diabetic patients. In general NIDDM patients are more likely to have raised LDL levels.

#### The electrocardiographic exercise test

This test is based on the premise that exercise increases the myocardial demands on the coronary blood supply which may be adequate at rest but inadequate during exercise. The exercise results in relative myocardial ischaemia and an inability of the coronary circulation to maintain the metabolic needs of the heart muscle. Consequently electrocardiographic manifestations which are normal or equivocal at rest may become abnormal and diagnostically significant with exercise. The test thus evaluates the balance between oxygen supply and demand

## DISCUSSION

In the study diabetic patients who were asymptomatic for ischaemic heart disease had a normal base line ECG were evaluated. The salient clinical data and exercise ECG profile of ischaemic heart disease were noted in detail. The incidence of latent coronary artery disease in diabetes only as a risk factor in this study was 29.3%. It is different from other observations in Indian population by various authors. In these reports the incidence is ranging from 7.3% to 51.0% in which diabetics associated with other risk factors were also included. Thus coronary artery disease contributes to significant morbidity in diabetics. The incidence of the latent coronary artery disease in men and women was in ratio of 1:1.7. In this study males who had positive ischaemic response for inducible ischaemia were 14(27.45%), and females had positive response in 8 (33.3%). Incidence between males and females noted by other authors are Root *et al.* noted incidence of IHD in males 38.2%, and females 32.3%, Gupta R *et al.* noted incidence of IHD in males 18.8% and females 10.5%, Gordon *et al.* noted incidence of IHD in males 7.3% and 15.3% females. The results of this study are concurrent with that of Gordon *et al.* A progressive increase in the incidence of ischaemic heart disease with increasing age was noted. In absence of non diabetic controls in this study no definitive interpretation can be drawn about this observation regarding significant increase of latent coronary artery disease in diabetic heart disease, Compared to non diabetic population despite similar trends in both. It has been currently hypothesized that diabetes especially type II diabetes and



cardiovascular disease are associated conditions not casually related. The hypothetically generally determined link between increase prevalence 3 of an uncommon allelic variant of apoprotein. AI-C-II-A/V gene cluster type II diabetes with increased coronary artery disease. Patients who had positive exercise ECG had reduced exercise tolerance The mean duration in positive patients was 7.29 minutes compared to negative, who had duration of exercise of 10.29 minutes. This observation supports that the coexisting incidence, and silent ischaemia in diabetics will influence the exercise tolerance. Patients who had positive test for inducible ischaemia had achieved lower METS (8.55-10.05) compared to patients with negative test (9.08-12.12 METS). This observation indicates possible metabolic influence on myocardial cell with effect on aerobic work capacity of type II diabetics. The present study indicates that increase in duration of diabetes has increased incidence of inducible ischaemia Similar studies by Jarret RJ, Gupta SB, Shipley, had reported that there was no straight correlation with the duration of diabetes to inducible ischaemia. This increased incidence of provacable ischaemia with increased duration of diabetes may correlate with associated advancing age of the patient, than isolated influence of the disease itself. The present study highlights that there is inverse relationship between mean HDL Cholesterol to incidence of inducible ischaemia. Similar observations were noted in the study by William P Castelli. The present study recorded linear relationship between level of cholesterol to incidence of inducible ischaemia that is higher the cholesterol higher is incidence of inducible ischaemia. Echocardiographic evaluation of all those patients who were positive for inducible ischaemia revealed regional wall motional abnormality in 6 out of 22 patients. Nineteen patients had normal Left Ventricular functions. Diabetes being a metabolic disorder influencing various components of metabolism might be responsible for dysfunction at cellular molecular level. This component of the influence of the disease on the myocardium is beyond the scope of this study. However there are number of reports about diabetic cardiomyopathy as a separate entity and just not a result of co-existing coronary artery disease. Another important finding was that 6 patients had diastolic dysfunction this observation indicates that Diabetes modifies ventricular compliance. If all the patients who were positive for inducible ischemia could be evaluated with coronary angiography the results would have been more supportive of definitive contribution of coronary insufficiency and could have ruled out false positive TMT for inducible ischaemia. Hence lack of coronary angiography is the limitation of this study.

## CONCLUSIONS

1. Female type II diabetics revealed relatively higher incidence of ischaemia when compared to males.
2. Type II diabetics with inducible ischaemia on TMT (Computerised Stress Test) had less exercise tolerance and achieved lower METS when compared to those who were negative for inducible ischaemia.
3. The incidence of inducible ischaemia had linear correlation with duration of diabetes.
4. There was inverse relationship of Inducible ischaemia with HDL cholesterol levels and linear correlation ship with total cholesterol levels.
5. Echocardiography revealed significant degree of regional wall motion abnormality and diastolic dysfunction among type diabetics with inducible ischemia.
6. Correlation of results of TMT with coronary angiography or Thallium perfusion studies is needed to uphold the real incidence of latent coronary artery disease. This is the limitation of the study.
7. The tread mill stress test is valuable non invasive method of diagnosing myocardial ischaemia among diabetics.
8. Diabetes is one of the major independent risk factor for coronary artery disease.

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