

# Diabetic Heart Disease – Current Problems and their Management

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## Summary

Diabetic heart disease (DHD) is the most important, contemporary and challenging management problem confronting the entire diabetes management team. The three major problems are: Coronary artery disease (CAD), autonomic cardiac denervation and diabetic cardiomyopathy (a specific heart muscle disease in diabetes).

Coronary artery disease (CAD) has a much higher incidence and mortality in diabetics than in non-diabetics. The disease has many atypical features including painless silent onset, delay in diagnosis, increased incidence of cardiogenic shock, atrioventricular and intraventricular conduction abnormalities, congestive heart failure, myocardial rupture and an increased incidence of reinfarction. There is an increased incidence of double and triple vessel disease and severe disease of left main coronary artery in diabetic than in non-diabetic subjects. Thrombolytic therapy, coronary artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA) are as useful in diabetics as they are in non-diabetics.

The development of autonomic cardiac denervation has serious repercussions in DHD since it is irreversible and mortality is as high as 50% after 3 years of diagnosis. A prolonged QT interval on the electrocardiogram and a relatively heightened sympathetic tone increases the likelihood of sudden cardiac death. Diabetic autonomic neuropathy (DAN) has also been identified in fibrocalculous pancreatic diabetes (FCPD) and has been evoked in the pathogenesis of diabetic cardiomyopathy.

Clinical, epidemiological and pathological data support the existence of a specific diabetic heart muscle disease. Both, systolic and diastolic dysfunction, have been identified in diabetic subjects even before the onset of cardiac failure (preclinical cardiomyopathy). Alloxan diabetic dog studies and studies on endomyocardial biopsy specimens and estimates of tissue lipids have established the morphological basis of this specific heart muscle disease.

## INTRODUCTION

Death from cardiovascular diseases predominate in patients with diabetes of more than 30 years duration and in those diagnosed after 40 years of age. Diabetic heart disease (DHD) is one of the most important challenging contemporary problems confronting the diabetologist, diabetic specialist nurse, dietician, diabetic health visitor and health education personnel. The significance of a high index of suspicion, early diagnosis and referral are as important as a modified diet prescription, exercise, rehabilitation and patient education.

### Problems in Diabetic heart disease [1]

#### Major Problems

- 1) Coronary artery disease.
- 2) Diabetic autonomic cardiopathy.
  - Parasympathetic.
  - Sympathetic.
- 3) Specific heart muscle disease (Cardiomyopathy)
  - microangiopathic cardiomyopathy.
  - metabolic cardiomyopathy.

#### Ancillary problems

- 1) Hypertension.
- 2) Hyperglycaemia.
- 3) Hyperinsulinaemia and insulin resistance.
- 4) Microalbuminuria and proteinuria.
- 5) Dyslipidaemia.
- 6) Rheological factors.

**Table 1**  
**Peculiar risk factors for CAD in diabetes mellitus**

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| <ol style="list-style-type: none"><li>1. Dyslipidaemia</li><li>2. Hyperinsulinaemia and insulin resistance</li><li>3. Hyperglycaemia</li><li>4. Microalbuminuria and proteinuria</li><li>5. Rheological abnormalities</li></ol> |
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**Table 2**  
**Peculiar clinical features of MI in diabetes**

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| <ol style="list-style-type: none"><li>1. Absence of pain</li><li>2. Atypical symptoms</li><li>3. Delay in hospital arrival</li><li>4. Delay in diagnosis</li><li>5. High in-hospital mortality</li><li>6. High incidence of complications</li><li>7. Worsening glycaemic control</li><li>8. High incidence of reinfarction</li><li>9. High incidence of multivessel disease</li><li>10. Severe disease of left main coronary artery</li><li>11. No circadian difference.</li></ol> |
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## Coronary artery disease (CAD) in diabetes mellitus (DM)

Risk factors peculiar to diabetics include hyperglycaemia, hyperinsulinaemia, haemobiological abnormalities and dyslipidaemias.

The relationship between hyperglycaemia and coronary artery disease has been addressed in the Chicago Heart Association Detection Project [2], Tecumseh Study [3] and Paris Prospective Study [4]. These studies have shown that asymptomatic hyperglycaemia is associated with an increased mortality from CAD.

Hyperinsulinaemia stimulates proliferation of arterial smooth muscle cells and lipid synthesis in the arterial wall and may thus be directly involved in atherogenesis [5]. Hyperinsulinaemia also raises blood pressure by increasing proximal tubular sodium reabsorption and activating the sympathetic nervous system [6, 7].

Haemobiological abnormalities in diabetics include an enhanced platelet activity, increased fibrinogen, increased factor VIII activity and decreased fibrinolytic activity [8, 9].

Lipid alterations in diabetics include hypertriglyceridaemia due to decreased activity of lipoprotein lipase, increased LDL levels and decreased HDL levels [10].

The major differences in the clinical picture between diabetic and non-diabetic CAD include

- 1) Blunted appreciation of pain results in a higher incidence of unrecognised infarctions in diabetics.
- 2) Atypical symptoms such as nausea, vomiting, fatigue, dyspnoea are more common in diabetics with infarction [11].
- 3) There is a delay in arrival at hospital and diagnosis of diabetics with infarction [12].
- 4) Anterior wall infarction is more common in diabetics than in non-diabetics [13].
- 5) Early mortality in diabetics who are in hospital is higher due to cardiogenic shock, atrioventricular and intraventricular conduction abnormalities, bundle branch blocks, myocardial rupture etc [1-4].
- 6) Glycaemic control worsens during infarction and ketoacidosis occurs in 4% of patient [14].
- 7) Late mortality in diabetics after discharge is higher due to high incidence of reinfarction [14].

- 8) Higher incidence of double and triple vessel disease and lower incidence of single vessel disease is seen in diabetic [15].
- 9) Severe disease of left main coronary artery is more common [16].
- 10) Thrombolytic therapy is as effective in diabetics as in non-diabetics. Presence of diabetic proliferative retinopathy is only a relative contraindication to the use of thrombolytic therapy [17].
- 11) CABG is as effective in relieving anginal symptoms in diabetic as in non-diabetics.
- 12) PTCA is an effective tool for relieving ischaemic symptoms, provided the coronary anatomy is suitable.
- 13) Aspirin is particularly useful in diabetics due to heightened platelet activity in uncontrolled diabetics.
- 14) There is no circadian difference in the occurrence of infarction in diabetics, since platelet activity is heightened throughout the day [18].

## Cardiac Denervation

**Table 3**  
**Salient features of autonomic cardiac denervation**

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| <ol style="list-style-type: none"><li>1. High mortality after diagnosis</li><li>2. Prolonged QT interval correlated with sudden cardiac death</li><li>3. Does not improve with glycaemic control</li><li>4. Occurs in FCPD</li><li>5. Tolerates general anaesthesia poorly</li><li>6. Involved in pathogenesis of cardiomyopathy</li></ol> |
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The important practical points regarding diabetic cardiac denervation are

- 1) Symptomatic autonomic neuropathy is an ominous sign. Mortality is 50% after 3 years of onset.
- 2) Parasympathetic fibres are always involved earlier than sympathetic fibres causing
  - a) resting tachycardia
  - b) attenuation of expected increase in heart rate and blood pressure exercise.
- 3) Sympathetic nervous system dysfunction occurs within 5 years of diagnosis of parasympathetic dysfunction. Predominant manifestation is orthostatic hypotension.
- 4) Prolonged QT interval and heightened sympathetic tone predisposes to life threatening arrhythmias and sudden cardiac death.
- 5) Diabetic autonomic neuropathy mainly improves with good metabolic control [19].
- 6) Autonomic nervous system can be involved as early as 2 years after the onset of FCPD [20].

- 7) Diabetics with cardiac autonomic denervation tolerate general anaesthesia poorly.
- 8) Diabetic autonomic neuropathy has been invoked in the pathogenesis of diabetic cardiomyopathy.

### Diabetic Cardiomyopathy

**Table 4**  
**Salient features of diabetic cardiomyopathy**

1. Preclinical cardiac dysfunction
2. Prolonged pre-ejection period (PEP)
3. Shortened LV ejection time (LVET)
4. Increase in PEP/LVET ratio
5. Prolonged isovolumic relaxation
6. Prolongation of early diastolic filling
7. Increased LVEDP and depressed end diastolic volume
8. Latent cardiac dysfunction – failure of ejection fraction to rise with exercise

#### *Clinicoepidemiologic studies*

- a) Rubler et al 1972 [21] found at autopsy that significant number of diabetics died of CHF in the absence of CAD, hypertension or valvular heart disease.
- b) Framingham study [22] noted two times higher incidence of congestive heart failure in diabetic men and 5 times higher incidence in diabetic women. This rise for heart failure persisted even after accounting for age, hypertension, obesity, hypercholesterolaemia and CAD.
- c) Hamby et al [23] found out an incidence of 22% for diabetes mellitus in a cohort with cardiomyopathy when compared to 11% diabetics in an age and sex matched cohort without cardiomyopathy.
- d) D'elia et al [24] found evidence for systolic and diastolic dysfunction in 59% of a diabetic cohort with renal failure in the absence of significant CAD.

Various invasive and non-invasive tests in clinical diabetes and experimental diabetes have provided evidence for the existence of a specific myocardial disease in diabetes mellitus.

#### *Pathogenesis*

Factors which contribute to diabetic cardiomyopathy include

- a) Diabetic autonomic neuropathy.
- b) Microangiopathy leading to tissue anoxia and fibrosis.
- c) Metabolic derangements.
- d) Growth hormone.

Catecholamine levels are significantly reduced in patients with diabetic autonomic neuropathy

(DAN), and the reduced levels correlate with abnormalities of diastolic function. Sympathetic stimulation improves LV contractility and also increases left ventricular relaxation rates. Thus LV systolic and diastolic dysfunction could be related to diminished sympathetic stimulation in many diabetic patients.

Small vessel changes include thickening of capillary basement membranes and presence of microaneurysms. Such micro-vascular damage may represent part of the spectrum of vasculopathy typically found in diabetics, as microaneurysms are not typically encountered in individuals with cardiomyopathy.

GH deficient dwarfs with diabetes lack the micro-vascular changes associated with diabetes, despite metabolic abnormalities similar to diabetics.

Enhanced responsiveness of collagen to growth hormone accounts for some of the interstitial changes seen in diabetics.

Depending on the predominant pathogenic factor, it can be a small stiff heart or a large dilated heart.

#### *Preclinical cardiomyopathy*

Diabetes mellitus is characterised by abnormalities of both systolic and diastolic function, which is seen much earlier than the development of overt congestive cardiac failure (CCF). Diastolic function is deranged much earlier than systolic function.

#### *Echocardiographic features [2, 5]*

Systolic dysfunction

- i) Prolonged per-ejection period (PEP).
- ii) Shortened LV ejection time (LVET).
- iii) Increase in PEP/LVET ratio.

Markedly elevated PEP/LVET ratios do not improve after treatment of hyperglycaemia, whereas modestly elevated PEP/LVET ratios respond to treatment of hyperglycaemia.

Diastolic dysfunction

- i) Prolonged isovolumic relaxation.
- ii) Prolongation of early diastolic rapid filling.
- iii) LV end diastolic pressure is increased (suggesting decreased compliance).
- iv) Decreased end-diastolic volume.

Latent cardiac dysfunction

- i. Failure of ejection is rise in response to exercise.

#### *Pathologic features [26, 27, 28]*

Vascular changes

- I. Arterial wall thickening.

- II. Intimal fibroblastic proliferation.
- III. Basement membrane thickening.
- IV. Intimal hyaline deposition.

Extra-vascular changes

- I. PAS + ve glycoprotein deposition.
- II. Wavy myocardium.
- III. Periarteriolar and scattered fibrosis,
- IV. Fatty degeneration.

*Treatment*

Management guidelines are same as in non-diabetics with the following exceptions

- I. Thiazides may worsen hyperglycaemia.
- II. Beta blockers may cause hypoglycaemia.
- III. Preload and after load reducing agents to be used with caution in-patients with autonomic denervation.

The role of intensive treatment of hyperglycaemia in the primary prevention or reversal of myocardial dysfunction remains to be elucidated.

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