Introduction
In diabetes mellitus, morbidity and mortality secondary to cardiovascular diseases has increased these days since the morbidity and mortality related to infections and ketosis has decreased. Diabetics mellitus (DM) has a greater prevalence of coronary artery disease (CAD), cardiomyopathy and congestive cardiac failure. Metabolic abnormalities and dyslipidemias associated with diabetes mellitus adversely influence atherosclerosis leading to coronary artery disease (CAD) and peripheral vascular disease (PVD).

Incidence of CAD in DM
The Framingham study has shown that cardiovascular mortality is twice in diabetic men and 4 times in diabetic women as compared with non-diabetic counter parts. Also the relative risk of acute myocardial infarction (AMI) of 50% higher in diabetic men and 150% higher in diabetic women. Prevalence of angina pectoris is 60% greater in diabetic men and 90% greater in diabetic women than in non-diabetics. Also CAD in more extensive (2-3 vessel disease) and more diffuse in a diabetic than in a non-diabetic. Incidence of left main coronary artery is higher (13%) in diabetic versus non-diabetic (6%). Sudden death occurs 50% more in diabetic men and 300% more in diabetic women. Also prevalence of silent myocardial infarction and silent myocardial ischaemia is more in diabetic. According to Framingham study, there is strong association of CAD and PVD. Presence of intermittent claudication in a diabetic should be taken as a clue to investigate for CAD.

How Important is Glycemic Control?
It is debatable whether glycemic control affects cardiovascular morbidity and mortality. Framingham study revealed that reduction in risk of CAD in DM depends more on prevention and control of associated risk factors such as control of hypertension, obesity, correction of dyslipidemias, cessation of smoking rather than glycemic control. But it is prudent and necessary to achieve tight glycemic control. Framingham study has highlighted the adverse effects of dyslipidemia in CAD in a diabetic. In uncontrolled diabetics, VLDL and triglycerides are raised. This is another reason to aim for tight glycemic control.
How does clinical presentation differ?
AMI in DM presents frequently with atypical symptoms such as breathlessness, nausea, vomiting and fatigue. These symptoms usually mimick symptoms of hyperglycaemia or hypoglycaemia, hence there may be delay in diagnosis of AMI. There is usually absence of typical chest pain. Owing to atypical presentation, patient may be admitted in internal medicine ward rather than coronary care unit which leads to delay in the treatment resulting in serious complications like cardiogenic shock and even death. That is the reason for increase in morbidity and mortality. In diabetes mellitus, there is greater prevalence of painless sudden death particularly during sleep. Silent myocardial ischaemia is evidenced during treadmill and thallium stress tests. Incidence of painless ST depression is twice in diabetic (75%) versus non diabetic (35%). It should be stressed that during AMI, glycemic control is essential. During acute coronary syndrome leading to myocardial ischaemia, heart shifts from aerobic metabolism with fatty acids as the primary fuel source to anaerobic metabolism which depends on glucose transport into cells facilitated by insulin. In presence of insulin deficiency, increased levels of ketones and free fatty acids are produced and these inhibit glucose transport.

Also during AMI, there is sympathetic overdrive and excess production of catecholamines which further cause reduction of insulin and lipolysis resulting in uptake of free fatty acids by the myocardium which are toxic for the myocardium. Hence during AMI, one sees hyperglycemia and hyperketonaemia which have a poor prognosis. Diabetic ketoacidosis is encountered in 4% of diabetics with AMI and it carries a poor prognosis (mortality up to 85%). Clinical features of ketoacidosis to some extent mimic features of AMI and that sometimes causes confusion.

Differences in circadian rhythm
In non-diabetics, Q wave AMI is more commonly seen during morning hours because of enhanced platelet aggregation during morning hours but this phenomenon of circadian rhythm is not seen in diabetic patients. In DM, Q wave AMI occurs evenly through the day due to increased platelet aggregation throughout the day. Also due to the same reason, silent AMI in diabetics shows morning peak and it persists through waking hours. Complication of autonomic neuropathy in DM may lead to sudden death in some cases of DM. There is relationship between cardiac autonomic neuropathy and prolonged QT interval which can result in severe cardiac arrhythmias and sudden cardiac death.

What are the differences in management.
The basic principles of treatment of diabetes mellitus and ischaemic heart disease are the same. But there are some special differences which we shall discuss.

1. **Aspirin**
   As there is increased platelet aggregability, aspirin is very beneficial in diabetics. However a word of caution for use of aspirin in diabetics with retinal haemorrhages. DAMAD study which in 267 diabetic patients with early retinopathy received aspirin and none showed worsening of retinopathy. From this study, it is clear that atleast in early retinopathy aspirin is safe. However its safety in severe cases of retinopathy is yet to be established.

2. **Thrombolytic therapy (TT)**
   In view of the atypical presentation of AMI (absence of chest pain), sometimes it becomes difficult in such cases to determine the exact time of onset of MI, hence physician may be in a dilemma regarding thrombolytic therapy. Hence TT is associated with a high incidence of haemorrhagic complications with increased mortality particularly in elderly diabetics. Hence in elderly diabetics, TT is advised only when one is certain about the onset of AMI and when it is massive myocardial infarction. Thirdly, one should do fundus examination to rule out severe proliferative diabetic retinopathy as it is considered as a relative contraindication for the use of
TT. However in TAMI trial which included 121 diabetics treated with TT, no haemorrhages were seen.12

3. Coronary Angioplasty (PTCA)
There are more chances of restenosis in diabetic than non-diabetic. DM is an independent variable risk factor predicting restenosis following PTCA. But report of Stein et al13 in which they compared 1133 diabetics and 9300 non diabetics undergoing elective PTCA over a 10 year period (1980-90), showed that PTCA in diabetics is associated with equally high success and low complication rates.

4. Coronary artery bypass graft surgery (CABG)
CABG is equally effective in diabetics as well as non diabetics in relieving ischaemic features, but long term survival following CABG remains usually lower in diabetics. Secondly due to extensive diffuse disease, diabetics require a large number of grafts but their late graft patency is similar to that of non diabetics. Peri-operative mortality is slightly higher in diabetics (7.1% vs 4.5%) and mortality is also higher due to poor sternotomy healing and associated renal failure. This leads to prolonged hospitalization.14

5. Management of associated risk factors
It is very vital that for proper management of coronary artery disease in DM, one has to aim to reduce progression of CAD and risk of second attack of acute coronary syndrome. Hence one has to find out other coronary risk factors such as hypertension, dyslipidemia, obesity, sedentary habits, smoking, hyperinsulinaemia and treat them aggressively. Diabetics have a greater tendency for plaque rupture. Lipid rich plaques have greater tendency to rupture than fibrous plaques.4 Hence tight control of dyslipidaemia is warranted.

6. Hyperinsulinaemia
Hyperinsulinaemia worsens CAD even in presence of normal blood sugar levels. It elevates growth factors and causes proliferation of smooth muscle cells. It is usually associated with high blood pressure and low HDL. Hyperinsulinaemia is usually associated with insulin resistance.

7. Congestive heart failure (CHF)
CHF is not uncommon in DM and is due to CAD, diabetic cardiomyopathy or associated hypertension.15 For management of CHF in DM, use of betablockers and thiazides leads to impaired insulin secretion. Also patients on insulin therapy may go in hypoglycaemia when non selective betablockers are used. In patients of DM with autonomic neuropathy (which causes impairment of arterial reflexes), one should be careful in using drugs which lower preload and afterload.

8. Secondary prevention
For secondary prevention, beta blockers have been found useful in diabetics as in non-diabetics. In Timolol myocardial infarction study, mortality rate in diabetics as well as non-diabetics were the same. But in placebo group, mortality rate in diabetics was twice that in non-diabetics. Timolol reduced the cardiac related mortality by 67% in diabetic patients. Timolol in the dosages for secondary prevention was well tolerated.16

9. Haemotological disturbances in DM
Blood viscosity is increased, which leads to increased shear forces leading to plaque rupture and infarct extension. In DM, there is increase in platelet aggregation, thromboxin A2, platelet specific protein B thromboglobulin, platelet factor 4 and plasma fibrinogen. All these alterations can lead to AMI and sudden death. In addition there is elevation of factor VIII levels, fibrinopeptide A and procoagulant Von-Willebrand factor.4
General guidelines for management

1. For management of DM with CAD, stress should be given on diet and exercise.
2. Oral hyclcaemic drugs should be avoided or used minimally. One should preferably use human insulins.
3. Avoid hypoglycaemia as it can result in ischaemic episode and arrhythmias.3
4. One should remember that drugs such as diuretics, corticosteroids, psychotropic drugs and betablockers elevate glucose levels whereas sulphonamides and aspirin decrease glucose levels.
5. In DM with autonomic neuropathy, some vasodilators and anti hypertensive drugs may cause postural hypotension17 and betablockers may mask hypoglycemic manifestations.3,16,18

References