INTRODUCTION

Type 2 diabetes mellitus (T2DM) popularly known as diabetes has been known to occur in Indian people since 500 BC. However, it is since last 40 years or so that the disease has assumed epidemic proportions with international ramifications affecting the Indian Diaspora all over the globe. India is now considered as diabetic capital of the world. Interestingly every fifth diabetic in the world is an Indian. Basically a non-communicable disease, it has evolved into a major national health problem because of its widely prevalent morbidity and associated cardiovascular mortality. Significantly the total mortality due to coronary artery disease (CAD) in diabetic subjects is higher in comparison to non-diabetic people. The incidence of MI and mortality due to it is comparable between diabetic patients with no history of MI and non-diabetic subjects with history of prior MI. These results and results from a few other studies have lead Adult Treatment Panel-III of the National Cholesterol Education Programme to label T2DM as a CAD equivalent mandating aggressive therapy.

PREVALENCE OF DIABETES / CAD IN INDIA

The current prevalence of T2DM in India has been estimated to be 6.2% which is predicted to increase to 7.6% by the year 2025. The plausible reasons for such a phenomenon rise in the prevalence of T2DM and/or CAD among native and migrant Indians are following:

a. Genetic predisposition due to insulin resistance attributed to consequent to initial deprivation followed by affluence, the so called thrifty genes;

b. Urbanization and industrialization leading to mass migration from rural to town, town to city, city to metropolis and motherland to abroad for better prospects and greener pasture. The sequence of this migration may not necessarily be in the order described above but straight from rural to metropolis or one metropolis to another metropolis or metropolis to abroad;

c. Increase in sedentary life style;

d. Increase in obesity particularly central obesity;

e. Increase in metabolic syndrome and diabetes;

f. Inadequate intake of fruits and vegetables;

g. Increased consumption of food high in glycemic index (high glycemic load)

h. Preponderance of atherogenic diets including fried and fast foods, processed foods that are high in calories, saturated and trans fats;

i. high prevalence of dyslipidemia characterised by high non-HDL cholesterol, Apo B/Apo A ratio, and total to HDL cholesterol ratio;

j. Low HDL-cholesterol and small dense dysfunctional HDL;

k. Tobacco consumption including smoke less tobacco products like surti, gutkha, pan masala etc.;
l. Poor awareness and control of cardiovascular disease risk factors such as smoking, high blood pressure, dyslipidemia and diabetes.

RISK FACTORS FOR DEVELOPMENT OF CAD IN T2DM

About 60% of diabetic subject succumb to coronary heart disease which makes CAD the leading cause of morbidity and mortality in diabetic patients. Diabetic macrovascular disease also has a more severe course with greater prevalence of multi vessel coronary artery disease and more diffuse elongated atheromas in affected blood vessels. This growing realization has lead to the birth of a new subspeciality of cardiodiabetology wherein cardiologists and diabetologists are joining hands to control the cardiovascular disease in diabetic patients and vice versa. The pathogenesis of CHD in diabetes is multifactorial and is contributed by many risk factors like hypertension, dyslipidemia, microalbuminuria, smoking, central obesity, tobacco chewing, previous MI, glycosylated hemoglobin and duration of diabetes etc.

BLOOD PRESSURE

Large epidemiological studies have shown a progressive and continuous relationship between systolic and diastolic blood pressure and risk of cardiovascular death. In UKPDS, a 10 mm rise in systolic blood pressure in diabetic patients was associated
with a 19% risk in stroke, 12% rise in heart failure and 17% rise in diabetes-related death.

DYSLIPIDEMIA
Diabetic dyslipidemia is characterized by hypertriglyceridemia, decreased HDL and increase in dense and small form of LDL. Raised LDL-cholesterol is a progressive and continuous cardiovascular risk factor in patients with diabetes. Similarly low HDL and high TG levels in diabetics carry high CAD risk. Even though, LDL levels may be low in diabetes, the quantitative change that is more of the smaller and denser forms of LDL make even these relatively lower levels of cholesterol dangerous. The protective action of HDL is also lost because of low HDL levels in diabetes. It is still not clear why despite normal or higher HDL—cholesterol in patients with type 1 diabetes there is increased cardiovascular risk.

Albuminuria
Although the association of CVD with higher levels of albumin excretion is well described; it only recently the association of CVD with microalbuminuria has been explored. In one of the first analyses of this association, Rachmani et al. noted that the risk of CVD in patients with diabetes increased almost 10-fold when albuminuria rose from 10 to 30 mg/day. Hillege et al. in evaluating the PREVEND data, broadened this association to the general population, showing increased cardiovascular risk with the lowest levels of albumin excretion. The emerging association between microalbuminuria and CVD reflects the underlying biologic complexity of albumin excretion, in which subtle fluctuations signal important physiologic changes within the vasculature. A retrospective analysis of the Heart Outcomes Prevention Evaluation (HOPE) found a continuous association between albuminuria and cardiovascular events beginning at levels as low as 4.4 mg/g of albuminuria. Therefore it is very important to realize that not only microalbuminuria but even microalbuminuria is an extremely important risk factor in the development of coronary artery disease in diabetes.

HBA1C
Role of HbA1C as a predictor of CAD in diabetic subjects continues to be a topic for discussion and future studies. The UKPDS showed that by keeping the HbA1C <7%, the reduction in risk of MI was of borderline significance. Study by Saleem et al. clearly showed that HbA1C is an independent factor influencing the severity of CAD as demonstrated by coronary angiography. Severity of CAD is correlated with the duration of DM and with poor control of diabetes as well. The American Diabetes Association is of the opinion that lowering HbA1C may be associated with reduction of macrovascular complications of diabetes mellitus. Further according to the European Society of Cardiology relationship between hyperglycemia and cardiovascular disease should be seen as a continuum and for each 1% increase in HbA1C there is a defined increased risk of cardiovascular disease.

POSTPRANDIAL GLUCOSE
There are ample epidemiological evidence which suggest that the effect of hyperglycemia on cardiovascular risk is independent of other known risk factors and the pathogenic role of hyperglycemia on the blood vessel wall already exists in the early stages of glucose intolerance. Postprandial, but not fasting, blood glucose is an independent risk factor for cardiovascular events in type 2 diabetes, with a stronger predictive power in women than in men, suggesting that more attention should be paid to postprandial hyperglycemia, particularly in women.

Fasting plasma and postprandial plasma glucose values reflect the recent status of diabetes in the patients as compared to HbA1C which represents glycemic status of the previous 90-120 days. Some studies have shown a positive correlation between postprandial glucose and cardiovascular disease risk whereas others have failed to do so. The MONICA study (2003) showed that the odds ratio for unknown myocardial infarction was 4.1 in women with impaired glucose tolerance as compared to NGT subjects. Similarly, the landmark Heinski Policeman Study demonstrated a higher risk of CVD mortality in patients with high postprandial glucose level. Briefly, postprandial glucose levels provide better information about the future risk of cardiovascular disease than fasting glucose and elevated postprandial glucose also predicts increased cardiovascular risk in subjects with normal fasting glucose.

SMOKING
The strong association of smoking with coronary artery disease is well established. Most recent studies have identified smoking as the strongest risk factor in both men and women under 40 suffering from acute coronary syndrome. Religa et al. found that of 100 women admitted with first myocardial infarction, 45% were smokers, while in the subset of patients below 45 years of age, the figure was 95%. In the epidemiological studies WOBASZ and NATPOL PLUS, in the general population about 25% women and 42% men were smokers many of them aged 18-31. It is believed that smoking would be playing a critical role in the development of coronary artery disease in diabetic patients. In fact the risk of CAD is likely to increase many fold in the combined presence of diabetes and smoking. This makes smoking an important modifiable risk factor for the prevention of CAD in diabetes.

TOBACCO
Nicotine contributes to the majority of harmful effects of smoking like coronary artery disease, hypertension and peripheral vascular disease. Nicotine increases circulating levels of catecholamines and free fatty acids thus affecting lipid metabolism contributing to higher levels of total cholesterol and lower levels of high-density lipoproteins. When snuff or chewing tobacco is used throughout the day, blood nicotine concentrations are similar to those seen with cigarette smoking. Use of chewing tobacco is extremely common in India and therefore chewing tobacco becomes an important modifiable risk for the prevention of coronary artery
Assessment of Cardiovascular Risk in Diabetes

**PREDIABETES**

Increased risk of CAD is well established with T2DM. Further many studies have shown that even prediabetes increases the risk of CAD and related mortality. Progression from IGT to diabetes is associated with mild deterioration, whereas reversion to normoglycemia is associated with improvement in risk factors in the risk of developing cardiovascular disease.

**IMPACT OF DIABETES MELLITUS ON CAD IN WOMEN**

Increased risk of CAD associated with diabetes is well established and prospective studies have consistently shown that the increased risk of CAD attributable to diabetes is greater for women than for men. Diabetes abolishes the advantage women have over men in surviving cardiovascular disease. Meta-analysis done by Warren et al. showed that the relative risk of death from CAD in diabetes is indeed greater for women (2.3) than for men (1.85). Even the Nurses Health Study done in the US found that the relative risk of fatal CAD was 8.7 for women with a history of diabetes and no CAD at baseline, 10.6 for women with a history of CAD and no diabetes at baseline and 25.8 for women with both conditions at baseline.

**CONTINUUM OF CARDIOVASCULAR DISEASE**

It is believed that T2DM, CAD, atherosclerotic CVA, and essential hypertension, are continuum of same clinical spectrum in a subset of CAD patients. Endothelial dysfunction may be the pathophysiological link between hypertension, T2DM and CAD. It is possible that endothelial dysfunction get accelerated due to environmental factors and hereditary factors in a subset of CAD/T2DM. The concept of CVS continuum is important in the sense that whenever someone encounters any case of T2DM, CAD, CVA, stroke and/or HTN in ethnic Indians; one has to think of the potential possibility of all five lesions at a later stage. A determined effort should therefore be made to exclude each one of these lesions at least in those who have a family history of CVS allied disorders or those who have manifest central obesity. It is well worth remembering that the process of atherosclerosis and/or diabetes sometimes starts right from conception in utero and progresses through the stages of foam cell formation ~ fatty streaks ~ atheroma ~ fibrous plaques ~ complicated plaques to the adulthood depending upon multiple factors like, maternal malnutrition, maternal smoking, environmental pollution, genes at the time of conception, diet and smoking.

**IMAGING TOOLS FOR PRE CAD MARKERS IN T2DM**

With the advancement in various imaging modalities it is possible to study atherosclerosis in sub-clinical stage and predict clinical
events of CAD in diabetic individuals. Structural changes like carotid intimal medial thickness (IMT) and functional changes like endothelial dysfunction and arterial stiffness can be demonstrated by various imaging modalities. These markers are found to be higher in diabetic subjects in comparison to non-diabetic controls. In CUPS study Shanti Rani et al. and Mohan et al. reported that the IMT values among diabetic subjects were significantly higher (0.95 mm) compared to normal subjects (0.74 mm). Moreover, carotid atherosclerosis defined as IMT >1.1 mm was significantly higher in diabetic subjects (20%) compared to non-diabetic subjects (1%). Similarly endothelial function, which was assessed by flow mediated dilation decreased significantly in diabetic subjects compared to non-diabetic subjects. Arterial stiffness using pulse wave analysis showed marked increase in stiffness in diabetic subjects.

Electron beam computed tomography (EBCT) is a non-invasive technology for evaluating the extent of coronary artery atherosclerosis that relies on the detection of coronary artery calcium (CAC). Recent studies have shown that the diabetic patients have a substantially higher prevalence of CAC. The amount of calcium deposited in the coronary arteries correlated with the pathological extent of atherosclerosis and the presence of stenosis as evaluated by coronary angiography which predicts future CAD events. A study by Sunita Schurgin (2001) has revealed significant increase in the prevalence of CAC scores; more than or equal to 400 (25.9%) as compared to the randomly selected (7.2%) and matched (14.4%) non diabetic control groups.

INDIAN DIABETES RISK SCORE (IDRS)

Recently ethnic specific risk score has been developed for early identification of diabetes in Indian people. Formulation of Indian Diabetes Risk Score (IDRS)

<table>
<thead>
<tr>
<th>Particulars</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
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<tr>
<td>&lt;35</td>
<td>0</td>
</tr>
<tr>
<td>35-49</td>
<td>20</td>
</tr>
<tr>
<td>&gt;50</td>
<td>30</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td></td>
</tr>
<tr>
<td>Waist &lt;80 cm (female), &lt;90 (male)</td>
<td>0</td>
</tr>
<tr>
<td>Waist ≥80-89 cm (female), ≥90-99 (male)</td>
<td>10</td>
</tr>
<tr>
<td>Waist ≥90 cm (female), ≥100 cm (male)</td>
<td>20</td>
</tr>
<tr>
<td>Physical activity</td>
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<td>Vigorous exercise or strenuous (manual)</td>
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<td>20</td>
</tr>
<tr>
<td>or mild to moderate physical activity</td>
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</tr>
<tr>
<td>or sedentary activities at home/work</td>
<td>30</td>
</tr>
<tr>
<td>Family history</td>
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</tr>
<tr>
<td>No family history</td>
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<td>Either parent</td>
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</tr>
<tr>
<td>Maximum score</td>
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Is an attempt in that direction Variables used in IDRS are: age, family history, regular exercise and waist. Individuals are classified as high risk (score >60), moderate risk score (score >30-50), and low risk (score <30) out of total score of 100(Table-1). IDRS has sensitivity and specificity of over 60% for a cut-off >60. This can be used as useful tool for detecting high risk diabetic individual in Indian scenario.

Interpretation: Score <30 low risk, score 30-50 medium risk and score >60 high risk for type 2 diabetes and cardiovascular diseases

CONCLUSION

The buzz word is “Think early and think beyond”

Type 2 diabetes mellitus is recognized as equivalent to CAD and thus carries the same risk as that of established CAD. It is thus prudent to look for the evidence of sub-clinical atherosclerosis and/or coronary artery disease in every patient who has diabetes mellitus for more than 3 years in elderly cases (male >60-years, females >50 –years). Similarly it is essential that each patient suffering from acute coronary syndrome should be subjected for oral glucose tolerance test after 72 hours of acute episode for detection of dysglycemia that is pre-diabetes or frank diabetes. It is advisable to ask for the history of coronary artery disease in the first degree relatives of diabetes and vice versa. It is good clinical practice to look for early evidence for other cardiovascular diseases like hypertension, cerebrovascular lesions, peripheral arterial disease, retinopathy and nephropathy in every case of diabetes and vice versa. At field level assessment high risk individual by applying Indian Diabetes Risk Score merits further exploration.

REFERENCES

10. Misra A, Khurana L. Obesity and metabolic syndrome in developing


