DISCUSSION

This, to our knowledge, is the first clinic-based study from western part of India conducted on recently detected Diabetes Mellitus patients. The study was undertaken to evaluate complications of diabetes mellitus and other risk factors for the development of diabetes at an early stage in recently diagnosed patients with the hope that, the results of the study may allow to make suggestions to improve the health status of people with diabetes.

The main findings of this study are that at the time of diagnosis

1. 46% patients with Type 2 Diabetes had microvascular complications and 15.3% had macrovascular complications

2. 60.6% patients with Type 1 Diabetes had DKA and 37.8% had to hospitalize

Out of the total 709 (427 males and 282 females) recently diagnosed Type 2 diabetes patients enrolled in the study, 622(87.7%) were having Type 2 diabetes which formed the core study population. 66(9.3%) had Type 1 diabetes, 10(1.4%) had Gestational diabetes (GDM), 3(0.4%) had Secondary diabetes (0.4%) and 8 (1.12%) had Impaired Glucose Tolerance (IGT). Out of three patients with Secondary diabetes, two had diabetes following pancreatitis and one had steroid induced diabetes.

TYPE 2 DIABETES PATIENTS & THEIR VARIABLES

DEMOGRAPHIC CHARACTERISTICS

Out of total 622 Type 2 Diabetes patients studied, 61.7% (384/622) were males and 38.3% (238/622) were females (Figure 41). Mean age of onset of the disease was 46.93±11.11 for males and was 48.95±10.55 for females. Mean height was 168±7.59 cms for males and 154.81±6.37 cms for females. Majority belonged to Hindu religion (83.8%) (Table 57 & Figure 42). 99.5%
(619/622) were literate (Table 58). 60% (85.2% males and 19.3% females) were working. 40% (14.8% males and 80.7% females) formed the non working group. Majority of males were working and majority of females were not working. (Table 59 & Figure 43)

PREVALENCE OF SYMPTOMS AT THE TIME OF DIAGNOSIS

The onset of Type 2 diabetes is usually subtle and many years may elapse before diagnosis. Harris et al. estimated a gap of 9 to 12 years between the onset of Type 2 diabetes and its clinical diagnosis. They subject themselves for testing only when they are symptomatic. It is evident from the fact that 92.8% (577/622) of study subjects were diagnosed due to symptoms. The majority of our patients (68.2%) had classic diabetic symptoms (nocturia, polyuria, polydypsia, and weight loss). Few patients had more than one group of symptom at time of diagnosis. Only 7.2% diagnosed without regard to symptoms (accidentally) during routine check up. In a similar study, 50% of the patients presented with some symptom and 8% were diagnosed on routine check up. In another study, polyuria, polydipsia and weight loss were the most common symptoms and were detected in 79% of the patients.

The other common symptoms with which the patient presented were weakness and fatigue (58.7%), leg pain, tingling, burning and numbness (44.9%). 17.7% presented with infection, 9.1% with history of blurred vision and 4.5% presented with sexual dysfunction. Occasionally, the first indication of the presence of Type 2 diabetes may actually be detected at the time of diagnosis of a diabetes complication. In our study, 0.3% (2/622) presented with long-term diabetic complications (cranial nerve palsy). (Table 60 and Figure 44)
EATING HABITS

The relation between improper dietary intake and inactivity and the Non communicable disease like diabetes is especially strong. i.e, diets extremely high in fats (especially animal fats); low in fruits, vegetable and complex carbohydrates.\textsuperscript{824}

The dietary pattern of patients was collected with the help of the STEPs questionnaire by using the interview technique.\textsuperscript{825,826}

In the present study, majorities (519/622, 83.4\%) of patients were vegetarian and very few (103/622, 16.6\%) patients were non vegetarian. There was no significant gender difference. Unlike Western populations, the frequency of non-vegetarian food intake was very low (once a week or once a month), with the exception of <3\% patients who were regularly having a non-vegetarian diet (Table 61). Meal pattern were variable and most of study patients had traditional concept of Breakfast/Lunch/Dinner. Most common form of cooking medium used was Oil & in liberal quantity. Surprisingly among the study subjects no body used blended oils. Sugar and jeggery is added practically in all the food items. Most of the patients had less than the recommended intake of vegetable & fruits, females had lower intake compare to males. The consumption pattern of fast foods amongst teenagers shows that deep fried foods like samosas, wada was more frequent in comparison of shallow fried foods like masala-dosa, hotdog, noodles etc. Consumption of baked food like pizza and pastries was also found to be high.

In general, the role of dietary factors in the Indian diabetes epidemic has been debated. Surprisingly, some studies have demonstrated that dietary intake does not appear to differ significantly between groups with or without diabetes in India.\textsuperscript{827,828} Consumption of traditional home-prepared rice and vegetables based meals in the vast majority of cases. A limitation of present
study is the lack of quantification of caloric and fat intake due to limited resources.

Further, evidence indicates that a diet low in total and saturated fat, high in plant foods especially in green and yellow vegetables and citrus fruits and low in alcohol is consistent with a low risk of development of metabolic disorders. One of the ways to delay the progress of this chronic degenerative disease is to shift from the "Affluent diet" to "Preventable diet" consisting of more cereals and pulses (legumes), less fat, more green leafy vegetables and moderate consumption of sugars.

Dietary records do however provide insight into issues faced in making recommendations to persons with or at risk of diabetes. In particulars, there are few carbohydrate alternations to white rice in the traditional diet. Where a focus on reading nutritional panel, calculating carbohydrate servings & a fat content and interpreting the glycaemic index, forms a standard part of diabetic dietary education in developed countries, this system is challenging when most foods are prepared from raw ingredients by a family member and shared around a large household. Diet sheets and portion calculators relevant to this area need to be developed.

With this it is important to ensure availability, acceptability and affordability of vegetables and fruits etc. throughout the year to enable populations to adopt healthy dietary guidelines.

HABITS

More than one forth of the study population had some form of habits. 9% were smoking, 19.5% were chewing tobacco/snuffing & 8.2% were consuming alcohol. Some patients had more than one habits. (Table 62)
TOBACCO USER

Total tobacco usage habit, in any form, in both males and females in the study subjects was 28.4%.

Regarding type of tobacco usage habit, the data revealed that the habit of using oral tobacco and cigarettes/rolled tobacco (Bidi) was higher in males than in females (44.0% Vs. 3.4%). This can be attributed to the fact that in the Indian population mostly men indulge in this unhealthy practice. This can be seen in another study where again the intake of tobacco was higher in males (26.1% vs. 1.7%).

Fewer females, however, indulged in this unhealthy behavior; and even in those who had tobacco usage habit, snuffing was more common (2.5%) and smoking was less common (0.8%)

ALCOHOL USER

Alcohol usage: About 8.2% of the study subjects had the habit of alcohol consumption. Alcohol consumption was more prevalent in males than in females (12.8% Vs. 0.8%)(Table 62). Gujarat being a dry state, details about frequency and amount of consumption may not have been disclosed by patients. Females in particular, were reluctant to mention about alcohol consumption due to social stigma. That might have resulted in underreporting.

Regarding the amount of alcohol consumed daily in the preceding 7 days, the majority (50%) of those who consumed alcohol were males who consumed beyond the prescribed limit for alcohol consumption (>2 standard drinks/day).

Sex, smoking and alcoholism were found to be non-significant factors. A recent report of WHO has also mentioned that consumption of an average of ≥40 g pure alcohol per day for women and ≥60 g for men is nonsignificantly
associated with diabetes.\textsuperscript{830,831} We also found similar results in the present study. However, partly it may be attributed to the small sample size of the alcohol users and secondly, the females were reluctant to mention about alcohol consumption due to social stigma. That might have resulted in underreporting.

The risk factors of today are the diseases of tomorrow. Identifying these risk factors in populations occupies a central place in the surveillance system because of the importance of the lag time between exposure and disease. Therefore, public health strategies have to be driven by the motive of identifying risk factors in populations, and countries need to know the profile of risk factors of populations in different settings.\textsuperscript{832}

FAMILY HISTORY

Asian Indians have been identified as one of the ethnic groups with a high prevalence.\textsuperscript{833,834} Familial aggregation of diabetes with a high prevalence among first-degree relatives and vertical transmission through more than two generations is commonly seen in Indians.\textsuperscript{835,836}

In the present study, 57.7\% had positive family history. 37.0\% had single parent with diabetes, 10.5\% had both parents with diabetes and 26.7\% had near relatives suffering with diabetes (Table 63 Figure 45). It shows high familial aggregation of T2DM in the Western Indian population.

There are limited data available about family history of diabetes in western part of India. In India, nearly 75\% of type 2 diabetic patients have first-degree family history of diabetes. In a study conducted in the Punjabi population of North India, about 80\% of the diabetic subjects had one or both parents affected.\textsuperscript{837}

The present study is clinic based rather than population-based in which self-reported diabetic patients were enrolled. This may be the reason for
difference in the incidence of family history of diabetes than that reported in other studies.

In the recent population-based study called Chennai Urban Population Study (CUPS) conducted on 1,262 individuals in Chennai in southern India, the prevalence of type 2 diabetes was higher among subjects who had positive family history of diabetes (18.2%) compared to those without (10.6%, p=0.0015). Moreover, 9.3% of subjects with family history of diabetes had impaired glucose tolerance (IGT—a pre-diabetic stage) compared to 5.0% of subjects without a family history (p = 0.016). The overall prevalence of glucose intolerance (diabetes + IGT) among subjects with two diabetic parents was significantly higher (55%) than those who had diabetic parent (22.1%, p=0.005) or those with two non-diabetic patient (15.6%, p<0.0001). The odds ratios of the risk for diabetes among subjects with one diabetic parent was 2.5 and this increased to 6.62 in subjects who had both parents affected by diabetes.838

The findings described in the study confirm and extend our knowledge of the dynamics of the present epidemic of T2DM in Western India.

AGE OF ONSET OF DIABETES

Age was found to be associated with the risk of DM. Those aged 40 years or more were found to have higher risk as compared to those younger than 40 years. Indians develop diabetes at a very young age, at least 10—15 years earlier than the Caucasian population839. The national urban diabetes survey in India also showed that more than 50% of the diabetic cases had the onset below the age of 50 years.840,841

The present data is in the line of earlier observation, shows that the onset of T2DM increases with age, especially after 30 years, and reaches a maximum (35.2%) at 41-50 years of age. In 61.6% the age of onset of diabetes was
below 50 years which are considered the potentially productive years of life. In 4.5% the onset was below 30 years (Table 64 and Figure 46).

A recent analysis by the International Diabetes Epidemiology Group comparing the profile of type 2 diabetes in the European and Asian populations showed that Indians had the strongest age associated risk for diabetes among all the groups. In the developed Western countries diabetes generally occurs in individuals aged > 65 years. In the developing countries onset of diabetes occurs at a younger age (45-65 years). Studies from India have shown a much younger age at onset of diabetes compared to the Western population. The recent DECODA study has made a comparative analysis of age at diagnosis of diabetes in different races. The overall effect of age on prevalence of diabetes differed considerably between ethnic groups even after correcting for other confounding factors such as BMI. The association between age and diabetes was higher in the Indian and the Maltese population compared to all other populations studies (Europeans, Chinese and Japanese).

The age and sex specific prevalence and the peak prevalence of diabetes were higher in Indian and in Singapore cohorts than in Chinese and Japanese cohorts.

With advancing age, lean body mass decreases and percent adiposity increases, but there may be little or no change in the total body weight. Aging is associated with sarcopenia, referred to as the universal and involuntary decline in skeletal muscle mass. This results in loss of muscle strength and contributes to eventual inability of the elderly to carry out tasks of daily living. The chief function of insulin is to facilitate glucose uptake by the muscles. A reduction in lean body mass means the eventual inability to dispose glucose. Reduced metabolically active lean tissue mass and physical activity levels in older people predispose them to obesity. This further increases insulin resistance.
An early occurrence of diabetes in the population has severe economic impact as severe morbidity and early mortality occurs in the most productive years of life. The diabetic subjects live long enough to develop the debilitating vascular complications of diabetes.

**PHYSICAL ACTIVITY**

Another worrisome factor is physical inactivity of Indians. Only a few studies are available but consistently reveal that Indians are less physically active as compared to white Caucasians.\textsuperscript{116-119} For example, in United Kingdom, Indian, Pakistani and Bangladeshi men were 14%, 30% and 45% less likely than the general population to meet the guidelines of physical activity, and these differences were more in women and other people.\textsuperscript{119}

The prevalence of physical inactivity among the diabetic patients in the present study was found to be 84.4%. Only eight subjects (1.3%) was involved in heavy work, they all were males (Table 65, Figure 47). The results of the present study are higher than figures (31-51%) given by the WHO.\textsuperscript{845}

This could be attributed to the fact that Gujarati, by enlarge, is business community and leave sedentary life. In the present study, nearly 50% males are businessman. They use of motorized vehicles and mechanization at workplaces, leading to physical inactivity. Similarly, high use of paid labor by housewives and use of mechanized means in kitchen preparations, leading to sedentary lifestyles in women.

The results corroborated with an urban community study from Rajasthan, where more than 70% of the subjects were categorized as having a sedentary lifestyle.\textsuperscript{846} In another study, a total of 76.6% of the females had a sedentary lifestyle, whilst this dropped to 56.7% among males in the 18-65 age group of the population of Pamplona, Spain.\textsuperscript{847}
Evidences are accruing to demonstrate that physical inactivity as an independent factor in triggering the epidemic of type 2 diabetes. The impact of physical inactivity is manifested more markedly in populations which had been accustomed to habitual heavy physical activity. Migration from rural areas to urban slums in metropolitan cities leads to obesity, glucose intolerance and dyslipidaemia. The risk of developing diabetes was more in subjects who followed a sedentary lifestyle. In Fiji, among Melansian and Indian men, the prevalence of diabetes was more than twice as high in those graded as sedentary or undertaking light activity as in those classified as performing moderate or heavy exercise.

Increasing urbanisation and mechanisation have further increased sedentary habits, which are also seen in young Indians. Interestingly, it is observed that substantial proportion of urban post-pubertal children and young adults in Delhi were sedentary. Mohan et al have shown that physical inactivity is associated with the components of the metabolic syndrome and CAD in this urban south-Indian population. Sedentary lifestyle may be critical for high tendency for insulin resistance in Indians and remains to be comprehensively investigated.

Physical activity has an impact on many of the components of the metabolic syndrome. The rapid globalization and industrialization occurring in developing countries has produced much advancement on the social and economic front. These improved socio-economic conditions have resulted in a decrease in physical activity and an increase in obesity, which has led to the increase in the prevalence of T2DM and its related complications in Indians. The data from this study suggests that those leading a sedentary lifestyle or involved only in household work develop diabetes more frequently than those whose occupation or routine life involved more physical work. South Asians and Asian Indians have been consistently shown to be less physically active when compared with other ethnic groups.
Moreover, increased intake of high-energy foods and an increase in psychosocial stress have proportionally increased the risk of disease even in relatively young adults between 25 and 35 years of age.

**STRESS**

Career is a word that comprises so many things within it. Competition, meeting deadlines, targets, follow ups, performance appraisals and lots more that keep us busy on the professional end so as to enhance the path of our career. As we chase these professional commitments stress levels are at their peak.

One of the contributing factors of Diabetes is stress. Given the modern lifestyles, most people find themselves amid a sea of tension and stress. It is difficult for them to avoid stress altogether.

Some of the evidences which we found from our study retrospectively show that out of 622 Type 2 DM patients studied almost 57% of patients were from age group 31-50 yrs- almost peak in their life where the stress level was at its peak. We had tried to differentiate population according to occupational status- then we found that almost 29.4% patients have their own business, 7.4% were professional, 18.0% were doing desk job.

The stress has mounted even more due to job-cuts, less or no increments as well. All this can have its impact on health -directly or indirectly and there can be many health disorders-like Diabetes, Depression, Insomnia, HT, False Appetite, Menstrual irregularity, CAD, Strokes etc. which are hazardous in the long run for a person..

Impact of stress, both physical and mental, is very strong on diabetogenesis, especially in those with a strong genetic background. A clinic-based prospective study has clearly shown the effect of stress on diabetes.
In mental stress, the body pumps out hormones to no avail. Physical stress, such as illness or injury, causes higher blood glucose levels in people with either Type of diabetes. Stress blocks the body from releasing insulin in people with Type 2 diabetes. The diagnosis of diabetes usually comes as a shock and is certainly a stressful time (Wijenaike, 2002; ADA, 2007).

In summary to avoid stress for maintain healthy life style is very important.

OBESITY

There is paucity on nationwide data on the prevalence of obesity. However, studies in different states of India provide some clues regarding the magnitude of the health threat due to this problem. Published data on obesity from different studies show that the prevalence of obesity ranges from 10 to 50%. However, the only nationwide study is the national health survey on women and this revealed a low prevalence rate. According to the Nutrition Foundation of India the prevalence of obesity is 1% for males and 4% for females in the slums while the corresponding figures for the middle socioeconomic class was 32.2% and 50% respectively.

In the present study, 82.3% (512/622) were overweight/obese which is high as compared to other studies (Table 66 & Figure 48). Present study is clinic based rather than population based, all study patients were self reported recently diagnosed Type 2 diabetes patients attending the clinic. This might be the reason of higher prevalence of obesity in the study population. In the Chennai Urban Population Study (CUPS), over 35% of the males in the middle-income group were obese compared to 13% in the low-income group. The corresponding figures for females were 33% and 24% respectively. Abdominal obesity among the middle income was 47.4% compared to 19.2% in the low-income group. The prevalence of diabetes
increased with in increase in quartiles of body mass index (BMI), the prevalence being 2.9%, 8.1%, 17.6% and 19.5% in the first, second, third and fourth quartile of BMI respectively. Prevalence of diabetes in subjects with abdominal obesity was significantly higher compared to those without abdominal obesity (27.8% vs 9.0%). The prevalence of impaired glucose tolerance (IGT) also with increase in quartiles of body mass index being 2.2%, 3.2%, 5.9% and 12.1% in the first, second, third and forth quartiles of BMI respectively and the increase was statistically significant (Trend chi square: 29.9, p<0.001). Prevalence of IGT in subjects with abdominal obesity (15.0%) was also significantly higher compared to subjects without abdominal obesity (2.6%). Body mass index showed a strong association with glucose intolerance both in Univariate and multiple logistic regression analysis. Moreover, even at lower BMI, categorized as low-risk according to WHO guidelines, the prevalence of diabetes was high among urban Indians.868

The average value of body mass index (BMI) in south Asians is lower than that seen in white Caucasians, Mexican-Americans and Blacks. Value of BMI in Asian Indians, however, increases as they become affluent and urbanized.869,870

ABDOMINAL OBESITY

It is now becoming increasingly clear that the regional distribution of fat plays a major contributory role for metabolic abnormalities. Abdominal adiposity assessed using waist circumference is considered to be more appropriate than generalized adiposity assessed by BMI.875-877 Despite relatively lower prevalence rates of obesity as defined by body mass index (weight in kg/height in square meters), Indians tend to have larger waist measurements and waist: hip ratios.871 and thus have a greater degree of central body obesity.
In the present study, 70.7% (440/622) of patients had central obesity and 53.4% (332/622) of patients had abnormal Waist Hip Ratio (WHR). (Table 67 & 68)

It is in agreement with several studies conducted so far. They have noted that high prevalence of abdominal obesity is particularly characteristic of the Indians. 872-875, 877-881, 886

Abdominal adiposity has also been reported among those with BMI < 25 kg/m². 878, 886 Further, although the average waist circumference in Indians appears to be lower, abdominal adiposity is significantly more than white Caucasians. 879, 887

Further, Indians also tend to have excess body fat and particularly abdominal and truncal adiposity. For any given waist circumference they also have increased body fat and moreover for any given body fat, they still have increased insulin resistance. 888-890

Several cross-sectional epidemiological studies suggest that obesity and abdominal obesity are strongly linked to diabetes. 891-893 Indeed, obesity is considered to be the link between insulin resistance and metabolic abnormalities which includes diabetes, hypertension and dyslipidemia, all of which are risk factors for coronary artery disease. 893

CHILDHOOD-OBESITY

In the present study, there were 5 children with Type 2 DM all were obese (BMI>25).

In developing countries such as India, especially in urban populations, childhood obesity is emerging a major health problem. 894 Studies from metropolitan cities in India have reported a high prevalence of obesity among affluent school children. 895-902
BLOOD PRESSURE

The prevalence of systemic hypertension was seen to be significantly higher in the study population. It was present in 57.9% (360/622) patients. There was no gender difference (male: 58.6%, female: 56.7%). (Table 69)

Prevalence of isolated systolic and isolated diastolic hypertension:

Based on the JNC-VII classification, isolated systolic hypertension (SBP ≥140 and DBP <90 mm Hg) was present in 7.5% of the subjects (7.5% of male and 7.6% of female) while isolated diastolic hypertension (DBP ≥90 and SBP <140 mm Hg) was present in 8.0% of the subjects (10.7% of male and 3.8% of female). Female had a lower prevalence of isolated diastolic blood pressure compared to male. (Table 69)

In a study, among the general population, isolated systolic and isolated diastolic blood pressure was present in 6.6% and 4.2% of the study population respectively. Female had a higher prevalence of isolated systolic blood pressure and lower prevalence of diastolic pressure compared to male. The SHEP (Systolic Hypertension in the Elderly Program) study showed that this type of high blood pressure is more common in older adults, especially in older female. Moreover, after menopause, there is a sharp increase in the prevalence of hypertension in female to levels that equal or surpasses that of male; this suggests that ovarian hormones participate in the protection afforded to premenopausal female. These may be the reasons for higher prevalence of isolated hypertension among older female in the present study.

RISK FACTORS ASSOCIATED WITH HYPERTENSION

Various risk factors have been associated with hypertension in epidemiological surveys. In the CUPS study, conducted by Mohan et al in
Chennai, age, body mass, waist hip ratio and glucose intolerance had a significant association with hypertension. The significant determinants of hypertension in the urban population of Jaipur were age, smoking and body mass index. In another study conducted in urban North Indians, age, higher body mass index, central obesity and higher socioeconomic status (SES) were independently and strongly associated with hypertension in both sexes, while higher dietary fat, salt intake and lower physical activity were weakly but significantly associated with higher prevalence and level of hypertension.

In the present study, the prevalence of hypertension steadily increased with age in both sexes and was 1.8% in male and 0.8% in female at the age group of 21-30 years, which increased rapidly and reached a prevalence of 19.5% in male and 15.1% in female at the age group of 51-60 years. (Table 70)

These findings were consistent with the present study findings which revealed that age, body mass index, smoking, serum cholesterol and triglycerides to be strongly associated with hypertension.

AWARENESS AND CONTROL OF HYPERTENSION

The study populations were categorized as normotensives (SBP<140 mm Hg and DBP<90 mm Hg), treated hypertensives (hypertensives under anti-hypertensive drugs) and untreated hypertensives. The mean BP among the normotensives was SBP: 118.53±10.62 mmHg, DBP: 78.79±5.49mmHg, among treated hypertensives it was SBP: 130.94±15.93 mmHg, DBP: 86.40±9.12mmHg and among untreated hypertensives it was SBP: 143.0±14.65mmHg, DBP: 91.25±11.05mmHg. (Table 71)

Of the total study subjects 57.9% (360/622) had hypertension. The proportion of subjects with self-reported hypertension was 207/622 (33.3%) (representing 57.5% of the total hypertensive subjects). Of the 207
hypertensive subjects, 169 (81.6%) were under treatment for hypertension. However, of these 169 individuals, only 80 (43.3%) had blood pressure under control (i.e. <140/90), which represents 22.2% of the total diabetic hypertensive group (Table 72, Figure 49-50).

Similar findings were observed by Mohan et al\textsuperscript{903} in an analysis done among the diabetic population. Of the total diabetic subjects (n = 365), 149 (40.8%) had hypertension. The difference between prevalence of hypertension among diabetic (40.8%, 149/365) and non diabetic subjects [16.1%, 320/1985] reached statistical significance (p<0.001). 56.4% of the diabetic population had undiagnosed hypertension. Of the known diabetic hypertensive subjects, 69.2% were on treatment for hypertension and of these 51.1% had their blood pressure under control. Thus overall, only 22.1% of the diabetic hypertensive subjects had their blood pressure under control. Among the diabetic population, treatment of hypertension was more common among male (male: 75.7% vs. female: 60.7%) while the control of blood pressure was more common among female (male: 46.4% vs. female: 58.8%).

The 'rule of halves' for hypertension states that: 'half the people with high blood pressure are not known, half of those known are not treated and half of those treated are not controlled'. If this rule is valid, then only one in eight of the hypertensive population would be receiving optimal treatment. An attempt was made to assess the applicability of the rule of halves in this study. Among the diabetic population with hypertension, 57.5% were aware of the condition, of whom 81.6% of them were on treatment and of these only 43.3% had their blood pressure under control i.e. (<140/90), which represents 22.2% of the total hypertensive group. Thus the 'rule of halves' is still valid in our study as far as hypertension is concerned.

\textit{PREVALENCE OF PRE HYPERTENSION:}

The present study had shown a large proportion of patients (173/622, 27.8%) were in the prehypertensive group (Table 72).
Prehypertension is not a disease category. JNC VII pointed out that BP related mortality is linear and that higher BP levels within what was earlier called 'high normal' or 'normal' range is associated with increasing morbidity and mortality. In the US population ≥20 years of age, 36% (62 million) had high-normal blood pressure or greater (systolic / diastolic blood pressure ≥130 / ≥85 mm Hg). Of the adult population of the NHANES in US, 61% has prehypertension or hypertension using the JNC VII definition. The Trial of Preventing Hypertension (TROPHY) study on individuals with high normal BP suggests clearly that the risk of cardiovascular disease begins to rise before the diagnosis of hypertension is evident.

Prehypertension is a designation chosen to identify individuals at high risk of developing hypertension, so that both patients and clinicians are alerted to this risk and encouraged to intervene and prevent or delay the disease from developing. Individuals who are prehypertensive are not candidates for drug therapy based on their level of BP and should be firmly and unambiguously advised to practice lifestyle modification in order to reduce their risk of developing hypertension in the future. Moreover, individuals with prehypertension, who also have diabetes or kidney disease, should be considered candidates for appropriate drug therapy if a trial of lifestyle modification fails to reduce their BP to 130/80 mmHg or less.

77.8% of diabetic hypertensive subjects still have not achieved adequate control, which underscores the urgent need to develop national strategies for prevention and treatment of hypertension in India. Although effective therapy has been available for more than 50 years, most persons with hypertension do not have their blood pressure under control. The US Department of Health and Human Services National health objectives for 2010 include reducing the proportion of adults with high blood pressure to 16%, increasing the proportion of adults with hypertension who are taking action to control it to 95%, and increasing the proportion of adults with controlled BP to 50%. The results of the present study shows that compared
to the US population there is long way to go to accomplish the goal of optimal control among the study population. Undoubtedly a similar situation exists in other parts of the country as well. It took at least 30 to 40 years of sustained effort to substantially improve hypertension detection and control in western countries, and the rates are still far from optimal.\textsuperscript{913} It is therefore obvious that considerable effort is needed to prevent or reduce the increasingly large burden of disease related to increasing rates of hypertension in countries in epidemiological transition, such as India.

LIPID ABNORMALITY

On applying NCEP and ADA guidelines we found out that nearly 78.3\% of the subjects (78.4\% males and 78.2\% females) had at least one abnormal parameter. Increased levels of Total Cholesterol (41.5\%), Triglyceride (50.5\%) and LDL-C (70.6\%) were found to be same both in males as well as females. However, decreased HDL-C (48.9\%) levels were found to be more in females (Table 73 & Figure 51).

Limited data available on diabetic dyslipidemia in recently detected type 2 diabetes. Our results are consistent with the previous studies conducted in different parts of the world. In a study performed in 1999-2000 in Slovakia (the Slovak population) on 3424 recently diagnosed type II diabetics aged up to 70 years 67.3\% had hypercholesterolemia, 66.5\% had hypertriglyceridemia.\textsuperscript{914}

In another study performed on recently diagnosed Type 2 diabetes in Iran, 24.5\% of the patients had high triglyceride (TG) levels, 32\% had high low-density lipoprotein cholesterol (LDL-C) levels and 36.5\% had low high density lipoprotein cholesterol (HDL-C) levels\textsuperscript{915}. 

425
In an analysis in UKPDS cohort followed up for nine years, it was noted that the Asian Indian population cohort had lower total cholesterol, LDL cholesterol and HDL cholesterol, but higher triglyceride compared to the White Caucasian and Afro-Caribbean cohort. This probably signifies that the Asian Indians are more insulin resistant, a fact that has been proved in many other studies comprising multi-ethnic population.916

The study clearly demonstrated that a very high percentage (92.4%) of females had low HDL-C levels. This could be attributed to 76.5% females who involved in house hold work, utilizing paid labor and 85.3% living sedentary life.

The significantly high levels of triglycerides and low levels of HDL-C observed in our population probably contribute to insulin resistance. Studies have shown that 53.7% males and 72% females have their HDL-C level below limits (<40 mg/dl in men and <50 mg/dl in women). Inter-ethnic comparison showed higher levels of serum triacylglycerols in adult Asian Indians,917,918 which manifests at a young age.918,919 Hypertriglyceridemia in Asian Indians was observed predominantly in people belonging to the high socio-economic strata920,921 as compared with the low socioeconomic strata rural populations. Low HDL-C levels are also characteristically seen in Asian Indians.918,922-924

The contributing factor for hypertriglyceridemia in our population could be our diet rich in carbohydrates.925 High TG levels have been associated with increased levels of small dense LDL which are considered to be highly atherogenic.926 Increased prevalence of low HDL has been reported earlier by Enas et al. who found that only 4% of Asian Indian male and 5% Asian Indian female had optimal HDL levels.927 Low HDL-C levels are stronger predictor of occurrence and reoccurrence of MI and stroke and are also associated with premature and severe CAD.928 Oxidative modification of LDL-
C is a key process of atherosclerosis and elevated LDL-C has been recognized as primary risk factor for CAD by NCEP — ATPIII.

Diet with high fat and calorie intake and lack of physical activity would be the major culprits, of dyslipidemia in our population. References have shown that our diets are rich in saturated fats. Besides it also involves overcooking of food which results in destruction of nutrients like folate, deep frying and refrying in the same oil leading to trans fatty acids formation which probably contributes to increase of Dyslipidemia in our population.929

METABOLIC SYNDROME (MS)

In the present study, prevalence of MS in recently detected Type 2 Diabetes patients is 61.1% (55.2% males and 81.9% females). (Table 74) There is scarcity in data on the prevalence of MS in Indians using IDF criteria; the few available studies are based on ATPIII criteria and one study using EGIR criteria. An earlier study in urban Indian adults aged 20-75 years, reported a prevalence of MS to be 41.1% using NCEP definition.930 The age-adjusted prevalence of MS based on ATPIII criteria in Jaipur (urban north Indian population) was 24.9%.931 Using EGIR criteria, the Chennai Urban Population Study (CUPS), reported an overall prevalence of MS to be 11.2% with a significant difference between the middle income (18.7) and low income groups (6.5%).932

Singapore National Health Survey, revealed a higher prevalence of MS among the Asian Indians (28.8%), compared to Malays (24.2%) and Chinese (14.8%).933 Prevalence rates of MS reported in Indians in Singapore are similar to that observed in the CURES study. The NHANES III in the US shows an age-adjusted prevalence of MS of 23.7% as defined by ATPIII criteria.934

Diabetes among Indian Americans study, a population-based study among migrant Asian Indians in US showed high prevalence of
hyperglycaemia (T2DM, 25%, impaired glucose tolerance 8%) and risk factors comprising metabolic syndrome. In particular, low HDL-C levels and hypertriglyceridaemia were prevalent in both genders and abdominal obesity was particularly prevalent in women. Overall, prevalence of the metabolic syndrome in migrant Indians varies from 20-32\%.

As subjects in the present study were self-reported recently detected Type 2 Diabetes patients, prevalence rates of MS reported in our study is higher as compared to other studies conducted in general population.

Various studies shown high prevalence of the metabolic syndrome in Indians, truly representative data from all regions of India are not available. Further, most investigators have not studied rural population which constitute ~70% of the population of India, and children and women.

Individuals with MS have two times higher risk for mortality due to myocardial infarction or stroke and three times as likely to develop, myocardial infarction or stroke compared to people without MS. Further they have a five-fold risk of developing type 2 diabetes (if not already present). MS has been indicated to be a risk factor and predictor for cardiovascular disease (CVD) and cardiovascular mortality.

The metabolic syndrome will likely to be increase further in the next several years, primarily because of the rapid increase in obesity. The health problems related to the metabolic syndrome will likely escalate dramatically.
MODIFICATION OF IDF DEFINITION - CONSENSUS STATEMENT:
It includes abdominal obesity [ethnic specific cut-offs of WC, and WC as a non-obligatory criterion (indifference to the IDF definition)], high triglycerides, low-HDL, dysglycemia (impaired fasting glucose/impaired glucose tolerance) and hypertension should be used. Three out of the five criteria have to be abnormal for diagnosing the metabolic syndrome.939

HbA1c
Table 75 & Figure 52 show HbA1c levels in newly detected type 2 diabetes patients at the time of diagnosis. 92.6% (576/622) of patients with type 2 diabetes had HbA1c >7 and 26.1% (162/622) had HbA1c > 10. Only 7.4% (46/622) had HbA1c <7.
Due to lack of symptoms and insidious onset of the disease as well as lack of awareness regarding the disease and fear of the unknown in spite of awareness, the diagnosis is often delayed by months to years. It might be the reason for elevated HbA1c at the time of diagnosis in majority of the patients. They subject themselves for testing only when they are symptomatic. The same is evident by the fact that 92.8% (577/622) of study subjects were diagnosed due to symptoms.

MICROVASCULAR COMPLICATIONS

Half of the patients (46%) newly diagnosed with Type 2 diabetes had already one or more microvascular complications present at the time of clinical diagnosis of Type 2 diabetes (Table 76 & figure 53). Harris suggests that the presence of diabetic complications at the time of clinical diagnosis of Type 2 diabetes indicates that complications of Type 2 diabetes are progressing, maybe as a consequence of untreated hyperglycemia or other factors, while diabetes remains clinically undiagnosed.940

In a study, they have observed that patients with history of diabetic complications before their clinical diagnosis of Type 2 diabetes carried a two fold increased risk of developing a new complication compared to diabetic
patients with out such history. They have also a fifty percent greater risk of dying.941

NEPHROPATHY

This, to our knowledge, is the first clinic-based study from western part of India on the prevalence of diabetic nephropathy in newly detected diabetes (NDD). Nephropathy was the most frequent complication in our study was present in 36.8%. Overt diabetic nephropathy was present in 10.0% and microalbuminuria was present in 26.8% (Table 76).

The prevalence of diabetic nephropathy varies widely from country and even among various ethnic groups in a particular country, ranging from 7-9% in the White UK population942 to 42% in Nauruans.943 The varying rates of prevalence reported by different researchers may also reflect the differing criteria employed to define diabetic nephropathy.

The predominant evidence from immigrant studies seems to support the premise that persons of south Asian ethnic origin are more susceptible to develop certain complications of diabetes, including but not limited to nephropathy. This observation was made initially by Allawi et al944 in the UK and later confirmed by Feehally and colleagues.945 Essentially similar conclusions were drawn by Shaw et al946 and Stewart et al947 in their studies on multi-ethnic populations in the Netherlands and Australia, respectively. However, studies on another multi-ethnic population in Singapore failed to show increased susceptibility of south Asians to diabetic nephropathy.948

Some studies 949–951 conducted in migrant Asian Indians in the U.K. and Europe have reported increased prevalence of diabetic nephropathy compared with white Caucasians.
We have little information on the prevalence of diabetic nephropathy from India, which is home to the largest number of diabetic subjects in the world. Our results are comparable with few clinic-based studies published on the prevalence of diabetic nephropathy in India. Viswanathan et al in 1991 reported the prevalence rate of microalbuminuria to be 28.5% in a cohort of 316 type 2 diabetes patients. In the same year, Gupta et al noted microalbuminuria to be present in 26.6% of type 2 diabetes patients studied by him in a clinic in north India. John et al, working in a teaching hospital in south India noted prevalence rates of 8.9% and 19.7% for diabetic nephropathy and microalbuminuria, respectively.

Mohan et al, working in a diabetes centre in south India, observed a prevalence rate of 36.3% for microalbuminuria and 6.9% for macroproteinuria among type 2 diabetic subjects. In neighbouring Pakistan, Shera et al in 2004 found that 20.2% of diabetic subjects had elevated urinary albumin excretion levels. More recently, in 2005, Ahmedani et al published the result of a multicentre study in Karachi in which 34% of diabetes patients were found to have microalbuminuria. In Sri Lanka, Weerasuriya et al reported that 29% of newly diagnosed diabetic subjects already had some elevation in urinary albumin excretion.

In a population based study done in south India, the prevalence of overt diabetic nephropathy was 2.2% and that of microalbuminuria 26.9%.

When compared with other population-based studies on diabetic nephropathy the prevalence of nephropathy was extremely high among Nauruans (75% in self-reported KD subjects and 63% in NDD subjects) and Pima Indians (47%). A population-based study in Egypt recorded a prevalence of albuminuria of 21% among KD subjects.

The large differences observed in the prevalence of nephropathy among different studies could be attributed to the differences in study design and
methodologies adopted for defining the disease. Many of the studies were clinic based, and this could have introduced a referral bias.

There could be several explanations for the lower prevalence of microvascular complications noted in south Asians. It is possible that due to wide publicity of the Diabetes Control and Complications Trial and the U.K. Prospective Diabetes Study results control of diabetes is improving globally, including in India, which could have resulted in lower rates of microvascular complications. Second, the prevalence of hypertension is known to be lower in native south Asians, and this may afford a relative protection against diabetic kidney disease.964 Finally, consequent to the greater awareness of the nephroprotective action of ACEIs and ARBs, usage of these drugs for preventing nephropathy has increased. This could also affect the prevalence rates of nephropathy compared with older studies.

**RISK FACTORS FOR NEPHROPATHY**

Multiple logistic regression analysis showed that, BMI≥25 (P=0.019) and high diastolic blood pressure (p=0.007), are significant predictors compared to subjects without nephropathy. (Table 77) Variables that could not reach up to statistically significant level but prevalence of nephropathy on higher side were systolic blood pressure, degree of glycemic control and associated retinopathy. There was no statistically significant difference between any of the other clinical or biochemical parameters in those with and those without nephropathy. None of the other variable studied was found to be associated with diabetic nephropathy either on univariate or multiple logistic regression analysis. These can be attributed to small sample size.

A clinic-based study conducted by Mohan et al found age, duration of diabetes, diastolic blood pressure, HbA1c and fasting plasma glucose levels to risk factors for microalbuminuria.503 Gupta et al reported HbA1c to be associated with microalbuminuria,501 John et al reported male sex, older age, longer duration of diabetes, poor glycaemic control and raised blood pressure
as risk factors for microalbuminuria, while Vijay et al. reported duration of diabetes, systolic and diastolic blood pressure, age of the patient and serum creatinine to be associated with proteinuria.

The major limitation of the study is that it is a clinic-based study and renal biopsies were not performed, as it is difficult to carry out these procedures in such a large study due to logistic and ethical reasons.

It is estimated that as of the year 2007, there are 40.9 million diabetic individuals in India. The prevalence of overt nephropathy in this study (i.e., 2.2%), when translated into numbers, would imply that ~850,000 individuals in India have overt nephropathy. Most patients with macroproteinuria eventually reach ESRD. The cost of a renal transplant in India is ~$5,000 U.S. (Rs. 2,50,000), which is unaffordable to the majority of people in India. The absolute number of subjects with diabetic nephropathy thus presents an economic burden to both the individual and the society. The large pool of microalbuminuria also suggests that there could be large increases in overt nephropathy with time, unless aggressive control of diabetes and hypertension is initiated. There is an urgent need to launch a national diabetes control program to tackle the potential economic burden due to diabetic nephropathy in India.

DIABETIC NEUROPATHY (DN)

Diabetic Neuropathy (DN) is heterogeneous in its clinical presentation. Diabetic peripheral neuropathies are a variety of syndromes which affect sensory, autonomic and motor nerve function. The commonest form, distal symmetric sensory polyneuropathy can affect virtually every tissue of the body and greatest source of morbidity and mortality in diabetes patients. Type 2 diabetes mellitus is frequently asymptomatic and the associated complications of diabetes like neuropathy may be the first clinical indication
of the disease. In the present study, 44.9% had leg pain, tingling, burning and numbness.

Although symptoms of DN may be prominent in uncontrolled diabetes, they are subjective and may be transient; quantitative assessment is difficult even in the clinic scenario. Most studies of DN have been performed in Western populations and there is a paucity of data in developing countries, particularly from India, where a large proportion of the population walks with bare feet. The few studies published on the prevalence of DN in India have been clinic based. Indeed, the Diabetes Atlas 2006 does not list a single population-based study on DN from south Asia. Few studies have been done to study the prevalence of neuropathy in newly diagnosed diabetes.

In the present study, 56.4% patients presented with neurological complication, 41.0% had impaired peripheral sensation and 15.4% had significant peripheral neuropathy. (Table 76)

The reported prevalence of diabetic neuropathy varies from less than 5 to 60% in different populations.

This could be attributed to different types of diabetes (e.g. Type 1 and Type 2 diabetes), the demography of the study population and different diagnostic criteria employed (pin-prick perception, clinical signs and symptoms, quantitative sensory tests or electrodiagnostic tests).

It is impossible to accurately approximate the true prevalence of diabetic neuropathy, because the criteria for diagnosis vary, epidemiologic studies are limited to patients receiving medical care, and diabetes remains undiagnosed in a large population of diabetes patients.

Quantitative sensory tests such as VPT are particularly suited to large studies because of the speed, ease and low cost.
Very few studies have reported on prevalence of neuropathy in Newly Detected Diabetes (NDD) subjects as most of the studies are restricted to Known Diabetes (KD) subjects.

In our study, 15.4% of the NDD subjects had neuropathy, which is lower than that reported in population-based study in CURES (19.5%)\textsuperscript{989} The cut-off for significant peripheral neuropathy in this study was more than 25\textsuperscript{V}. Where as the cut-off for DN in CURES\textsuperscript{989} was derived from the normal values of the non-diabetic control population and a VPT $\geq 20$ V was used to define neuropathy.

Using vibration sensation Nielsen et al\textsuperscript{990} observed neuropathy in 38\% of their patients and Cheng et al\textsuperscript{991} in 33.9\% among their Taiwanese patients of diabetes. However Ratzman et al\textsuperscript{992} and Pirart\textsuperscript{993} observed a lower prevalence of diabetic peripheral neuropathy in 6.3\% and 7\% respectively in their studies. Weerasuriya et al\textsuperscript{994} observed 9.8 \% of their diabetics had evidence of diabetic neuropathy at the time of diagnosis in their study from Sri Lanka. Ashok and his colleagues\textsuperscript{995}, observed a prevalence of neuropathy in 5.4\% of their patients with type 2 diabetes at the time of diagnosis.

The prevalence of neuropathy in this study would have been much higher if nerve conduction was used to screen for neuropathy, as it has higher sensitivity compared with biothesiometry.\textsuperscript{996} However, it is extremely difficult to perform nerve conduction studies in large studies.

The prevalence of neuropathy in this study was much higher than that reported in population-based studies in Mauritius (3.6\%)\textsuperscript{978} Australia (7.1\%)\textsuperscript{983} and Egypt (13.6\%).\textsuperscript{979} This might reflect a longer period of undiagnosed diabetes in Indian population and it may be a reflection of the low sensitivity of the biothesiometry method.

In another study conducted in Manipur, 29\% of the newly diagnosed patients of type 2 diabetes had clinical and electrophysiological evidence of diabetic peripheral neuropathy.\textsuperscript{997} This finding were identical with the finding of
27.8% by Franklin et al 998 Hamman et al 999 also found the prevalence of diabetic peripheral neuropathy in 29.7% and 26.9% in their study among the non-Hispanic whites and Hispanics respectively.

**RISK FACTORS FOR NEUROPATHY**

Multiple logistic regression analysis showed that, increasing age (>60, p=0.010), and association of retinopathy (p=0.019) were significant predictors compared to subjects without neuropathy (Table 78). There was no statistically significant difference between any of the other clinical or biochemical parameters in those with and those without neuropathy. None of the other variable studied was found to be associated with diabetic neuropathy either on univariate or multiple logistic regression analysis. These can be attributed to small sample size.

The primary risk factor for diabetic neuropathy is hyperglycemia.1000 The annual incidence of diabetic neuropathy in the DCCT was approximately 2% in conventionally treated patients, but that rate dropped to 0.56% in intensively treated type 1 diabetes mellitus patients.1001 The UKPDS failed to support a similar correlation between the incidence of neuropathy and glycemic control in type 2 diabetes patients, but the progression of diabetic neuropathy is dependent on glycemic control in both type 1 and 2 diabetes patients, and the pathologies are considered similar.1000-1002 The duration of diabetes also increases the risk of neuropathy, but the association between duration and prevalence may depend in part upon patient age, which itself is a risk factor.1000,1003 Cigarette smoking, alcohol consumption, hypertension, height, and hypercholesterolemia are all considered independent risk factors for diabetic neuropathy.1000,1003,1004

The limitation of the study is that, being a cross-sectional study, no inferences on cause and effect can be drawn. Another limitation of this study is the use of biothesiometry to define neuropathy, as it is a subjective method and therefore dependent on the subject’s cooperation and response.
This assesses only large fibre neuropathy and small fibre neuropathy (e.g. loss of temperature sensation) would be missed by this technique; however, we felt this was the best technique for a large clinic-based study.

As India is already home to over 40 million people with diabetes, the fact that over one-quarter of them would have neuropathy translates to over 10 million people with neuropathy, many of whom would not even know they have diabetes. This underscores the need for a National Diabetes Programme to help reduce the burden as result of diabetes in India and other developing countries.

RETINOPATHY

Retinopathy was the most frequent ophthalmic complication, present in 4% (25/622) patients (Table 76). Background Diabetic Retinopathy was present in 3.2% (20/622) patients, Preproliferative Diabetic Retinopathy was present in 0.5% (3/622) and Maculopathy was present in 0.3% (2/622).

In a similar study, Rema et al\textsuperscript{1005} in a study of 438 consecutive newly diagnosed type 2 diabetic patients, reported that 7.3% already had diabetic retinopathy, detected by four-field retinal colour photography at the time of diagnosis of diabetes.

In another population based study done by Rema et al\textsuperscript{1006}, among the known diabetic subjects, 20.8% had diabetic retinopathy while 5.1% of newly detected diabetic subjects had diabetic retinopathy. Prevalence of Diabetic Macular Edema (DME) in the total diabetic population was 5.0% while among the known diabetic subjects it was 6.3% and 1.1% among the newly diagnosed diabetic subjects.\textsuperscript{1006}
The limitation of the present study was that DR was diagnosed by ophthalmoscopy. This may be the reason of lower prevalence of retinopathy in the present study as compared to this study.

These data are strikingly lower than those reported in Europe, where the prevalence of retinopathy at diagnosis has been reported to vary from 20% to 35%.1007-1009 In the United Kingdom Prospective Diabetes Study (UKPDS)1009 the prevalence of diabetic retinopathy at the time of diagnosis of diabetes was 35%, which was phenomenally higher than other studies. In UKPDS, the study subjects were much older than those in the present study.

In studies conducted in USA, the prevalence of retinopathy at the time of diagnosis of Type 2 diabetes varied from 10-21%.1010-1012 Studies done in Australia in the newly detected diabetes1010 showed a prevalence rate of 9.9%, which is consistent with the prevalence in India. In a study by Stratton et al, in Type 2 (non-insulin-dependent) diabetes patients, 37 per cent of whom already had retinopathy at diagnosis.1013 The Asian Young Diabetes Research (ASDIAB) study, in which young diabetic subjects of age 12 to 40 years were recruited in several Asian countries also showed a lower prevalence of DR in Indians compared with other Asian groups.1014

Multiple logistic regression analysis showed that, only systolic blood pressure (odds ratio [OR]: 2.95, p: 0.027) was significant predictor compared to subjects without retinopathy (Table 79). Variables that could not reach up to statistically significant level but prevalence of retinopathy on higher side, were age, associated nephropathy and CAD. There was no statistically significant difference between any of the other clinical or biochemical parameters in those with and those without retinopathy. None of the other variable studied was found to be associated with diabetic retinopathy either on univariate or multiple logistic regression analysis. These can be attributed to small sample size.
In the present study, Retinopathy was more common among the male (5.2%, 20/384), compared with female (2.1%, 5/238). The same was observed in clinic (sex ratio – 2:1) and in the population-based data from CURES (males-21.3% vs females-14.6%) and the Hyderabad study. A similar male preponderance has been reported by the UKPDS study, and a study of Pima Indians. However, the reason for this is unclear and merits further investigation.

A study done in the Joslin clinic patients in US, showed increased prevalence of DR in females compared to males in the older-onset group, although PDR was present equally in both sexes.

Although the actual percentage of DR observed in the present study is low, if one were to extrapolate these results to all of India, the number would still be quite staggering. Presently there are more than 31.7 million diabetic individuals in India, and if 17.6% have DR, this would translate to more than 5.6 million subjects with DR. Furthermore, the number of diabetic subjects is expected to increase to 79.4 million by 2030, which could translate into a heavy economic burden and compromise the quality of life. This emphasizes the need for routine retinal screening of diabetic individuals to detect DR in the early stages.

MACROVASCULAR COMPLICATIONS

PERIPHERAL VASCULAR DISEASE (PVD)

Peripheral vascular disease (PVD) is a major cause of morbidity and mortality especially affecting the elderly population. The prevalence of PVD is multifold higher in patients with diabetes compared with age- and sex-matched nondiabetic subjects, and this may be because of hyperglycemia, hypertension, hyperlipidemia, platelet factors, and other factors that are increased in diabetic subjects. Recent estimates by the World Health Organization show that India already has the largest number of
diabetic patients in any given country, and this trend will continue in the future.\textsuperscript{1022}

Unfortunately, there is very little epidemiological data on PVD in either migrant Indians or individuals from the Indian subcontinent. Earlier clinic-based reports suggested that PVD is less common among Indian diabetic patients in the U.K.\textsuperscript{1023}, South Africa\textsuperscript{1024}, and Southern India\textsuperscript{1025}.

The main finding of the present clinic based study is the prevalence of PVD is 8.3. (Table 80 & Figure 55)

In a population-based study, prevalence of PVD in newly diagnosed diabetic subjects was 3.5\% and 7.8\% in known diabetic subjects.\textsuperscript{1026} They noted that PVD was uncommon until middle-age and then the prevalence rate increased dramatically.

The prevalence of PVD is lower than that reported from Netherlands \textsuperscript{1027}, the U.K. \textsuperscript{1028,1029}, and the U.S. \textsuperscript{1030}. It is in marked contrast to the high prevalence rate of CAD reported in Indians.

Thus, this study confirms earlier clinic-based data that the prevalence of PVD is low among Indians if ABI is used as the criterion for the diagnosis of PVD.\textsuperscript{1025}

This result is comparable to that in a recent report from Sri Lanka \textsuperscript{1031} but is considerably lower than that reported from Rochester \textsuperscript{1032} and the Hoorn Study \textsuperscript{1027}.

A prospective study among 613 type 2 diabetic patients from Tanzania, Germany and India was conducted to determine the differences in underlying risk factors and clinical presentation of foot problems.\textsuperscript{1033} It was reported that PVD was frequent in Germany while in Tanzania and India it was far less
This lower prevalence of PVD is most likely due to the lower age of the population and the lower age at onset of type 2 diabetes in Indians. As the population ages one can expect the prevalence of PVD to substantially increase even in India. A lesser prevalence of PVD and yet higher prevalence of amputation rate among Indians is due to progressive infection.

A couple of hospital-based studies have reported the prevalence of PVD in type 2 diabetic patients. In a study conducted in 3,010 type 2 diabetic subjects, 4.0% had PVD, these included 15.1% with gangrene and 17.6% who had undergone amputations. In another hospital-based study on 4,941 subjects, the prevalence of PVD was 3.9%. There was a slight female excess in PVD patients. PVD increased with increase in duration of diabetes. A hospital-based study from Bikaner in north-west India, recruited 4,067 type 2 diabetic patients. PVD was diagnosed using Doppler. The study showed that among diabetic the prevalence of PVD was 24.6%. This study also describes the various risk factors associated with PVD.

The prevalence of PVD has been shown to be higher among diabetic subjects compared to non-diabetic subjects.

The differences in prevalence rates may be because of the differences in the subject selection, sample size, and other factors, they could also reflect true differences in prevalence of PVD in different ethnic groups. This suggests that different susceptibility factors may operate in different populations. Alternatively, it could also be because the prevalence of certain well known risk factors, e.g., smoking, could be less common in certain populations. Finally, it could simply be a reflection of the younger age structure of the population, as shown by a steep increase in prevalence rates of PVD in those patients >70 years of age. The differences between the prevalence rates of CAD and PVD in our population are quite striking. Thus, whereas CAD occurs with increased prevalence and at a younger age (premature CAD), PVD appears to show the opposite trend, i.e., lower prevalence and occurrence in
older age-groups. This finding suggests that the pathogenic mechanisms for CAD and PVD could be different. In addition, our results suggest that screening for CAD using the ABI \textsuperscript{1019,1044} is unlikely to be useful in a South Asian population.

Multiple logistic regression analysis showed that, there was no statistically significant difference between any clinical or biochemical parameters in those with and those without PVD. These can be attributed to small sample size.

Indeed, the risk factors for PVD itself appear to differ in different populations. A study from China \textsuperscript{1045} reported that hypertension, diabetes, elevated serum cholesterol, LDL cholesterol, triglycerides, fibrinogen, and hyperglycemia are associated with PVD. A U.S. study showed diabetes to be the major risk factor for PVD \textsuperscript{1046}. In Greece, serum triglycerides alone were found to be associated with PVD in diabetic subjects \textsuperscript{1047}. A prospective study on type 2 diabetes showed triglycerides, HDL cholesterol, hypertension, and smoking as risk factors for PVD \textsuperscript{1048}. Other reports showed microalbuminuria \textsuperscript{1049}, homocysteine \textsuperscript{1050}, and lipoprotein( a) \textsuperscript{1051} to be associated with PVD.

The criteria for assessment of PVD, in this study, was a decreased ABI measured using a peripheral Doppler. This method is considered to be a reliable method for detecting PVD \textsuperscript{1052}. Earlier studies have suggested that an ABI <0.9 has a sensitivity of 95% for detecting angiogram positive disease, whereas a ratio of $\geq 0.9$ almost always excludes PVD \textsuperscript{1053}. ABI is thus considered a suitable method to assess PVD for epidemiological and clinical studies. However, there are some limitations to the use of peripheral Doppler because calcified non compressible arteries occur with increased frequency in patients with diabetes \textsuperscript{1054}. One cannot rule out the possibility that, if angiography or duplex color Doppler studies had been done, the prevalence of PVD might have been higher.
In summary, this clinic-based study using the ABI shows that the prevalence of PVD is quite low among western Indians. One should, however, be cautious in interpreting these results. The population of India is steadily aging and the prevalence of diabetes is rising sharply. Thus, one cannot rule out the possibility that, in the future, PVD could emerge as a very significant cause of morbidity and mortality, even in India. Another limitation is that the sample size is small. However, the sensitive methods used for detection is the strength of the study.

PVD can have a substantial economic impact on the individual, family and society due to limb loss as this disease can result in both direct and indirect costs. It can also decrease the quality of life. Finally PVD is a manifestation of atherosclerosis, it could also be a predictor of fatal atherosclerotic events like myocardial infarction and stroke.

CORONARY ARTERY DISEASE

Asian Indians have considerably higher prevalence of premature coronary artery disease (CAD) and standardized mortality rates for CAD compared with Europeans, Chinese and Malays. A report from the Study of Health Assessment and Risk in Ethnic Groups (SHARE) indicates a significantly higher risk of cardiovascular events among South Asians compared with Europeans and Chinese. Within the Indian subcontinent, a dramatic increase in the prevalence of CAD has been predicted in the next 20 years due to rapid changes in demography and lifestyle consequent to economic development. Earlier studies in Asian Indians have shown that classical risk factors do not explain the excess of CAD seen in this ethnic group. It is also possible that the risk factors for CAD could differ considerably between native and migrant Indians because of differences in diet, physical activity, body weight and lifestyle changes consequent to affluence and cultural changes consequent to migration.
As shown in Table 80 & Figure 55 show the prevalence of CAD in the study population is 7.2%.

There are limited data available about prevalence of CAD in newly detected Type 2 diabetes. The PODIS shows comparatively low figure of 4.5% of CAD in newly detected diabetics.\textsuperscript{1068}

Ramachandran in 1998 \textsuperscript{1069} has reported prevalence of CAD in diabetics as 14.2% (3.9% - established cases + 10.3% based on ECG criteria) in the population based study in Chennai. While Mohan et al \textsuperscript{1070} at Chennai in 2001 found prevalence of 21.4% (Known diabetes 25.3% and newly diagnosed diabetes-13.1%). Similarly in other studies Gupta PB et al have reported prevalence of CAD in diabetics as 19\% \textsuperscript{1071}.

In the ICMR multicentric study which was carried out in different hospitals in 1984 – 1987, prevalence of CAD in diabetic was in males 8.1\% and in females 4.7\%.

Several studies have reported \textsuperscript{1072} higher incidence of diabetes and CAD in persons who had low birth weight but become obese in adulthood. Children having born small but had grown heavy (or tall) were the most insulin resistant and had the highest levels of cardiovascular risk factors \textsuperscript{1073}.

Multiple logistic regression analysis showed that, only alcohol (p=0.016) was significant predictor compared to subjects without CAD (Table 81). Variable that could not reach up to statistically significant level but prevalence of CAD on higher side were age and degree of glycemic control. There was no statistically significant difference between any of the other clinical or biochemical parameters in those with and those without CAD. None of the other variable studied was found to be associated with CAD either on univariate or multiple logistic regression analysis. These can be attributed to small sample size.
Several studies have shown that the prevalence rate of conventional risk factors in Indians is not significantly higher as compared to other ethnic groups/populations (except for diabetes). However this does not in any way reduce their importance in causation of CAD in Indians. As compared to previous study in 1995 in similar population, he has observed significant increase in the number of people with obesity, diabetes and dyslipidemia.

The differences observed in the prevalence of CAD among different studies could be attributed to the differences in diet, physical activity, body weight and lifestyle changes consequent to affluence. It could also be due to differences in study design and methodologies adopted for defining the disease. Many of the studies were clinic based, and this could have a referral bias.

PROGNOSIS AND COURSE OF CORONARY ARTERY DISEASE IN DIABETIC PATIENT

Mortality after acute myocardial infarction in diabetic versus non-diabetic patients is already greatly increased during hospital stay. As an example, a retrospective study by Yudkin and colleagues demonstrated a hospital mortality of 24.7 per cent in 380 non-diabetic (patients defined by normal HbA1c values) after infarction versus 42.2 per cent in diabetic patients, which is almost doubled.

Medium- and long-term survival is also decreased in diabetic patients with coronary heart disease. In the aforementioned Finnish observation trial by Heffner et al. only a little more than half of the patients with Type 2 diabetes survived the 7 year observation time after myocardial infarction.

Similar results were seen in the diabetes subgroup analysis of the placebo arms of the statin intervention trials, such as the 4S-trial. 

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In the OASIS trial, which was conducted in six different countries, male patients with diabetes mellitus admitted due to unstable angina or non-Q-wave infarction showed a 1.5-fold increased mortality in the following 2 years compared with non-diabetic patients. In female diabetic patients the 2 year mortality rate was even twice as high.\textsuperscript{1078}

Coronary heart disease in diabetic patients shows significantly more frequently a multi-vessel disease pattern with diffuse coronary sclerosis than in non-diabetic patients. Acute coronary syndrome in diabetic patients leads more often to impaired left ventricular function. The occurrence of cardiac dysrhythmias also seems to be higher. The primary size of infarction, however, does not differ significantly.\textsuperscript{1079}

CONCLUSIONS

The prevalence of CAD among Indians is increasing rapidly. Urgent steps are needed to modify lifestyle by increasing physical activity, modifying diet and making aggressive use of statins as part of the preventive strategy to reduce risk factors and, thus, the burden of CAD in this population.

SEXUAL DYSFUNCTION

As shown in Table 82, 7.3\% males (28/384) had sexual dysfunction as a presenting complain. No female had similar complain.

The exact prevalence of sexual dysfunction in general as well as diabetic population is not known, the consensus is that the problem is not uncommon in male diabetic subjects. The prevalence of erectile dysfunction in male diabetic subjects varies between 30 to 70\%, the average being 50\% and increases as age advances. Sexual dysfunction in a male diabetic subject may occur at an early age and could be the presenting symptom of diabetes. The females were reluctant to mention about it due to social reason. That might have resulted in underreporting.
Erectile failure is the common sexual dysfunction in a male diabetic subject. Causes of erectile failure in a diabetic may be metabolic, psychogenic, endocrine, neurological, and vascular and drug induced or mixed. Alterations in any one of the factors can result in sexual dysfunction. In a known diabetic the organic causes are the commonest, comprising about 85% of the cases, psychological problems account for about 10% and in the remaining 5%, the cause is not known.

NEUROGENIC CAUSES:

Increased incidence of erectile failure in a male diabetic subject seems to be primarily a result of diabetic autonomic neuropathy. This observation was substantiated by bladder function studies. The pelvic parasympathetic nerves (Nervi erigentes) that lead to erection also innervate the bladder and involvement of those nerves is demonstrated by the abnormal cystometrogram. Autonomic neuropathy assessment in male diabetic subjects with erectile failure revealed greater involvement of parasympathetic nerves.

VASCULAR CAUSES:

Both macro and micro-vascular complications of diabetes may confound the clinical picture of diabetic erectile failure. Severe vascular lesions involving the distal aorta and iliac arteries as in Leriche’s syndrome may also result in erectile failure. Small blood vessel disease (micro-angiopathy) may further interfere with normal penile function. Whether neuropathy in a male diabetic subject can influence vascular lesions with subsequent production of erectile failure is still subjudice. Invariably male diabetic patients with arterial occlusive disease secondary to arterioscleroses do also have corporal veno occlusive dysfunction due to pan cavernosal alteration in corporal tissue compliance.
DRUG INDUCED ERECTILE FAILURE:

Since diabetic subjects receive a number of drugs for control of diabetes and its complications, they may suffer from the side effects of these drugs. Some of these drugs (methyl dopa, reserpine, atenolol, clonidine, pindolol, prazocin, verapamil and guanethidine) may cause erectile failure in a male diabetic subject. Withdrawal of these drugs may restore potency.

PSYCHOGENIC CAUSE:

Failure to attain penile erection due to organic causes puts a man into strain and repeated unsuccessful attempts leads to psychological stress and the vicious cycle perpetuates. In any sexual dysfunction, psychogenic cause always exists and male diabetic subjects are no exception to this. In psychogenic erectile failure the onset is abrupt, libido is diminished and nocturnal and special situation erection is present.

History and physical examination may indicate the probable cause of erectile failure.

SEXUAL PROBLEMS IN DIABETIC WOMEN:

The equivalent of impotence in a woman is absence of vaginal lubrication during intercourse. They may also suffer from fatigue, depression, changes in perimenstrual blood glucose control, vaginitis, decreased sexual desire and an increased time to reach orgasm. A distinct clinical entity ‘Clitoral neuropathy’ has been reported. This is usually mistaken for candidial vaginitis since it produces paresthesias over the genitalia.

In conclusion, both women and men with diabetes are at increased risk for sexual dysfunction. In men, sexual dysfunction is related to somatic and psychological factors, whereas in women with diabetes, psychological factors
are more predominant. A diabetic subject presenting with sexual dysfunction requires utmost sympathy and deft handling. The patient and the spouse should be educated on the effects of the chronic disease on the sexual function and further counseled to adapt well to the new situation.
CUTANEOUS MANIFESTATIONS

Cutaneous manifestations generally appear subsequent to the development of diabetes, but may be the first presenting sign or even precede the diagnosis by many years.

As shown in Table 83, 16.4% (102/622) have cutaneous manifestations. Out of 102 patients, 55 were males and 47 were females. 9.3% (58) had infection like boils, perputitis, candida albicans infection of the female genitalia and paronychia. 1.6% (10/622) had Vitiligo and 5.4% (34/622) had Acanthosis Nigricans. Out of all complain related to cutaneous manifestation; pruritus was the most common complain.

There are limited data available on cutaneous manifestations in newly detected Type 2 diabetes. In a clinic based study, out of 150 consecutive known diabetes mellitus patients, some form of cutaneous involvement was present in 66%. Diabetic thick skin in the form of finger pebbles was the most common manifestation (49.49%), followed by fungal and bacterial infections (34.34%).

Braverman found cutaneous manifestations in 30% of patients, whereas Romano et al., Nigam and Pande, Mahajan et al., Yosipovitch et al., Wahid and Kanjee found these in 60, 61, 64, 71 and 82% respectively. Similar frequency was reported by Romano et al., whereas Nigam and Pande reported higher frequency.

The prevalence of cutaneous manifestation in the present study was 16.4% in NDD. It is lower as compared to previous studies conducted in KD.

The occurrence of cutaneous manifestations was directly correlated with obesity status, the duration of diabetes and uncontrolled diabetes. As the duration of diabetes increases, there is non—enzymatic glycosylation of dermal collagen and mucopolysaccharides, leading to various cutaneous manifestations.
Uncontrolled diabetes increases the risk of development of microangiopathy and related complications or sequelae. A higher percentage (87.87%) of patients with cutaneous manifestations had systemic complications like hypertension, coronary artery disease, peripheral vascular disease, nephropathy, retinopathy and peripheral neuropathy as compared to diabetic patients without cutaneous manifestations (37.24%) \(^\text{1080}\). Similar values of 89 and 55.5% were reported by Mahajan et al,\(^\text{1084}\) and Shemer et al,\(^\text{1090}\) respectively. Hence the cutaneous manifestations correlate with systemic manifestations of diabetes.

**CUTANEOUS INFECTIONS**

The prevalence of cutaneous infections in the present study was 9.3%. It is lower than previous studies in which prevalence of cutaneous infections was 20% to 50% in known diabetics.\(^\text{1091,1092}\) Poor diabetes control might be the cause or the consequence of the concurrent infection. The infectious disorders can be of fungal or less commonly bacterial origin.\(^\text{1091}\)

Candida albicans infection especially of the female genitalia occurs with greater severity and frequency in poorly controlled diabetes. The presence of pruritus vulvae and the coexistence of culture proven candida in a non pregnant woman can alert clinicians to the onset of diabetes. Balanitis, balanoposthitis, and phimosis may be less common than candida infections in women, but are presenting manifestations of diabetes in uncircumcised men.\(^\text{1093}\)

Generalized pruritus is not associated specifically with diabetes, but if it occurs dry skin is commonly the cause, Localized anogenital pruritus (pruritus vulvae and balanitis) may be the presenting symptom of diabetes.\(^\text{1094}\)
ACANTHOSIS NIGRICANS (AN)

Acanthosis nigricans is a dermatologic condition associated in some cases with hyperinsulinemia. Children with this condition are 1.6 times to 4.2 times as likely as those without it to have hyperinsulinemia. The association of acanthosis nigricans with hyperinsulinemia has led to speculation of a possible further association with type 2 diabetes. The natural history of acanthosis nigricans with respect to type 2 diabetes has not been determined, but evidence suggests the acanthosis nigricans may be a risk factor for type 2 diabetes. A readily apparent, rapidly identifiable physical examination marker identifying patients at increased risk for type 2 diabetes could stimulate discussions of lifestyle modifications in the primary care setting. Lifestyle interventions can prevent or delay disease onset by as much as 58%, making identification of high-risk patients a priority in primary care. All patients with unexplained AN should be screened for insulin resistance.

A. Kong et al have observed that children and adults with a family history of type 2 diabetes had more than twice the prevalence of acanthosis nigricans compared with those without such family history. The prevalence of acanthosis nigricans increased as BMI increased and was higher in those with hypertension. They also observed that among children and adults with more than one type 2 diabetes risk factor (family history of type 2 diabetes, overweight, hypertension, and minority race/ethnicity, defined as race/ethnicity other than white, non-Hispanic), the prevalence rate of acanthosis nigricans increased successively with each additional risk factor. Patients with acanthosis nigricans were 1.97 times as likely as those without it to have type 2 diabetes. Patients who were older, obese, and had more than 1 risk factor were also more likely to have the disease.

Vitiligo may precede the onset of clinically evident diabetes and also occurs more frequently in families of diabetic patients. There appears to be no
difference in the clinical course of Vitiligo even if associated diabetes is well controlled.

In conclusion, the skin is involved in diabetes quite often. Whenever patients present with multiple skin manifestations, their diabetic status should be checked and controlled; or if they are obese, a high index of suspicion should be kept regarding their diabetic status.

Acanthosis nigricans can be used to rapidly identify those patients with multiple risk factors for type 2 diabetes mellitus. Because lifestyle changes have been proven to reduce the incidence of type 2 diabetes in high-risk adults, acanthosis nigricans may provide primary care clinicians with an efficient method for identifying patients who would most benefit from lifestyle modification interventions.

Diabetics are more prone to develop bacterial, fungal and viral infections. Patients with recurrent furuncles or carbuncle should always be investigated for diabetes. Monilial balanoposthitis and vulvo-vaginitis as well as extensive ring worm infections are common amongst diabetic. Pruritus vulvae is quite frequent in diabetic females.

**TYPE 1 DIABETES MELLITUS**

Out of total 709 patients studied, 9.3% (66/709) patients were diagnosed as having Type 1 DM. 60.6% (40/66) were male and 39.4% (26/66) were female. The mean age of onset of disease was 14.5 years in male & 12.9 years in female. In 78.8% the age of onset of diabetes was below 20 years. Majority belonged to Hindu religion (90.9%) and the rest were from other religion. 60.6% (40/66) had Diabetic Ketoacidosis (DKA) at the time of diagnosis and 37.8% (25/66) were hospitalized at the time of diagnosis. The reasons for hospitalization were DKA in 36.4% (24/66) patients and severe hyperglycemia in 1.4% (1/66) patient. (Table 84)
Diabetic ketoacidosis (DKA), the metabolic outcome of very low levels of effective insulin action, can be a life-threatening complication. Despite the high morbidity and cost of DKA at diagnosis of diabetes, there are no recent estimates of its prevalence in the Indian population. Although predictors of DKA in children with established type 1 diabetes have been studied\textsuperscript{1106} little is known about predictors of DKA that precede diagnosis. Worldwide studies have shown that DKA is present in 15% to 67% of youth at the time of diagnosis.\textsuperscript{1107} In the present study, 60.6% (40/66) had Diabetic Ketoacidosis (DKA) at the time of diagnosis which is comparable.

Studies have suggested that DKA at the diagnosis of diabetes is more frequent in younger patients, in populations with lower socioeconomic status, and in countries with a lower incidence of type 1 diabetes where diabetes awareness is low.\textsuperscript{1108,1109,1110} Type 2 Diabetes may also present with DKA, but the prevalence and predictors of such a severe presentation of type 2 diabetes in youth have not been systematically studied.

In a large, population-based study\textsuperscript{1140} "on Presence of Diabetic Ketoacidosis at Diagnosis of Diabetes Mellitus" the major finding is that a substantial percentage (29.4%) of youth in the United States who are currently being diagnosed with type 1 diabetes present with potentially life-threatening ketoacidosis. This estimate is similar to those reported 10 to 20 years ago from several European countries\textsuperscript{1108,1109,1111,1112}

Comparisons with previous studies in the United States and elsewhere suggest that the risk of DKA at diagnosis has not improved decisively over the past 20 years. In Colorado, over the past 23 years, the proportion of children with type 1 diabetes who have presented with DKA at the time of diagnosis has decreased only modestly, from 38% in 1978–1982 to 29% in 1998–2001.\textsuperscript{1113,1114} On the other hand, the incidence of type 1 diabetes in youth is doubling every 2 decades,\textsuperscript{1115,1116} and several studies have reported increasing rates of type 2 diabetes in youth, especially in nonwhite ethnic groups.\textsuperscript{1117,1118,1119} Although the rates of DKA are somewhat lower, with
more youth with diabetes, in the absence of community efforts to increase public awareness of the early symptoms of diabetes, DKA is likely to remain a major cause of morbidity and health care expenditures in youth.

Currently, there are few population-based epidemiologic data on the prevalence and predictors of DKA at the time of presentation of type 2 diabetes in youth. In this study, using a large number of patients with type 2 disease from several settings and geographic areas, they found that 9.7% of youth with type 2 diabetes presented with DKA. This finding is consistent with previous reports.\textsuperscript{1120,1121} DKA in adults occurs in those with ketosis-prone diabetes and particularly in nonwhite persons with type 2 diabetes.\textsuperscript{1122,1123} Finding suggests that DKA at diagnosis should not be used to exclude the diagnosis of type 2 diabetes, at least in patients <20 years of age.

Their data confirm previous reports suggesting that lack of insurance and less favorable health insurance are associated with more severe onset of diabetes in youth.\textsuperscript{1124,1125,1126}

They did not find any significant differences in the prevalence of DKA among different racial and ethnic groups in univariate and multivariate analyses. This is consistent with a previous report on predictors of recurrent DKA in the US youth with type 1 diabetes,\textsuperscript{1106} where rates were similar in Hispanics and non-Hispanic whites. In contrast, young Asian children in the United Kingdom had 8 times the risk of presenting in DKA as did non-Asian children of the same age.\textsuperscript{1127}

In the present study, in 78.8% the age of onset of diabetes was below 20 years. It is in agreement with the previous studies,\textsuperscript{1106,1109,1124,1125} in which they found that the prevalence of DKA was significantly higher among younger children, reaching 37% in those aged 0 to 4 years. The strong association with younger age was independent of indicators of socioeconomic status, suggesting a biological, rather than a social phenomenon. Although DKA is overlooked in some younger children, with presenting symptoms such
as vomiting and respiratory distress initially ascribed to less-specific diagnoses, a body of evidence points toward a shorter prodromal period in younger children. In developed countries, earlier studies have suggested that as many as 1% of children used to die at the diagnosis of diabetes. The situation in India may be worse.

The mortality in DKA is still as high as 0.31%, that translates into 47 potentially preventable deaths among an estimated 15,000 children and adolescents diagnosed in the United States annually. Complications of DKA, especially brain edema, account for nearly all of the deaths at diagnosis of diabetes in this age group.

The study also shows that, among youth, the use of health care resources at the diagnosis of diabetes is very high, with more than half of the patients being hospitalized and nearly half (44%) of the hospitalizations because of DKA.

In the present study, 37.8% (25/66) were hospitalized at the time of diagnosis. The reason for hospitalization was DKA in 36.4% (24/66), which is also comparable.

Many US children are hospitalized for a few days at diagnosis of diabetes, but some of these hospitalizations might be avoided if adequate reimbursement and safe outpatient alternatives for initial care existed. In Colorado, the availability of a tertiary type 1 diabetes outpatient care center has contributed to a decline in hospitalization at diagnosis from 88% in 1978–1982 to 46% in 1998–2001; correspondingly, however, the proportion of hospitalizations because of DKA increased from 44% to 63%. High rates of hospitalization increase the cost of diabetes care at the time of diagnosis. In USA, the annual cost of treating DKA in patients of all ages, at diagnosis and later on, exceeds $1 billion; newly diagnosed patients account for 25% of this cost.
In light of the increasing incidence of diabetes in the United States and worldwide, a high index of suspicion on the part of parents and health care providers may reduce the cost of initial diabetes care. Early recognition of the classical triad of polydipsia, polyuria, and polyphagia with weight loss (present also in many cases of type 2 diabetes before diagnosis) is essential, as is awareness of the variable presenting symptoms, for example, vomiting or rapid breathing in a young child. An intensive community intervention to raise awareness of the signs and symptoms of childhood diabetes among school teachers and primary care providers in a region of Italy was found to reduce the prevalence of DKA at diagnosis of type 1 disease from 83% to 13%.1134

In the United States, the Diabetes Autoimmunity Study in Youth, an observational study following children at high risk for type 1 diabetes by periodic testing for diabetes autoantibodies, levels of hemoglobin A1c, and random blood glucose, demonstrated that the clinical course of diabetes is milder in youth diagnosed without DKA.1135 Children followed by the Diabetes Autoimmunity Study in the Young were rarely hospitalized and did not develop DKA at diagnosis of diabetes, in contrast to community control subjects with and without a family history of diabetes. They also had nearly normal hemoglobin A1c values at diagnosis, with significantly lower requirements for insulin in the first year of illness. This milder clinical course at diagnosis may have very important long-term implications because near-euglycemic control at onset occurring spontaneously1136 or achieved by intensive insulin treatment1137 has been shown to preserve the secretion of insulin. Residual endogenous insulin secretion, as shown by the Diabetes Control and Complications Trial, predicted a 65% lower risk of severe hypoglycemia1138 and a 50% lower risk of the progression of diabetic retinopathy.1139

In majority of children, Diabetic ketoacidosis can be an initial presentation of diabetes. Family physician has to be alert when a child presents with evidence of dehydration or hyperventilation or drowsiness or with polyuria,
and polydipsia. Increased public awareness concerning the symptoms and signs of Type 1 Diabetes is warranted. Improved access to care may additionally reduce the severity and costs of initial treatment in Type 1 Diabetes.
INTRODUCTION

Diabetes Mellitus is a disease-complex involving multiple systems of the body. Diabetes is the fifth most common cause of return visits in office based practice with only hypertension, pregnancy, otitis and well-child where visits may be required more frequently.\(^{1141}\) It is a chronic disease requiring lifelong management on the part of the patient and the physician. The management of diabetes requires patience, commitment and has to be focused and individualized. Continuity of care and being able to provide education along with specific therapy is extremely important. Chronic disease management requires an entire system of care by a team of providers to supply the necessary range of expertise, a system of information to track care and risk factors, and a system to provide patient education to encourage self-management. Many providers underestimate the time and expertise involved in building this systematic approach. Much of the difficulty of providing good care is a "system problem," not a "person problem."\(^{1142, 1143}\) Diabetes care should be organized to be practical, cost-effective, flexible and individualized. Updated and repetitive information helps improve care. The impact of organised diabetes care can be measured on various health care practices like improved rates of glycated hemoglobin estimation, foot inspection, low-density lipoprotein cholesterol control and decreased rates of hospitalization because of foot infections and smoking.

RATIONALE OF 'ORGANISED' DIABETES CARE

The goals of diabetes care are

- Sustained improvement in health status of people (children as well as adults) with diabetes and a life approaching normal expectation in quality and quantity.
• Prevention and cure of diabetes and of its complications by intensifying research effort.

Zgibor et al in a clinic-based study showed better process outcome in patients followed by specialists as compared with non specialist care.\textsuperscript{1144} Similar results were published in another report by Hellman et al in a private practice endocrinology setting in which longitudinal data were available over a 14-year follow up.\textsuperscript{1145} Additionally, Zgibor et al pointed out that many studies in Europe, have reported lower rates of proliferative retinopathy, other long-term clinical complications and mortality in patients who receive care in specialized diabetes centers. A long-term follow-up from the Pittsburgh Epidemiology of Diabetes Complications Study also showed that specialist physicians and clinics contribute to better outcome for patients with type1 diabetes.

Thus diabetes care should be a comprehensive and coordinated effort to improve the outcomes which could be measured as health status, clinical status, patient satisfaction, and cost of therapy of all diabetic patients seen at an “Organised Diabetic Clinic”

**COMPONENTS OF A DIABETES CLINIC**

**PATIENT DATABASE (REGISTRY)**

The patient database (Table 85) forms one of the most important components of a diabetes clinic organization. It provides useful information about the complete profile of the patient. Computerised patient records help to organize medical data into a coherent flow sheet for rapid review. The computerised patient database can also be programmed to provide related useful information such as: (a) number of patients with different types of diabetes (b) association of a particular type of diabetes with each type of diabetes- related complication. Each new patient receives a specific ‘Diabetes Clinic Registration Number’. The data in the computer is programmed in such a way that by punching the registration
number, the last name or first name, or the city from which he comes, one is able to retrieve his complete profile.

The registry helps the practice of diabetes to be interactive and helps the doctor and his patients to manage their diabetes, its related complications and their key clinical measures better. An updated registry may, for example, remind the diabetologist which patients need HbA1C monitoring. The diabetes registry also helps in analyzing data which then answers questions about whether the patients are deriving benefit in clinical outcome.

**Table 85** The Database Sheet of Each Patient (Manual Record and Computerized) has the Following Essential Details

<table>
<thead>
<tr>
<th>Personal Details</th>
<th>Name, Age, Sex, Husband’s/Father’s Name, Complete Address, Phone numbers, email ID, name of referring doctor, Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History</td>
<td>Yes (in grandparents, parents, siblings, children / others)</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Age of onset of Diabetes</td>
<td></td>
</tr>
<tr>
<td>Symptoms of Diabetes</td>
<td></td>
</tr>
<tr>
<td>Clinical Examination</td>
<td>Anthropometric details: height, weight, BMI, Waist circumference, Blood pressure(lying/ sitting), Cardiovascular, Central Nervous system, Gastrointestinal, Foot examination, retinal examination</td>
</tr>
<tr>
<td>Laboratory Investigations</td>
<td>Blood sugars, HbA1c, Renal functions(Blood urea, serum creatinine, urinary protein, Microalbuminuria), lipid profile, other investigations: ECG, Chest skiagram, Thyroid Profile</td>
</tr>
<tr>
<td>Clinical Diagnosis(Coded)</td>
<td>Type 1 Diabetes / Type 2 Diabetes/ Gestational Diabetes / other types</td>
</tr>
<tr>
<td>Complications</td>
<td>All Coded</td>
</tr>
</tbody>
</table>
DIABETES-SPECIFIC LABORATORY SERVICES

The laboratory needs to be standardized, accurate and reasonably priced. Investigations which need to be done on a regular basis include blood sugars, blood urea, serum creatinine, urine protein, micro albumin, lipid profile, liver enzymes, thyroid functions, and glycated hemoglobin. An electrocardiogram is also required. Chest skiagram and other relevant examinations are arranged.

PATIENT EDUCATION MATERIAL

Patient education forms the corner stone of treatment of chronic diseases such as diabetes mellitus. Amongst the important components of the diabetes clinic environment are ‘Patient educational posters’ on the walls of the waiting area. These need to be in the vernacular language. The posters should have material directed to all aspects of diabetes care. They must be changed periodically to avoid monotony. Audio-visual education is of value for people in the waiting area. New patients are grouped and educated together. Question-answer session after a lecture help to improve learning. Patients receive education for diet, investigations related to diabetes treatment, complications of diabetes, podiatry care and for prevention of diabetes in other members of the family.

PARAMEDICAL PERSONNEL AND STRICT GLYCEMIC CONTROL

DCCT\(^9\) clearly demonstrated the benefits of coordinated efforts in achieving glycemic control. The strict glycemic goals achieved in this study was made possible only through close cooperation between the physicians and a number of other paramedical personnel viz. diabetes educators, dietitians and behavioural specialists. In a practical clinical care setting, however, this may not always be possible. At the same time it can be said that the success in achieving strict glycemic control would depend to a great extent on the level of involvement of paramedical personnel.
DIETARY ADVICE SERVICE

This is an important component of any diabetes clinic. A dietitian or a nutritionist in consultation with the diabetologist plays a vital role in the management of diabetes. Dietitians are available and are generally part of diabetes management teams in most hospital care settings. Diet has always been the key to the success of any diabetes treatment regimen and hence the role of a dietitian in planning and monitoring the diet of diabetic patients is of crucial importance. In one survey, only 20% of patients reported visiting a dietitian over the past year\textsuperscript{1146} and we need to work seriously to improve this figure. The dietitian is invaluable in guiding the patient to make the right food choices. The dietitian can contribute significantly by making a thorough assessment of the patient which would include anthropometric and current dietary assessments, and then evaluate risk and accordingly provide counseling on diet and lifestyle.\textsuperscript{1147} Dietary assessment should include, besides nutrient intake, a detailed account of food preferences and habits, which should help construct a comprehensive diet plan with a high likelihood of compliance. This is an essential component of any successful dietary management and would therefore determine the success of diabetes management overall.

In addition to planning and advising the patient on the details of dietary choices and providing diet charts the patient can follow, the dietitian should also make every effort to provide nutrition education to the patient on various facets of diabetic diet and lifestyle as well as the need to closely adhere to the same. Frequent follow up to monitor the implementation and compliance of dietary advice also needs to be undertaken by the dietitian from time to time. Chandalia et al\textsuperscript{1148} demonstrated that patient's nutritional knowledge improved significantly after nutritional counseling and this improved control of diabetes significantly.
DIABETES EDUCATOR / DIABETES NURSE SPECIALIST

The Diabetes Educator could give advice about foot care, review of insulin injection techniques or discuss self-monitoring, eye examination, measurement of Glycosylated hemoglobin, micro albuminuria and the importance of control of blood pressure and lipid levels. Complications of diabetes and sick-day care are other issues which could be discussed.

REFERRAL ADVICE

Referring the patient at the appropriate time for foot care, a retinal examination or a cardiac work-up is an important component of ‘organised diabetes care’. The ophthalmologist then may advise fluorescein fundus angiography or laser photocoagulation. Similarly a patient needs referral advice for nephrology/cardiac evaluation or podiatric check up.

IMPROVED DIABETES CARE IN PRACTICE: THE ORGANISATION PROCESS

The ‘organization process’ requires that one pays attention to the following to improve diabetes care in practice. Several standards, guidelines and consensus statements have been developed by many organizations. They should set and modify these according to patient needs and requirements and try to stick to them to provide comprehensive care.

DO NOT FORGET TARGETS

Make a list of what has to be done. Flow charts can help as important reminders, at all desks in the clinic.

REMEMBER WHAT TO DO

Simple paper charts help providers remember that care for patients has several components and each one needs attention. This information can also be formatted as a flow sheet to track recommended screening procedures.
Brightly colored stickers can be used to indicate high-risk conditions, such as a high-risk foot.

PLAN A 'PREVENTIVE CARE VISIT'

One can have effective preventive care if the visit is scheduled for that. Patients need to know what they would be learning about a particular complication on their next visit in addition to their routine investigations. Since complications related to diabetes are initially asymptomatic, a visit designated for example for foot care could be more productive.

DISTRIBUTION OF TASKS

Office staff must be given materials for various tests or services needed periodically. For example different staff members could be made responsible for scheduling investigations like a glycated hemoglobin, a cholesterol test or a timely eye referral or a foot examination. The staff can also direct the patient for education service in a particular area. For example, foot examinations are more likely to occur if nurses have patients remove their shoes before the doctor arrives in the examination room.1149

EMPOWER PATIENTS

In any chronic disease management, patients should be active participants in taking care of their disease. Patients can serve as powerful reminders and collaborators in their own care.

HOW DOES ORGANISED DIABETES CARE BECOME EFFECTIVE?

Organized diabetes care improves both short-term and long-term outcomes. Organized diabetes care are helpful in the following ways:
BETTER AND UPDATED INFORMATION

The diabetologist and his team have updated scientific information which is transformed into clinical practice for the patient’s benefit.

CONTINUITY OF CARE AND DELIVERY OF FREQUENT REPETITIVE INFORMATION

Continuity of care can improve care for persons with diabetes mellitus. The provider would be more likely to know when tests are needed and treatment changes are indicated. Continuity might, therefore, have even greater benefits for persons with diabetes than it does for the general population. Frequent and repetitive information has a better retention value. For example, when a patient on each visit hears about the importance of better blood pressure control or sees a poster about the benefits of foot care, he or she gets the message better and the retention of information is long lasting. A more recent study suggested that higher provider continuity, might lead to better glucose control.

MONITORING OF MEDICAL COMPLIANCE

Compliance of therapy is the essence of any good treatment protocol. An organised diabetes clinic improves when staff are trained in monitoring. Thus compliance is increased.

ONGOING TEACHING AND PATIENT-DIABETES TEAM INTERACTION

This allows the patient to continually reassess his/ her treatment and make appropriate adjustments. A periodical interaction between the patient and the diabetes-team serves as an excellent platform for monitoring of the disease, change therapy to improve short-term goals and thereby prevent complications. It also helps in early detection complications and timely intervention. For productive interactions to occur, practice systems must ensure that provider teams have requisite expertise, appropriate patient
information, organized clinical practice support and, that patients have ready access to self-management support resources.

FAMILIAR PERSONNEL

The patient on arrival in the clinic feels comfortable with the same staff and this has an overall advantage.

FOLLOW EVIDENCE - BASED CLINICAL GUIDELINES

The outcome at the diabetes clinic can be improved significantly if the staff is trained to follow evidence-based clinical guidelines for various parameters.

RETINAL SCREENING

All patients with type 2 diabetes at diagnosis or at presentation to the centre and all patients with type 1 diabetes beginning five years after diagnosis are subjected to annual dilated eye-examination performed by a retinal specialist. The staff at the centre checks the reminder sheet and plans the examination. Having realized the importance of retinal examination over a period of time, patients themselves volunteer for the eye test.1153

FOOT CARE

The purpose of this examination is to identify persons at high risk for developing foot ulcers in the next few years because of neuropathy, deformities, or peripheral vascular disease.1154,1155 All patients with type 2 diabetes have foot screening examination annually from the time of diagnosis, and all patients with type 1 diabetes should have this examination annually beginning 5 years after diagnosis.

SCREENING FOR MICROALBUMINURIA

All patients undergo a screening for microalbumin on an annual basis since it is an important marker for cardiovascular disease.1156
ADVICE FOR BLOOD PRESSURE CONTROL

Control of blood pressure is as important as good glycemic control. Organized diabetes care helps in ensuring that this becomes a regular check index when assessing a patient in follow-up. New Targets of blood pressure control and its importance need to be communicated to the patients as well and should be applied to non pregnant adults with either type 1 or type 2 diabetes.1157

ADVICE ON CARDIAC RISK REDUCTION

Since diabetes carries a great cardiovascular risk and is responsible for majority of diabetes-related hospitalisation and premature death, it becomes imperative for the diabetologist and his team to pay special attention to factors which will eventually reduce cardiac risk.1158

GLYCEMIC MANAGEMENT TO TARGET HBA1C LESS THAN 7%

A guideline suggesting how and when to use diet, exercise, oral hypoglycemic agents, and insulin are discussed in detail with the patients with the aim of reducing HbA1C to less than 7 %.1159

PREGNANCY AND GLYCEMIC CONTROL

It is of paramount importance to have special clinic personnel dedicated for the care of women with pregestational type 1 and type 2 diabetes or gestational diabetes. These patients will require specific nutritional instructions and also very strict glycemic control for a good fetal outcome.

COUNSELING ABOUT HABITS

A sincere and persistent effort should be made by the diabetologist and his team to motivate his patient to discontinue tobacco (smoking/chewing/snuffing and alcohol.
GUIDELINE IMPLEMENTATION

Guidelines can be implemented in several ways.

CONTINUING MEDICAL EDUCATION

Continuing medical education programmes are useful to implement guidelines. This includes lectures and workshop on several aspects of diabetes care like retinal screening, foot care, screening of, microalbuminuria and glycemic management. Active participation of the patients improves compliance and ultimately clinical outcomes.

PATIENT-SPECIFIC DECISION SUPPORT

Specific patient education materials exist for each guideline requiring patient self-management activities. For example a small pamphlet containing information on protective foot care, importance of self monitoring of blood glucose are distributed to patients and then discussed on subsequent visits.

MEASURE GUIDELINE IMPLEMENTATION

As providers of diabetes care, it becomes imperative to assess how one is doing and are various guidelines being implemented and with what success. These are helpful in improving care in the future.

PATIENT SELF-MANAGEMENT PROGRAM:

Practice and implementation of self-management behaviour plays an important role in the control of disease. For example, a detailed plan is drawn up for a patient ready to actively participate in self- monitoring of blood glucose. With proper education, more patients come forward for self-management program.
EVALUATION OF THE IMPACT OF THE PROGRAM

This is assessed by an annual survey of randomly sampled patients. They are asked to answer questions in a proforma, for example on screening for microalbuminuria or retinal screening or foot care.

ADVANTAGES OF ORGANISED DIABETES CARE

Observational studies have indicated that endocrinologists in private practice and in institutional settings are able to provide process outcomes significantly different than those of generalists, and are comparable to those achieved in the Diabetes Control and Complications Trial.

IMPROVEMENT IN SHORT-TERM CLINICAL OUTCOMES

Studies have demonstrated that the involvement of diabetes-specialist clinics and diabetes team management have a significant impact on such short-term, clinically significant outcomes as cost for diabetic ketoacidosis, length of hospital stay, emergency room visits and hospitalizations, hypoglycemia, and foot infections. In the Medical Outcomes study report by Greenfield et al in 1996, endocrinologists fared better than family physicians in the Mean Summary Clinical Outcomes Index, which includes [HbA1c], foot ulcers, foot infections, albumin excretion, systolic and diastolic blood pressure; visual acuity, vibration sense, and serum creatinine.

IMPROVEMENT IN LONG-TERM CLINICAL OUTCOMES

In the study by Hellman et al in a private endocrinology setting, doctors intensively, followed 209 people and reported that they developed significantly less end-stage renal disease, had fewer cardiac events and had lower overall mortality rates compared with 571 patients who had been followed by standard community care. Attention to this model of service would provide long-term benefits in a number of practice settings.
A DAY AT THE DIABETES CLINIC

REGISTRATION/APPOINTMENTS

All patients should be seen with an appointment to provide best care. Patients being given an appointment are (a) requested to report at the Registration Desk after about 10 hours of fast, (b) get all previous medical record, and up to date prescription and present medication. Registration desk fills up details including address and phone numbers.

MEASUREMENTS

The out patient clinic nurse records height, weight and waist circumference.

MEETING THE DIABETES DOCTOR

This is a critical part of the patient examination. On the first visit, it is a detailed history taking (including personal history, family history, history of medication, physical activity) and clinical examination which includes blood pressure recording, examination of feet, inspection of insulin injection sites (in a patient already on insulin), The Doctor will then advise blood tests and other necessary special tests.

BLOOD SAMPLES

Blood sample is taken by one of the clinic nurses for various investigations.

SPECIAL TESTS

Then, as per the advice by the diabetologist, other special test like ECG/ Echocardiography/ TMT, Fundoscopy / Eye check Biothesiometry, ANS testing, X-Ray, USG, Doppler, Foot scan are carried out.
REVIEW OF REPORTS

Once the test reports are ready, doctor will overview reports, adjust the treatment and gives the prescription. Depending upon the test reports, he then advises consultation with other members of the diabetes team, the dietician and the diabetes educator.

SPECIALIST’S CONSULTATION

Based on the clinical examination and result of reports, patient is advised to consult specialist like Ophthalmologist, Cardiologist, Nephrologist, Podiatrist.

THE DIABETES DIETICIAN

The Diabetes Dietitian discusses diet with the patient. The dietician recalls the diet being taken by patients and advises about diet. Dietitian also advises about healthy eating choices, food exchanges. The diet advised should be tailor made according to patients demand, choices and requirement. Diet advice should help in maintaining ideal body weight.

THE DIABETES EDUCATOR

The diabetes educator plays a very important complimentary role to the diabetes doctor. He or she can guide the patient about various aspects of diabetes management including prescription of exercise and yoga.

DIABETIC SUPPLY CENTRE

Diabetic Patients needs different supply for the effective management.

- Therapeutic agents (Insulin, Oral Hypoglycemic agents)

- Diabetes monitoring (testing equipments for blood sugar & urine testing)

- Dietary supplements
Educative material (on diabetes & related complication and nutritional tips)

A diabetes supply centre is essential at the clinic to help people with diabetes, to obtain all supply under one roof & reduce cost by offering attractive discount on medicine as well as supplies.

THE NEXT APPOINTMENT

The reception desk then gives the next appointment for the patient to be seen by the doctor when the reports are ready and then medication has to be planned.

SUMMARY

Organized care, with its enforcement of information on each visit, improves clinical outcomes in the management of Diabetes Mellitus. Among the many components of an ‘organized diabetes clinic’, the patient database is the most important; it provides patient information and can be designed to be interactive for reminders about periodic investigations and data analysis. Diabetes specific laboratory investigations, patient education material, services of a diabetes educator and a dietician, and proper referral for foot care or a retinal examination are the other important components of an organized diabetes clinic. There should be a constant effort to improve quality of care and much of this is achieved by properly distributing various tasks among staff members of the diabetes clinic. Empowering patients is also helpful. Updated information, delivery of the same information repetitively, a better adherence to clinical guidelines, ongoing teaching programmes which include patient-diabetes team interaction and an overall dedicated and committed staff help in achieving this goal.

Guidelines should be followed properly and methods to measure guideline implementation should be adopted. Organized diabetes care improves both short-term and long-term clinical outcomes. Short-term clinical outcomes like
Length of hospital stay, emergency room visits, and attacks of hypoglycemia are lessened. Long-term clinical outcomes show improvement in the form of significantly less end-stage renal disease, fewer cardiac events and lower overall mortality rates.

'Organized diabetes care' over years can make a significant difference on various health practices. Specific intermediate-targeted outcomes include increased rates of retinal screening, increased performance and documentation of foot inspection and risk-related education, increased testing for microalbuminuria, increased testing for HbA1C, reduced HbA1C levels; and improved patient satisfaction.
PREVENTION OF DIABETES IN INDIANS

STAGES IN THE NATURAL HISTORY OF DIABETES

Fortunately, in the natural history of diabetes, there is a long pre-diabetic stage, during which adequate prevention strategies can help delay the onset of diabetes. Surprisingly, in spite of the enormous progress in understanding the natural history of diabetes, efforts taken for prevention of diabetes are all still grossly inadequate.

The various periods opportunity for the prevention and the consequences of diabetes with number of modifiable risk factors are illustrated in Figure 26.1. Diabetes usually progresses from impaired glucose tolerance (IGT) or pre-diabetes stage to an early asymptotic stage to onset of clinical diabetes and then to the stage of complications. The three points in the natural history of the disease where prevention is possible are depicted in Figure 56.

FIGURE 56: Stages in the natural history of diabetes

(Adopted from Type 2 Diabetes in South Asians: Epidemiology, Risk Factors and Prevention under the Aegis of SASAT)
PRIMARY PREVENTION

Prevention of the emergence or development of risk factors in population groups in which they not yet appeared by taking action prior to the onset of disease, which removes the possibilities that a disease will ever occur. This may be achieved by modifying environment and behavioural risk factors through mass education\textsuperscript{1169} susceptible individuals or populations.\textsuperscript{1170}

SECONDARY PREVENTION

Refers to action which\textsuperscript{1171} halts the progress of a disease at its incipient stage and prevents complication”. The specific interventions are early diagnosis and adequate treatment may reverse the disease or reduce its progression and the development of complications.

TERTIARY PREVENTION

Defines as “all measures available to reduce or limit impairments, diabetic complications and disabilities, there by minimising and controlling suffering caused by diabetes and to rehabilitate the patients.

PRIMARY PREVENTION OF DIABETES

There are two main primary prevention strategies include high-risk and population approaches.

It is indeed difficult to apply any intensive preventive strategy to the whole population for simple logistic and cost considerations. Hence, more practicable strategies have to be thought of such as general education towards healthy lifestyle, healthy town planning; invoking help from food industries for marketing of healthy foods. Such global methods may not necessarily be effective or may only have a marginal effect. These have not
been studied systematically anywhere. Most frequently advocated approach at present is intensive interventional strategy applied to highly susceptible groups. These groups can be identified by the presence of risk factors for the development of diabetes. Prospective intervention studies have also documented the benefit of lifestyle modifications in preventing diabetes in high-risk individuals. This means that there is a need for identifying high-risk individuals if we are to prevent diabetes.

SCREENING FOR HIGH-RISK GROUPS

Screening would be ideal to detect the early stage/pre-diabetes and prevent diabetes. The American Academy of Family Physicians Policy and US Preventive Services Task Force (USPSTF) concluded that there are insufficient evidence for recommending for or against routine screening of asymptomatic individuals for diabetes. However, according to the ADA, individuals aged 45 and above must be regularly screened while those who are at high-risk, e.g. those with IFG and IGT or belonging to a high-risk ethnic group (e.g. Asian Indians) must be screened with a shorter screening interval.

This Approach has the advantage of directing appropriate interventions as well as providing potential motivation for individuals to make the necessary changes to reduce the impact of disease. A number of prospective studies conducted in impaired glucose tolerance subjects have shown a reduced progression to diabetes by controlling weight, diet and increasing exercise. Disadvantage of the high-risk approach is that individual or group interventions are costly, need to be sustained for long periods and that it does not alter the underlying cause of the disease in the whole population as prevention and control measures are limited to those at risk.
Risk scores based on simple anthropometric, demographic and behavioural details have been computed to detect high-risk individuals, as selective screening instead of mass screening for diabetes, would be cost-effective and less laborious.

Recently, risk scores have been developed specifically for the Indian population based on the risk assessments made in epidemiological studies.

DIABETES RISK SCORES

The risk score developed by Ramachandran et al is shown in Table 13. An ROC procedure showed a cutoff score of ≥21 having sensitivity and specificity close to 60%.

INDIAN DIABETES RISK SCORES (IDRS)

Mohan and his team has recently developed an Indian Diabetes Risk Score (IDRS), based on the data from Phase 3 of CURS which recruited a representative population of Chennai.

IDRS requires answers to four simple questions and waist circumference.

The four questions are:

What is your age?
Do you have a family history of diabetes? If yes, does your father or mother or both have diabetes?
Do you exercise regularly?
How physically demanding is your work (occupation)?

The waist circumference can be replaced with a pant (waist) size measurement in centimeters for men. In those who do not know their waist size, it can be measured using a simple inch tape around the navel area. The score is derived to give a total score of 100.
They categorized individuals as having high-risk (score ≥ 60) moderate risk (score of 30-50) and low risk (score < 30) for diabetes. IDRS which has a sensitivity and specificity of over 60% for a cut-off > 60, it possible to do a selective screening for Indian population.

The usefulness of IDRS is that it is simple, low cost, less labour intensive and easily applicable for mass screening programmes.

INTERVENTION TO PREVENT DIABETES

Though diabetes is an inherited disorder, behavioural changes or pharmacological interventions can help in the prevention of diabetes. Lifestyle modifications, inclusive of dietary modification, regular physical activity and weight reduction are indicated for prevention of diabetes. Landmark studies like the Da Qing study,\textsuperscript{1172} Finnish Diabetes Prevention study,\textsuperscript{1173} the Diabetes Prevention Programme (DPP)\textsuperscript{1174} and STOP-NIDDM study\textsuperscript{1184} have clearly documented that diabetes can be prevented by lifestyle changes or pharmacological intervention.

As India is facing an epidemic of diabetes, the time has come to start actively trying to prevent diabetes in the community. This would need several steps:

AWARENESS OF DIABETES

Across India, the awareness of diabetes is low. In a survey\textsuperscript{1185}, only 60% of respondents being aware of the disease before their diagnosis.

EDUCATION

Diabetes education has become an essential part of any modern diabetes control program. The philosophy of self-care and health education for an improved long-term quality of life is probably best illustrated in diabetes.\textsuperscript{1186}
Acquiring knowledge and skills in instituting diet, exercise, medication and self-monitoring is critical to a successful management program for diabetes patients. This would not only require a reasonable professional wisdom but also involves adequate patient education to empower the diabetic patient to manage his own condition.

In a study evaluating the education needs of diabetic patients with low socio-economic and literacy levels, 100 patients with diagnosed diabetes were interviewed for assessment of their knowledge of diabetes. Overall diabetes awareness (ODA) for the group was poor (mean score 34%) while their knowledge of self-monitoring was very poor (23.7%). ODA correlated with socio-economic status and education level but not with age and duration of diabetes. However, knowledge of complications and self-monitoring improved with increasing duration of diabetes. Patients were not aware of food exchange (89%), glucometer (88%) and benefits of exercise (81%). females had uniformly lower scores than males for all aspects of diabetes studied. The study highlighted the inadequacy of existing diabetes education methods and pointed to the difficulties in educating low socio-economic, low-literacy, and multi-lingual patient groups particularly women. This again emphasized the critical role of para medical personnel in diabetes care. Another study reported that more than half the diabetic patients attending a hospital did not know whether good long term control of diabetes prevented complications. Knowledge regarding individual complications was equally poor. A study of the knowledge, beliefs and practices of diabetic patients showed a large gap between knowledge and action and reinforced the need for increased efforts towards patient education regarding diabetes. Viswanathan et al found that awareness of general foot care principles and basic facts about foot complications were poor. In a study carried out to assess oral health education among diabetic patients it has been reported that a majority of them did not know the factors in diabetes that can contribute to oral ill health including the need for good glycemic control.
A large cross-sectional community-based survey called the Chennai Urban Rural Epidemiology Study (CURES)\textsuperscript{1193}, carried by us in Chennai, south India, showed that the awareness of diabetes is very low. Nearly 25% of Chennai residents were not even aware of a condition called diabetes and knowledge about complications of diabetes was even worse. Moreover, even among self-reported diabetics, knowledge and diabetes and its complications was poor and less than 50% only knew that the diabetes is preventable.

Diabetes education programmes have been shown to reduce the frequency of acute metabolic complications and have been particularly effective in decreasing hospital admissions due to diabetic ketoacidosis\textsuperscript{1194} and severe hypoglycemia\textsuperscript{1195} all of which are important components of diabetes care. However, the benefits of education on glycemic control among diabetic subjects are not as dear.\textsuperscript{1196-1198}

In the context of chronic complications, diabetes education strategies have been most effective in reducing foot ulceration and preventing leg amputations\textsuperscript{1199,1200} particularly in high-risk individuals. High risk patients are those with neuropathy, peripheral vascular diseases, and those with other foot abnormalities viz callosities or deformities. The risks of amputations have been shown to decrease by 45-85% and this protection can persist for up to 10 years.

All the above-mentioned studies underscore the need for an urgent, focused and targeted education program for diabetic patients as well as the general public.

LIFESTYLE CHANGES

Studies in the west have consistently demonstrated the relationship of physical activity with not only diabetes but also with coronary artery disease. The results from the CUPS, suggest that only 6.2% of the urban population exercised regularly which is very worrying in the context of the double epidemic of diabetes and coronary artery disease. Urbanisation has resulted
in sedentary lifestyle due to occupational changes from traditional manual labourer jobs to white-collar jobs along with use of automobiles for transport. In addition affluence has led to more and more Westernised culture resulting in unhealthy food styles, which further adds to the increase in lifestyle related diseases. The influence of urbanisation and affluence on physical activity and dietary pattern on the prevalence of diabetes clearly shown in the CUPS study. In the CUPS study, in the middle-income group, proportion of subjects with heavy grade physical activity was five-fold (5.2%) lesser than the low-income group (27.1%). Over 60% of the middle income group had a sedentary lifestyle demonstrating the effect of affluence on physical activity. In keeping with the reduced physical activity, the prevalence of all lifestyle related diseases were higher in the middle-income group compared to the low-income group. Thus it is clear that encouraging physical activity and continuation of fibre rich, less energy dense foods is of permanent importance.

Given the heritage in our country, yoga and meditation, may be good preventive measures for diabetes. Several studies report on the beneficial effect of the practice of yoga on diabetes. However, long-term property planned prospective studies are required to authenticate the benefits of yoga.

Figure 57 suggests the prevention strategies for diabetes at an individual level. As Indians develop diabetes 2-3 decades earlier than Europeans, it is suggested to screen for diabetes in individuals aged ≥35 years. Obese subjects and subjects who are diagnosed to have pre-diabetes should be advised for weight reduction strategies by regular exercise and dietary changes. Screening for diabetes at regular intervals is suggested in these subjects.

Misconception regarding risk factors for diabetes along with lack of awareness about diabetes could lead to escalation of diabetes in India unless
mass awareness programmes are conducted. The best advice would be to increase physical activity and change dietary patterns to reduce weight by at least 5%. As 5% reduction in weight can prevent obesity, diabetes and coronary artery disease. Communities must be motivated to initiate preventive programmes by mass awareness camps. Educating about the deleterious effects of diabetes and emphasising strategies for prevention of diabetes at the community level is the urgent need of the hour.

**Figure 57** Screening/prevention of diabetes and related complications.

(Adopted from *Type 2 Diabetes in South Asians: Epidemiology, Risk Factors and Prevention under the Aegis of SASAT*)
POPULATION STRATEGY

The aim of this approach is to lower the mean level of risk for the entire population and influence favourably as a whole irrespective of individual risk levels by increasing physical activity, improving diet and reducing obesity. This not only increases the chance of preventing high-risk individuals from developing diabetes, but also reduces the chance of individuals with low-risk becoming high-risk.1205

POPULATION STRATEGIES-EMPIDEMIODOLOGICAL EVIDENCE

INTERVENTION PROGRAMMES

Compelling evidence now exists that diabetes can be prevented or delayed in subjects with impaired glucose tolerance.1206-1209 This evidence has held consistently across different populations, in different countries, among men and women, and in all age and racial and ethnic groups. Impaired Glucose tolerance is the first stage in the course of diabetes and also a major problem from the quantitative point of view.1210 According to International Diabetes Federation, at least 300 million people worldwide have impaired glucose tolerance1211 and the prevalence varies widely from 3 to 10% in European population.1212 It is much higher in some newly industrialized nations and groups with high prevalence of diabetes, such as Asian Indians with the recent Chennai Urban Rural Epidemiology Study (CURES) noting a prevalence of IGT of 10.4%.1213 Subjects With impaired glucose tolerance (IGT) are at increased risk of developing diabetes and from an important high-risk group for actions aimed at preventing the disease.1211,1214-1216

Various studies like Diabetes Prevention Programme (DPP) demonstrated that both medication and lifestyle interventions can delay or prevent progression from impaired glucose tolerance (IGT) to diabetes.1217 The study also demonstrates the intensive lifestyle intervention reduced the incidence
of diabetes by 58% compared to 31% reduction by metformin intervention.\textsuperscript{1217} The Da Qing study\textsuperscript{1218} compared diet, exercise and diet plus exercise with a no-treatment control group and found that all three lifestyle approaches reduced the risk of developing diabetes by 31.46%. The Finnish Diabetes Prevention Study\textsuperscript{1219} of 522 overweight subjects with IGT showed that a lifestyle intervention designed to produce weight loss by improved dietary and physical activity reduced the risk of diabetes by 58%. The prospective study on the association between regular exercise and the subsequent development of diabetes in the US male physicians, demonstrates that exercise reduces the development of diabetes even after adjusting for BMI.\textsuperscript{1220} In the Malmo study,\textsuperscript{1221} BMI decreased by 2.4% in the intervention group and only 10.6% of the intervention group developed diabetes over 5 years compared with 28.6% of the control group.\textsuperscript{1221-1223}

The American\textsuperscript{1224} and Finnish\textsuperscript{1225} prevention studies illustrate the benefits in a developed country. In a developing country, China, the Da Qing study also showed substantial preventive benefit of exercise, diet, or a combination of the two. Various studies comparing lifestyle interventions and pharmacological therapies to prevent diabetes are currently underway.\textsuperscript{1226} However, implementing diabetes prevention in the general population is a challenging.

PROMOTION OF PHYSICAL ACTIVITY—EPIDEMIOLOGICAL EVIDENCE

The intervention studies discussed above were carried out in a number of ethnic groups/populations and these studies have targeted either high-risk groups or were done in a research or clinical setting. However, implementation of such prevention programme at the community level presents a great challenge, but is the need of hour. Community and population-based approaches have been tried in very limited number of studies and this is an area that needs further work, especially given the strong the environmental components working to reduce physical activity and
increase energy intake. Community-based interventions may be the most economically feasible, if they can be shown to be effective.

NEW APPROACHES TO THE PROBLEM

Following are the few community-based intervention programs being carried out by All India Institute of Diabetes and Research & Yash Diabetes Specialities Centre (Swasthya), Ahmedabad

1). LIFE STYLE MODIFICATION CAMPS

Highlights of the meet

Target population- people with diabetes or with high risk for developing diabetes

- Education by experts
- Screening for diabetes and their risk factors & complications
- Diet advice
- Yoga - flexibilities, asanas, pranayam & meditation
- Duration: 10-15 days learning phase. Thereafter maintenance phase for one year.
- Around 1000 people participate in each camp

2). EDUCATION

Education continues to be a key component in the prevention and treatment of diabetes. Low cost educational material including pamphlets, posters, booklet, flash cards, and CDs on diabetes have been developed in both English and the regional language Gujarati) are distributed to the public, free of cost. A short documentary film has been produced on diabetes highlighting its causes, sings, and symptoms, associated complications, management, prevention strategies and its social and economic impacts is telecast on various popular television and radio channels. These will help the person affected to make decisions that have a direct impact on their health.
Diabetes education empowers people with diabetes by encouraging them to take responsibility for their health and enabling them to manage their condition themselves.
Figure 58 Life style modification camp

Figure 59 Conduct of mass screening programme for diabetes
3). EARLY DIABETES DETECTION BY SCREENING

Diabetes can develop slowly over a period of years. And a person may be asymptomatic, but still develop diabetes-associated eye, kidney, or heart problems. Because of these serious long-term consequences of diabetes, it is important to detect the early by screening in order to prevent or delay damage to heart, kidney, nerves, blood vessels or eyes. With this early detection we may be able to take therapeutic measures, which will allow us to reverse or at least to slow down the rate of progression of the complications. To achieve this goal, a large scale-screening program has been started.

4). EXHIBITION FOR GENERAL PUBLIC

Conducting exhibition emphasizes the need for carrying the right messages regarding diabetes right down to the masses. It includes education, awareness, screening and evaluation, for diabetes as well as complications. Two major diabetes exhibitions have been organized in Ahmedabad during the last 5 years, which have been attended by several thousand of people.

5). AWARENESS CAMPAIGNS

Conducting community-wide campaigns helps to improve the health of communities by developing or strengthening social networks and by improving community members sense of cohesion and collective ability to bring about change.

These campaigns are be large-scale, intense, highly visible, community-based with messages directed to large audiences through different types of media, including television, radio, newspapers, movie theatres, billboard, and mailings. Mass media appeared to be successful in promoting awareness and interest in exercising.
Figure 60 Diet exhibition

Figure 61 Meet for Type 1 diabetic children
6). DIABETES PREVENTION PROGRAM

A massive diabetes prevention program is under way at Ahmedabad. The main aim of the program is to implement a massive public awareness program on diabetes reaching out to thousands of people and conduct large scale opportunistic screening of people. It will help people in preventing diabetes and leading a longer, healthier life. Through this program, large-scale public awareness campaigns were being conducted with active participation of the community.

7). DIET EXHIBITION

The main aim is to increase awareness and to clear prevailing misconception about diet. In which nearly 1500 freshly prepared food items are put for the display. It included display of calorie content of different food stuffs, various food exchanges, fiber rich foods, low calorie sweets etc.

8). MEET FOR TYPE 1 DIABETIC CHILDREN

The main aim of the meet is to change the social environment in such a way that instead of hiding the disease, children with Type 1 diabetes should feel pride for the disease.

HIGHLIGHTS OF THE MEET:

Education through audio-visual media by the experts in a fun-filled and entertaining atmosphere. (Diabetologist/Pathologist/Diabetician/Educator/Podiatrist/Paediatrician/Psychiatrist/Psychologist) about the disease including self injection techniques & self monitoring of blood sugar.
Importance of Yoga.
Nutritious and tasty diabetic food
Recipe contest
Certificate-achievement/marriage/self injection
Felicitation of the child for best control of Diabetes
Eye check up.
Free distribution of books and other material.
Free insulin to poor
All these accompanied by competitions, games, drama (with a message), gifts and prize distribution to all the children.

The Meet is being organized every year. All patients of Type 1 diabetes in Gujarat State (situated in the western part of India) are taking advantage of this unique opportunity.
The increased prevalence of diabetes in India is attributed to the aging population structure, urbanization, the obesity epidemic, and physical inactivity. While all these factors contribute to the epidemic of diabetes, early life exposures are emerging as potential risk factors. The "fetal origin of disease" hypothesis proposes that gestational programming may critically influence adult health and disease. Gestational programming is a process whereby stimuli or stresses that occur at critical or sensitive periods of development, permanently change structure, physiology, and metabolism, which predispose individuals to disease in adult life.

Traditionally and convincingly, lifestyle modification and drug interventions have proved to delay or postpone the development of overt diabetes in persons diagnosed to have impaired glucose tolerance. This is a post primary prevention strategy. The primary prevention of Type 2 DM at best would mean to keep genetically or otherwise susceptible individuals normoglycemic and not only preventing Type 2 DM from developing. The primary prevention is more important than post primary prevention, as this effort is likely to reverse or halt the epidemic of disease. Women with Gestational Diabetes Mellitus (GDM) are an ideal group for the primary prevention of diabetes as they are at increased risk of developing diabetes predominantly Type 2 DM as are their children. Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. Women with GDM have an increased lifetime risk of developing diabetes, at over 3 times compared to controls at 16 years after index pregnancy. By 17 years of age one-third of children born to GDM mothers have had evidence of IGT or Type 2 DM. In an ongoing community based project sponsored by World Diabetes
Foundation. 33% of the women who developed GDM had maternal history of diabetes.

The familial predisposition to type2 diabetes mellitus is mediated by both genetic and intrauterine environmental factors. The contribution of the genetic factor may be due to the major role played by maternal mitochondrial DNA in the transmission of disease. The ovum is well supplied with mitochondria but the sperm contains a few and even those few do not persist in the offspring. At fertilization, it is the nucleus of the spermatozoa that enters the ovum and thus all the cytoplasm, mitochondria and mitochondrial DNA are exclusively maternally inherited. Maternal inheritance is attributed to mutation in the gene(s) present on mitochondrial DNA and is transmitted invariably by an affected mother to her progeny. However studies have also shown, low genetic risk for diabetes, exposure to hyperglycemia in utero significantly increases the risk of diabetes in adult life. In an elegant study Sobngwi et al concluded that exposure to diabetic environment in utero was associated with increased occurrence of impaired glucose tolerance and a defective insulin secretory response in adult off springs, independent of genetic predisposition to type 2 diabetes. Yet another study revealed that children exposed in utero to maternal diabetes are at a higher risk of obesity and diabetes than their unexposed siblings, suggesting that the increased risk to the exposed offspring is not exclusively genetic. These observations clearly indicate the need to focus on the intra uterine environment.

The maternal fuels – glucose, amino acids and lipids (mixed nutrients) are in excess in women with glucose intolerance due to decreased insulin secretion or action. They cross the placenta and stress the fetal beta cells. The fetus responds to the mixed nutrients by secreting large quantities of insulin. This results in increasing adiposity and accrual of visceral fat that eventually causes decrease in fetal pancreatic reserve and the infant is at risk for developing subsequent diabetes. On the other hand, intrauterine malnutrition causes intrauterine growth retardation and this under nutrition is associated
with decreased pancreatic reserve. Thus both small-for-dates infants and large-for-dates infants are at risk for subsequent diabetes.1240

In India, both undernutrition and overnutrition exist during pregnancy. There are two reported studies in India which are related to the size at birth to future risk at type 2 diabetes. In Mysore, low—birth weight did not increase the risk of diabetes but babies who were short and fat (higher body mass index, BMI) at birth were at increased risk1241 Fall et al speculate that the rise in Type 2 diabetes in Indian urban populations may have been triggered by mild obesity in mothers, leading to glucose intolerance during pregnancy, macromonic changes in the fetus and insulin deficiency in adult life.1241 Yet another study's by Yajnik et al attributes high prevalence of Type 2 DM and IGT in Indian people may be linked to poor fetal growth.1242 Same author also suggests that Type 2 DM in India may be programmed in fetal life, hence diabetes prevention will have to start in early life (in – utero ) and continue in later life.1243 The importance is that the intrauterine milieu, whether one of nutritional deprivation or one of nutritional plenty, results in changes in pancreatic development and peripheral response to insulin that may lead to adult - onset GDM and Type 2 DM.1244 The aim should be to help the pregnant women to have infants born with weight appropriate for gestational age (AGA) by adequate and appropriate nutrition and maintaining fasting plasma glucose < 90mg and peak plasma glucose < 120mg.1245

In Pima Indians, the population with the highest known rate of diabetes, a study found that the increased exposure to diabetes in utero and childhood obesity accounted for most of the increased prevalence of diabetes over the past 30 years.1246 if the diabetic intrauterine environment is substantially contributing to the obesity and diabetes epidemics, populations that have a high prevalence of diabetes will continue to be disproportionately affected by these epidemics, resulting in a perpetual widening of health disparities between racial and ethnic groups.1227
transgenerational epidemiology and etiology of diabetes and develop simple, economical, and effective prevention strategies.\textsuperscript{1227}

These observations call for the screening for the glucose intolerance during pregnancy and ensuring adequate nutrition for the developing fetus. Though ADA recommends selective screening, the universal screening is essential in all Indian pregnant women as they have a 11-fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women.\textsuperscript{1247} The ADA diagnostic criteria based on a 3-h OGTT, was originally validated against the future risk of maternal diabetes and not on fetal outcome. This ADA criteria is accepted in USA and are little used elsewhere.\textsuperscript{1248} The WHO criteria of 2-h PPG $\geq 140$ mg/dl identifying a large number of cases may have a greater potential for prevention and is being followed in many parts of the world.\textsuperscript{1249}

The screening for glucose intolerance is usually performed around 24 - 28 weeks of gestation. But a statistically significant number of GDM mothers deliver big babies despite good glycemic control in the third trimester.\textsuperscript{1250} This is due to the undetected glucose intolerance in them in the early weeks of gestation that influences the fetal growth.\textsuperscript{1251} Fetal pancreatic islets of Langerhans differentiate during the 10\textsuperscript{th} and 11\textsuperscript{th} week of development and begin to release insulin in response to nutrients as early as 11\textsuperscript{th} - 15\textsuperscript{th} weeks of gestation.\textsuperscript{1252,1253} The priming of the beta cell mass in early gestation may account for the persistent fetal hyperinsulinemia throughout pregnancy and the risk of accelerated growth, even when the mother enjoys good metabolic control in later pregnancy.\textsuperscript{1254} Alterations of intrauterine environment in particular, the development of hyperinsulinemia is strongly associated with the development of obesity and IGT during childhood and puberty.\textsuperscript{1255} Early maternal metabolic imprint may affect the fetal growth. This observation implies that screening is to be performed in the first trimester itself as the fetal beta cell recognizes and responds to maternal glycemic level as early as 16\textsuperscript{th} week of gestation.\textsuperscript{1256} The criteria recommended WHO is simple and cost effective and is practiced in many centres\textsuperscript{1257,1258} and the one-step procedure
of WHO (2-hr PPG ≥ 140 mg/dl) serves dual purpose of both screening and diagnosis.\(^{1259}\)

Over the next 2 to 3 decades there will be 80 million reproductive age women with diabetes in the world. Of these 20 million will live in India alone creating a potential for extremely high rates of maternal and infant morbidity.\(^{1260}\) Women who had GDM, develop overt diabetes at a young age, substantially increasing their lifetime risk of developing complications from diabetes. A recent national survey reported the prevalence of IGT in the age group of 20-29 and 30-39 years as 12.2% and 15.3% respectively.\(^{1261}\) No gender difference was seen in the prevalence of IGT\(^{1261}\). Yet another observation was that the prevalence of GDM corresponds to the prevalence of IGT within a given population.\(^{1262}\)

Outcome of the screening for glucose intolerance during pregnancy has given an insight for the phenomenal increase in the incidence of diabetes. The development of glucose intolerance during pregnancy has a long term consequence for the progeny. The epidemiological studies in Pima Indians has documented that more than 50% of children born to mother with GDM developed glucose intolerance by 35 years of age.\(^{1263}\) Hence a policy to identify GDM and its consequences on the infant, 75-gm OGTT has been recommended to all the women in the population during the 3\(^{rd}\) trimester of pregnancy\(^{1263}\). In a study Dr. Sheshiah found 16.55% having GDM in our country. The offsprings of these women are at risk of developing glucose intolerance in the future just like Pima Indians. A high prevalence of glucose intolerance during pregnancy might have been occurring in continuum, which has been documented now by our study.\(^{1264}\)

In conclusion,\(^{1265}\) increasing maternal hyperglycemia is associated with increasing pregnancy morbidity and increased likelihood of subsequent diabetes in the mother. In addition, maternal hyperglycemia has a direct effect on the development of fetal pancreas and is associated with increased susceptibility to future diabetes in the infant an effect which is independent
of genetic factors. Among ethnic groups in South Asian countries, Indian women have the highest frequency of GDM necessitating universal screening for glucose intolerance during pregnancy in India. Probably the undiagnosed glucose intolerance that has been occurring in the past has resulted in the increased prevalence of diabetes in India. Moreover, women who have GDM, because of their high diabetes risk and young age, are ideally suited to be targeted for lifestyle or pharmacologic interventions to delay or prevent the onset of overt diabetes (Fig. 62).

Figure 62  Lifestyle/Pharmacologic intervention to delay/prevent the onset of overt diabetes.

GDM

Intervention with MNT/Insulin

New Born – Appropriate for Gestational Age

Prevention of Obesity & IGT in Offspring

Hence, an important public health priority is prevention of diabetes, starting with maternal health pre and post conception. Preventive measures against Type 2 DM should start during intrauterine period and continue throughout life from early childhood.

The timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition
may prevent in all probability the vicious cycle of transmitting glucose intolerance from one generation to another. The Govt. of Tamilnadu accepted this view and promulgated an order by which the screening for glucose intolerance has become mandatory in all medical college hospitals, district head quarters hospitals, taluka head quarters hospitals and block level primary health centres and non governmental institutions. Hope the Govt. of India also adopts this policy.

"No single period in human development provides a greater potential (than pregnancy) for long-range 'pay-off', via a relatively short-range Period of enlightened metabolic manipulation" – Norbert Frienkel.
Preventive approaches to diabetes complications can be categorized into three levels, first the early approach where early detection and appropriate treatment are the cornerstones for delaying the onset of the diabetic complications.

Once some complication sets in, preventing progression of the same would form the second approach or the intermediate approach by introducing specific drugs and lifestyle intervention for combating complications.

Third would be the late approach where complications have reached a very critical stage and interventional procedures like surgery are required to ameliorate progression to end stages of the complications (Figure 63).

**Figure 63** Strategies to protect target organ damage diabetic subjects

(Adopted from RSSDI Textbook of Diabetes Mellitus 2nd edition)
EARLY DETECTION OF DIABETES COMPLICATIONS
(SCREENING)

Early detection of diabetes complications by routine screening is an important aspect in prevention of diabetes complications. Screening is beneficial in diseases, which impose a significant burden on the society, where the natural history is known and intervention in early stages can prevent further progression of the disease. Diabetes satisfies all these criteria. Several studies have clearly demonstrated that intervention at an early stage can help in preventing morbidity and mortality. The American Diabetes Association (ADA) in its clinical practice recommendations has indicated the frequency of screening for various complications of diabetes.

DIABETIC RETINOPATHY: Even if visual symptoms are absent, initial retinal screening is recommended at the time of diagnosis for type 2 diabetic subjects and for type 1 diabetic subjects, within 3-5 years after diagnosis of diabetes when patients is age 10 years or older. Thereafter, an annual screening is recommended for all diabetic subjects regardless of the type of diabetes (Table 86). Since retinal screening involves pupil dilatation, a detailed eye examination by an ophthalmologist is advisable. In patients with any degree of retinopathy, more frequent examinations are indicated. In diabetes complicating pregnancy a comprehensive eye examination at the first trimester and a close follow up throughout pregnancy is recommended by the ADA. Retinal colour photography helps to document early retinal lesions while Fundus Fluorescein Angiography (FFA) helps to document diabetic macular edema and subtle new vessels in the retina.

DIABETIC NEPHROPATHY: In the natural history of diabetic nephropathy, excretion of low but abnormal levels of albumin in the urine is considered as the initial stage and is referred as microalbuminuria, which is also, regarded as incipient nephropathy. Detection at this stage is helpful, as sufficient evidence has accumulated to show that intervention at this stage prevents progression of the disease and indeed sometimes even reverses to
normoalbuminuria stage. In addition to hyperglycemia, hypertension is also a contributing factor for diabetic nephropathy, which could also be controlled using adequate measures. Thus detection of microalbuminuria in diabetic subjects is crucial to prevention of overt diabetic nephropathy. According to the ADA clinical practice recommendations, annual screening of microalbuminuria is recommended in type 1 and type 2 diabetic subjects. The easiest method as suggested by ADA for diagnosis of microalbuminuria is measurement of the albumin to creatinine ratio [ACR] in a random spot collection. Microalbuminuria is diagnosed if ACR is 30µg/ mg of creatinine while ACR 300µg/mg of creatinine is categorized as clinical albuminuria. Care should be taken while diagnosing microalbuminuria because conditions like exercise, urinary tract infection, marked hypertension; heart failure and acute febrile illness can cause a transient increase in excretion of albumin in the urine. As day-to-day variability has been observed in albumin excretion, at least two to three collections within a time span of 3 to 6 months is required for diagnosis of microalbuminuria.

**DIABETIC NEUROPATHY:** Though neuropathic pain is one of the important causes of morbidity in diabetic subjects, unlike microalbuminuria there is no direct measure for screening of peripheral neuropathy. Several tests may be necessary to designate a subject as having diabetic neuropathy. To determine the small fibre function, protective sensation in the feet, temperature discrimination threshold and skin integrity tests could be used. For large myelinated fibres, vibration perception threshold [VPT] using biothesiometry has been shown to be a good predictor of foot ulceration. Though not used for routine purposes, motor and sensory conduction velocities gives an assessment of function of large myelinated fibres. Wasting, weakness and ankle reflexes would indicate alterations in motor nerve function. For detecting sensory nerve dysfunction, vibration using tuning fork, sensitiveness to monofilament and pinprick should be useful. Annual screening for peripheral neuropathy is recommended using measures suggested in Table 86.
Table 86 Screening Schedule for Diabetic Complication

<table>
<thead>
<tr>
<th>Complication</th>
<th>Test to be done</th>
<th>First Screening – When?</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macrovascular Complication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>Examine pedal pulses, Auscultate for bruits, Peripheral Doppler-ankle brachial index</td>
<td>At diagnosis for type 2 diabetes; As clinically appropriate for type 1 diabetes</td>
<td>Annually</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>12 lead Electrocardiography</td>
<td>At diagnosis for type 2 diabetes; As clinically appropriate for type 1 diabetes</td>
<td>Annually</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Microvascular Complication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>Retinal Screening – Ophthalmoscopy / fundal photography Visual Acuity</td>
<td>At diagnosis for type 2 diabetes; 3-5 years after diagnosis for type 1 diabetes</td>
<td>Annually</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic Nephropathy</td>
<td>Microalbuminuria – spot urine</td>
<td>At diagnosis for type 2 diabetes; 3-5 years after diagnosis for type 1 diabetes</td>
<td>Annually</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>Foot Examination Assess protective sensation in feet (Semmens – Weinstein 10G monofilament) Plantar Pressure measurement</td>
<td>At diagnosis for type 2 diabetes; As clinically appropriate for type 1 diabetes</td>
<td>Annually</td>
</tr>
</tbody>
</table>

MACROVASCULAR DISEASE: A common cause of foot amputations in diabetic subjects is peripheral vascular disease [PVD]. As lower limb amputations are preventable, detection at an earlier stage is advisable. Most of the diabetic subjects are symptom free for PVD. Subjects with asymptomatic PVD not only have a higher risk for frank PVD but also an increased risk for cardiovascular deaths.1283 One of the easiest measures for
detecting PVD is ankle brachial index \(<0.9\) measured by peripheral Doppler. This has been shown to have a sensitivity of 70 to 97% and specificity of 89 to 97%. In addition, studies have shown ankle brachial pressure index to be a good predictor of subsequent cardiovascular events. Sophisticated measures for assessing PVD include Duplex Doppler studies and angiography.

Coronary artery disease [CAD] can often be asymptomatic and early screening is therefore advantageous, in preventing major events. Since diabetes is considered as a risk equivalent for CAD routine screening for CAD in these patients is justified. The recommended initial test for routine screening for CAD is resting electrocardiography (ECG). This provides evidence of previous silent myocardial infarctions and silent or inducible myocardial ischemia. Cardiac stress test (Treadmill) is useful in detecting latent CAD but the test has a substantial false positive and false negative rates. Thallium-201 scintigraphy, exercise echocardiography, and ambulatory ECG are less commonly used for screening purposes. Another test, which is gaining importance in the field of cardiology, is measurement of carotid intimal medial thickness [IMT]. Several studies have indicated IMT to be a strong predictor for cardiovascular events. IMT has been clearly shown to be higher among diabetic subjects compared to non-diabetic subjects. IMT has also shown to be a good predictor for cerebrovascular disease. However, this measurement requires a high-resolution ultrasound. Recently functional changes in the artery, which can be assessed by determining the endothelial dysfunction and arterial stiffness, have been shown to be indicative of future cardiovascular events. These measurements also require sophisticated instruments like high resolution B mode ultrasonography system or SphygmoCor apparatus.

**PREVENTION OF DIABETES COMPLICATIONS**

The metabolic consequences of diabetes include hyperglycemia, hypertension and dyslipidemia. Landmark trials and intervention studies have clearly
documented the beneficial effects of glycemic control, blood pressure control and lipid control in delaying the onset of complications:

GLYCEMIC CONTROL

Evidence from various studies suggests a continuous relationship of hyperglycemia with microvascular complications (retinopathy and nephropathy) and neuropathy.\textsuperscript{1296-1298} It has been shown that for every 1% decrease in glycosylated haemoglobin [HBAC1] there is dramatic decrease in prevalence of complications. However, the effect of glycemia on macrovascular disease is not so clear.

GLYCEMIC CONTROL AND PREVENTION OF MICROVASCULAR COMPLICATIONS:

Three landmark studies on glycemic control in diabetes namely the Diabetes Complications and Control Trial (DCCI), the United Kingdom Prospective Diabetes Study (UKPDS) and Kumamoto study\textsuperscript{2} have dearly documented the beneficial effects of glycemic control in preventing microvascular complications (Table 87).

\textbf{Table 87} Glycemic Control and risk reduction of microangiopathy in Intervention Studies

<table>
<thead>
<tr>
<th></th>
<th>DCCT(27) (Type 1 Diabetes)</th>
<th>UKPDS(28) (Type 2 Diabetes)</th>
<th>Kumamoto(54) (Type 2 Diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Studied</td>
<td>n = 1441</td>
<td>n = 5102</td>
<td>n = 110</td>
</tr>
<tr>
<td>Duration of follow up</td>
<td>9 years</td>
<td>10 years</td>
<td>6 years</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>76%</td>
<td>21%</td>
<td>69%</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>56%</td>
<td>33%</td>
<td>70%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>60%</td>
<td>-</td>
<td>57%</td>
</tr>
</tbody>
</table>

A meta analysis by Wang et al\textsuperscript{1299} on 16 randomized trials estimated the impact of glycemic control over progression of microvascular complications. It summarized that "long term intensive blood glucose control significantly reduced the risk of diabetic retinopathy and nephropathy".
GLYCEMIC CONTROL AND MACROVASCULAR COMPLICATION

Earlier studies in the western population like the Whitehall study, Honolulu Study, PASY study and several others have shown that hyperglycemia contributes to cardiovascular disease. Indian studies have shown that the risk for CAD increases with increase in plasma glucose.

In the UKPDS study, by glycemic control alone, the risk reduction of myocardial infarction was reduced by 16% but this just missed statistical significance \( p=0.052 \) leading to the conclusion that by glucose control alone, macrovascular complications cannot be prevented.

Based on the several studies result the consensus today is that though hyperglycemia plays a major role in complications, to prevent macrovascular complications in diabetic patients tight control of factors like hypertension and dyslipidemia are equally important. Table 88 summarizes, the current evidence with respect of control of risk factors and prevention of diabetic complications.

**Table 88 Benefits of risk factor control on diabetes complication**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Retinopathy</th>
<th>Nephropathy</th>
<th>Neuropathy</th>
<th>Macrovascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose Control</td>
<td>Definite Benefit</td>
<td>Definite Benefit</td>
<td>Definite Benefit</td>
<td>Possible Benefit</td>
</tr>
<tr>
<td>Blood Pressure Control</td>
<td>Definite Benefit</td>
<td>Definite Benefit</td>
<td>Unknown value</td>
<td>Significant Benefit</td>
</tr>
<tr>
<td>Lipid Control</td>
<td>Possible benefit</td>
<td>Possible benefit</td>
<td>Possible benefit</td>
<td>Significant</td>
</tr>
<tr>
<td>Smoking</td>
<td>Benefit unclear</td>
<td>Benefits unclear</td>
<td>Unknown value</td>
<td>Significant Benefit</td>
</tr>
</tbody>
</table>

HYPERTENSION CONTROL

Blood pressure is another key factor which can affects both micro as well as macro vasculature. Over 50% of type 2 diabetic subjects may have hypertension. In the present study 57.9% have hypertension. It has been hypothesized that both type 2 diabetes and hypertension have common
pathogenic mechanisms. Controlling blood pressure is an important aspect in treating complications, as untreated hypertension results in declining renal function.\textsuperscript{1308}

Based on PROCAM study\textsuperscript{1309} and other studies, the goals recommended for blood pressure for diabetic subjects both by the ADA as well as the JNC VII are lower than those recommended for non-diabetic subjects.\textsuperscript{1310, 1311}

\textbf{HYPERTENSION CONTROL AND MICROVASCULAR COMPLICATION}

Hypertension hastens the progression of diabetic retinopathy. The UKPDS study addressed the issue of hypertension control in reducing microvascular complications. A 10/5 mmHg reduction in blood pressure yielded a 34\% reduction in risk of diabetic retinopathy.\textsuperscript{1312} The EUCLID study, which assessed the impact of lisinopril on microvascular complications in type 1 diabetic subjects, suggested a decrease in progression of retinopathy, among the drug intervention arm compared to placebo.\textsuperscript{1313}

ACE inhibitors and angiotensin II receptor antagonists have been shown to have greater benefits in diabetic subjects in preventing progression of microalbuminuria to macroalbuminuria stage.\textsuperscript{1278, 1314-1319} Further, ACE inhibition has been shown to be beneficial in diabetic subjects at all stages of nephropathy. In microalbuminuric patients, ACE inhibitors reduce the progression to macroalbuminuria and in macroalbuminuric patients, they reduce the decline in glomerular down the progression of nephropathy independent of their effects on blood pressure.\textsuperscript{1319} In the MICRO-HOPE study, ramipril treatment was associated with a decreased risk of development of overt nephropathy.\textsuperscript{1279} Over all; hypertension control seems to be beneficial in reducing both nephropathy and retinopathy in diabetic subjects.
**HYPERTENSION CONTROL AND MACROVASCULAR COMPLICATION**

UKPDS, HOT trial, CAPP study, MICRO-HOPE study and summary of several other studies have shown a remarkable reduction in cardiovascular mortality are depicted in Table 89.1319,1320-1323

**DYSLIPIDEMIA AND MICROVASCULAR DISEASE**

Some intervention studies have shown lipid control could help prevent diabetic nephropathy1324, but not many studies have assessed its role in diabetic retinopathy. Although studies have shown serum lipids to be associated with microvascular complications the effect of intervention with lipid-lowering therapy has not been widely investigated.

**Table 89** Antihypertensive Agents that Reduce Cardiovascular Risk in Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Hypertensive in the Elderly Program (SHEP)1320</td>
<td>Diuretics: Chlorthalidone &amp; β-Blokcer . Atenolol</td>
</tr>
<tr>
<td>Heart Outcome Prevention Evaluation (HOPE)1319</td>
<td>ACE inhibitor- Ramipril</td>
</tr>
<tr>
<td>United Kingdom Prospective Diabetes Study (UKPDS)1312</td>
<td>ACE inhibitor – Captopril β-Blocker – Atenolol</td>
</tr>
<tr>
<td>Appropriate Blood Pressure Control in Diabetes (ABCD)1321</td>
<td>ACE inhibitor – Enalpril</td>
</tr>
<tr>
<td>Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trials (FACET)1322</td>
<td>Ace Inhibitor – Fosinopril</td>
</tr>
<tr>
<td>Losartan Intervention for End Point Reduction in hypertension study (LIFE)1323</td>
<td>Angiotensin Receptor Blocker – Losartan</td>
</tr>
</tbody>
</table>

**CONTROL OF DYSLIPIDEMIA AND MACROVASCULAR DISEASE**

Cross-sectional, prospective and interventional studies have consistently documented the association of dyslipidemia with cardiovascular disease.1325-1327 Lipid control plays a major role on the course of than that of
microvascular disease; Several intervention studies have very clearly demonstrated the positive benefits of lipid control in cardiovascular disease.\textsuperscript{1328}

More than 50 clinical trials have supported the clinical benefit of cholesterol management in prevention of cardiovascular disease.\textsuperscript{1329-1332}

**MULTI-FACTORIAL APPROACHES TO PREVENTION OF CVD IN DIABETICS**

Although in clinical practice, most diabetologists advise simultaneous control of blood glucose, blood pressure and lipids so as to take care of all the above mentioned risk factors, there were no studies on the effect of tackling all these risk factors on macrovascular complications until the recent Danish Steno 2 study.\textsuperscript{1333}

The Steno 2 study had two arms, the conventional and intensive group with eighty type 2 diabetic individuals in each. The treatment regimen focused on glycemic control, hypertension control, lipid control and antiplatelet therapy, with the intensive group having a lower target than the conventional group. There was a significant decrease in the glycosylated hemoglobin values, systolic and diastolic blood pressure, serum cholesterol and triglyceride levels in the intensive group compared to conventional group. This decrease resulted in lower risk of cardiovascular disease, nephropathy, retinopathy, and autonomic neuropathy. The risk reduction in cardiovascular events observed in this study is higher than other studies, which have used single-factor intervention strategies, targeting glycemic control, hypertension control or lipid control. Results from this study emphasised the need for a multi-factorial approach to prevent cardiovascular disease in diabetic subjects.
LIFE STYLE MEASURES

Lifestyle changes like dietary modification, regular exercise and cessation of smoking has been suggested as measures to reduce cardiovascular disease.\textsuperscript{1334} One of the most important modifiable risk factor for prevalence of both PVD and CAD is cessation of smoking. One of the life style intervention programmes which included smoking cessation showed clinical benefits for subjects with PVD.\textsuperscript{1335} Cessation of smoking has been constantly emphasized particularly in subjects with high risk for vascular disease.\textsuperscript{1335, 1336}

Though dietary modification is always a challenge as the dietary patterns differ in different countries, there are a few strategies, which could be of benefit to everyone. 1) Type of fat: substituting saturated fat and trans- fatty acids with non-hydrogenated mono-and poly-unsaturated fats 2). Improving quality of carbohydrate: Substitute high glycemic index (GI) foods with low GI ingredients and increase intake of cereals rich in fibres. 3) Reduce salt intake.\textsuperscript{1337}

Physical activity has shown to have a strong relation with coronary artery disease.\textsuperscript{1334} A prospective study on 8302 Finnish men and 9139 women aged 25 to 64 years without a history of antihypertensive drug use, coronary heart disease, stroke, and heart failure at baseline showed that subjects with heavy grade of physical activity had low prevalence of hypertension.\textsuperscript{1334} Exercise helps in weight reduction and also reduces cholesterol levels which would prevent vascular disorders.

A multi-drug approach coupled with life style measures would be ideal to prevent the onset of complications. However, once complications set in, specific measures to tackle the consequences of the complications have to be incorporated into the patient’s treatment regimen.
INTERMEDIATE APPROACH FOR PREVENTION OF DIABETES COMPLICATIONS:
These approaches are specific for diabetes related complications as suggested in Table 90.

**DIABETIC RETINOPATHY:** The Diabetic Retinopathy Study [DRS] assessed the effect of pan-retinal photocoagulation on the risk of vision loss from PDR. Photocoagulation significantly reduced visual loss and this effect persisted throughout the entire follow up. The ETDRS study investigated the timing for initiating photocoagulation and suggested that scatter photocoagulation be deferred in eyes with mild to moderate non-proliferative diabetic retinopathy. By timely screening for retinopathy and aggressive use of photocoagulation both the sight threatening forms of retinopathy namely proliferative diabetic retinopathy and microaneurysms can be effectively tackled.

Table 90 Strategies for prevention of diabetes complication

<table>
<thead>
<tr>
<th>Complication</th>
<th>Early Approach</th>
<th>Intermediate Approach</th>
<th>Late Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic Retinopathy</td>
<td>Glycemic Control</td>
<td>Photocoagulation</td>
<td>Vitreo-retinal Surgery</td>
</tr>
<tr>
<td></td>
<td>Blood Pressure Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipid Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic Nephropathy</td>
<td>Glycemic Control</td>
<td>ACE inhibitor</td>
<td>Dialysis Transplantation</td>
</tr>
<tr>
<td></td>
<td>Blood Pressure Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipid Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>Glycemic control</td>
<td>Gamma Linolenic acid</td>
<td>Prompt intervention</td>
</tr>
<tr>
<td></td>
<td>Foot Wear</td>
<td>Alpha Lipoic acid</td>
<td>(antibiotics,local</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drugs for relief of pain</td>
<td>surgery)</td>
</tr>
<tr>
<td>Macrovascular Disease</td>
<td>Glycemic Control</td>
<td>Antiplatelet Drugs</td>
<td>Revascularization</td>
</tr>
<tr>
<td></td>
<td>Blood Pressure Control</td>
<td></td>
<td>Surgery</td>
</tr>
<tr>
<td></td>
<td>Lipid Control</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DIABETIC NEPHROPATHY:** The measures taken for regressing the progression of diabetic nephropathy include tight blood pressure control, use of ACE inhibitors, and protein restriction in diet. Protein restriction in type
1 diabetic subjects reduced the decline in glomerular filtration rate.\textsuperscript{1340} Similarly, creatinine clearance decreased more slowly in subjects with low protein diet compared to those on high protein diet.\textsuperscript{1340}

**DIABETIC NEUROPATHY:** For painful peripheral neuropathy, the drug recommended is tricyclic antidepressant drugs, phenytoin, carbamazepine and topical capsaicin.\textsuperscript{1281} NSAIDS should be used with caution as these could be of great risk in subjects with renal insufficiency. The new drugs in market containing gamma linolenic acid, alpha lipoic acid and methylcobolamine have been reported to be of some benefit.

**MACROVASCULAR DISEASES:** Drugs, which are considered to be of great use in preventing cardiovascular diseases, include aspirins and anti-platelet drugs. According to a meta analysis on 6 large studies which involved 23,072 patients without and 6,458 patients with diabetes admitted for non-ST-segment elevation myocardial infarction or unstable angina, diabetic subjects have more benefit by using GP IIb / IIIa inhibitors compared to non-diabetic subjects.\textsuperscript{1341}

**LATE APPROACH FOR PREVENTION OF DIABETES COMPLICATIONS:**

This forms the last step and is used in the end stages of the diabetes complication. The late approaches have been sequenced in Table 90. Viteri-retinal surgery is used to regain sight in those with bleeding due to proliferative retinopathy and in cases of retinitis proliferans and retinal detachment. Dialysis and kidney transplantation are used in end stage renal failure with good results. In macrovascular disease, interventions like angioplasty and by pass surgery have been used with varying degrees of success. New types of stents like the drug-eluting stents are considered to be major breakthroughs in preventing restenosis.\textsuperscript{1342} However, it can be appreciated that most of these are not curative but palliative therapies and it is better to try to prevent patients going into these late stages of complications.
Owing to the importance of multi-factorial approach to drugs, poly pharmacy is the rule. An important task for the pharmaceutical industry is to try to develop combinations of drugs that are safe and effective thereby helping the diabetic patient to live an easier, longer and healthier life despite diabetic.