Ann Natl Acad Med Sci (India), **43(1):** 55-77, 2007

Alarming Increase of Diabetes Mellitus and Coronary Heart Disease in India. What are its Causes and how can we contain it?

OP Gupta and Sanjeev Pathak
Emeritus Professor of Medicine, BJ Medical College, Ahmedabad

Abstract

The last 30 years have witnessed a malignant increase in prevalence of diabetes mellitus (DM) in our country particularly in urban areas (1). This is also true for the rising number of coronary heart disease (CHD) patients in the country (2-5). Further, the occurrence of CHD in DM has now acquired epidemic form, which has become a major health problem in the conglomeration of life style diseases in the South East Asia region (1).

Many studies have consistently shown that people with diabetes are 2 to 4 times more prone to develop CHD as compared to non-diabetics (4-7). Several special features have been attributed to the occurrence of CHD in diabetics (1). It tends to occur at an early age, is usually more extensive and severe or is found in virulent form which is rapidly progressive. Post-menopausal women with diabetes are especially at higher risk for CHD than men (8,9). Further, the patients of CHD with diabetes have worse prognosis (10,11). An excessive CHD mortality among diabetic individuals has been reported in a number of prospective studies encompassing a variety of ethnic and racial groups (12,13). However, currently as a population, Indians are most susceptible to all the three entities namely CHD, diabetes and occurrence of CHD in diabetes (14,1).

In the last two decades, with the rapid progress in several areas, now India as a country is transforming itself from developing to a developed nation. With the increasing trend in several life style

Correspondence: Dr. O.P. Gupta, Emeritus Professor of Medicine, BJ Medical College, Ahmedabad, E-mail: opgupta.dr@gmail.com.

diseases, we will have to make enormous efforts to contain them. Therefore, in this article, attempts have been made to identify the present epidemiological situation of DM and CHD, India specific risk factors responsible for their increase and efforts required to be made for containing and later arresting this alarming increase.

Alarming Increase of DM and CHD

Prevalence of DM in India

The World Health Organisation (WHO) earlier (15,16) has projected that the global prevalence of type 2 DM will more than double from 135 million in 1995 to 300 million by the year 2025. Recently, International Diabetes Federation and WHO have reported very disturbing estimates, that in the year 2003 at least 194 million people are having DM worldwide and in the year 2010 there will be 225 million diabetics (17). Thus, the previous estimates seem to be grossly underestimated as these figures are now projected to rise from 300 to 333 million in 2025.

As shown in Table-1, the greatest increase will be in India from 35.5 million in 2003 to 73.5 million in 2025. While in China and USA, there will be less increase in the numbers during the same period. Currently India as a country has got the largest number of diabetics in the whole world.

Type 2 DM is the commonest form of diabetes globally as well as in India. It constitutes more than 95% of the diabetic population in our country. The prevalence of diabetes has shown increasing trend in the last three decades in India. Since 1938, prevalence studies of DM have been conducted in our country (1). These studies have been carried out in different places, in various age groups and by using different methods of examination (urine, blood or both). Only in 1970s, the methodology was somewhat standardized and the prevalence studies became more uniform. Most of these significant studies conducted from 1959 onwards have been listed in Table-2.

Table 1: Estimated Top Ten Countries and Number of Adults with diabetes in 2003 and 2025 (17)

Country	2003 (in millions)	Country	2025 (in millions)
India	35.5	India	73.5
China	23.8	China	46.1
USA	16.0	USA	23.1
Russian Federation	9.7	Pakistan	11.6
Japan	6.7	Russian Federation	10.7
Germany	6.3	Brazil	10.7
Pakistan	6.2	Mexico	9.0
Brazil	5.7	Egypt	7.8
Mexico	4.4	Japan	7.1
Egypt	3.9	Germany	7.1

(IDF Report – Diabetes Atlas 2003)

The earliest study of prevalence of DM by Patel *et al* in Mumbai (1959) reported the occurrence of 0.98%, which

Table-2: Studies of Prevalence of DM in India from 1959 to 2006

Year	Author	Place	Prevalence Rate (%)	
			Urban	Rural
1959	Patel JC *et al*	Mumbai	0.98	
1970	Gupta, OP	Ahmedabad	1.12	
1970	Moses	Madras	1.26	
1970	Tripathi *et al*	Cuttack	1.20	
1971	Tripathi *et al*	Cuttack	2.30	
1972	Ahuja *et al*	New Delhi	2.30	
1972	Jaya Rao	Hyderabad	2.40	
1973	Mukherjee AB	Kolkata	0.70	
1973	Parmoshware	Bangalore	0.01	
1975	Gupta OP	Ahmedabad	2.16	
1975	Mutallik G	Pune	1.48	1.10
1975	Pai *et al*	Trivandrum	1.81	1.00
1975	Tripathi BB	Cuttack	1.40	0.60
1975	Chetri *et al*	Kolkatta	1.63	1.48
1978	Gupta, OP	Ahmedabad	3.80	1.93
1979	Johnson *et al*	Madurai	0.50	
1984	Murthy *et al*	Tenali	4.70	
1986	Patel JC	Bhadran		3.80
1988	Ramachandran *et al*	Kudremkh	5.00	
1989	Kodali *et al*	Gangarathi		2.20
1989	Rao *et al*	Eluru		1.60
1991	Ahuja *et al*	New Delhi	6.70	1.53
1992	Ramachandran *et al*	Madras	8.20	
1997	Ramachandran *et al*	Madras		2.40
1999	Ashabai *et al*	Chennai	11.60	
2000	Ramachandran *et al*	National	17.40	
2000	Ramankutty *et al*	Kerala		2.50
2001	Misra *et al*	Northern	10.30	
2004	Sadikot *et al*	National		2.7
2005	Mohan V	Chennai	15.50	
2006	Basavangowdappa	Mysore		3.77

has increased to 15.5% in Chennai in 2005 in urban area (18).

From Table 3 it can be seen that the prevalence rate of diabetes in urban population of our major regions of India has increased from 0.95–3.8% in 1978 to 9.3–16.6% in 2001. This indicates enormous increase in prevalence rate in urban areas within 23 years in different regions of India.

Table 3: Increasing Trend of Prevalence of DM in India : Comparison between ICMR Study (1978 – Urban only (19) and National Urban Diabetes Survey 2001-NUDS (20)

City	Region	Prevalence in %	
		1978	2001
Ahmedabad	West	3.8	-
Pune	West	1.86	-
Mumbai	West	-	11.6
Kolkata	East	1.78	9.3
Cuttack	East	2.02	-
Trivandrum	South	1.83	-
Chennai	South	-	12.4
Bangalore	South	-	16.6
Hyderabad	South	-	11.7
Delhi	North	0.95	13.5

Epidemiology of diabetes in Migrant Indians

The incidence and prevalence of many diseases get altered as populations migrate from its original country to other places. In case of diabetes, uniform increase is seen in the prevalence rate in

Indian population migrated to various countries over several decades. In United Kingdom (UK), Asian Indian men had four times higher prevalence of diabetes than their British counterparts. Similarly data from South Africa, Tanzania, Malaysia and Singapore also show higher prevalence of diabetes in Asian Indians than the native population and other migrant populations. The possible explanation could be the combined effects of genetic and environmental factors like psychological stress, lifestyle changes, acquired obesity and thrifty phenotype situation

Impaired Glucose Tolerance and Impaired Fasting Glucose

Several studies have indicated that impaired glucose tolerance (IGT) precedes the development of frank DM. Hence, IGT has acquired great importance in recent times. From field studies, many reports have mentioned about higher prevalence of IGT than diabetes. Ramachandran *et al* from Chennai, in their study have reported the prevalence of IGT as 13%, which is significantly higher than DM (5%) in the same population below 40 years of age. Ashabai *et al* also reported higher prevalence of IGT (25.2%) as against the prevalence of DM (17.4%) in a selected urban population in Chennai. Similarly in another study of age and gender standardized prevalence of DM and IGT in National Urban Diabetes Study, the prevalence of IGT was found to be higher than prevalence of DM in majority of the cities.

Laying emphasis on impaired fasting glucose (IFG), in a study, Misra *et al* have reported higher prevalence of IFG as 15.2% than that of DM (10.3%) in the same population. Sadikot *et al* in their prevalence of diabetes in India study (PODIS) (21) have reported IFG rate as 3.68% (4.89 in urban and 2.27 in rural population). Similarly Basavngowdappa *et al* have in 2006, reported prevalence of IFG as 2.8% in rural population in Mysore (22).

What are the causes of increase of DM & CHD?

From the above reports it is observed that in the last about three decades there has been significant increase in prevalence of diabetes both in urban and rural population in different regions of the country. Several views have been expressed for this epidemic to pandemic rise of diabetes in India. Some factors seem to be common globally while some seem to be specific to India. An attempt has been made to list them in Table-4 and Table-5.

After studying the prevalence rates in different countries in the world, American Diabetes Association has identified certain risk factors, which are common to most of the countries. It is now reasonably well established that risk of developing type 2 DM increases with age, obesity and lack of physical activity. It is also more common in individuals with family history of diabetes and in the members of certain racial and ethnic groups. Most of the recent increase in

Table 4: Studies on Prevalence in Migrant Indians in different countries

Country	Year	Age	Prevalence	Population Screened
UK	1990	>20	M/F 11.2/8.9	Asian (mostly Punjabi)
UK	1995	>15	7.4	Hindu Community
Tanzania	1991	>15	9.1	Bhatia Community
Tanzania	1995	>15	15.6	Hindu Indians
Mauritius	1990	>25	12.4	Indians
Singapore	1992	18-69	12.3 10.1 7.7	Indians Malays Chinese
South Africa	1994	>25	9.1	Indians
USA	1991	>15	9.1	Indians

diabetes is lifestyle related. In India also the dramatic rise in prevalence of DM is closely associated with change in lifestyle like relative physical inactivity, central obesity and change in food habits particularly increased consumption of energy-rich fast foods. As emphasized earlier, there has also been progressive

Table 5: Global major risk factors for Type-2 DM (American Diabetes Association) (23)

- Family history of DM (Parents or siblings with DM).
- Race, ethnicity.
- Obesity (20% over desired body weight or body mass index >24 (kg/m2)
- Habitual physical inactivity
- Impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
- Hypertension >140/90mm of Hg in adults
- Triglyceride level > 250 mg/dl and/or HDL cholesterol of <35 mg/dl
- History of gestational diabetes and/or delivery of a baby weighing >4 kg.
- Polycystic ovary syndrome

Table 6: Additional Indicators for High Risk of Type 2 DM in India (24)

- Central obesity: raised waist hip ratio (WHR, Men >0.9, Women >0.85)
- Tuberculosis especially with atypical presentation or non-healing disease.
- Any other recurrent infection or ulcer
- Premature arteriosclerosis
- Stress hyperglycaemia
- Persons on drugs causing glucose intolerance
- Low birth weight due to intrauterine malnutrition.

  They are at risk to develop type 2 DM during adulthood.

  (Thrifty phenotype hypothesis).

urbanization, industrialisation and modernisation resulting in increased competition leading to enhanced stress. It has been reported that increase in stress is accompanied by various changes mentioned above which lead to imbalance of neuro-endocrine system and increases the risk for developing type 2 DM. These factors affect Indian population comparatively at younger age, particularly so in males.

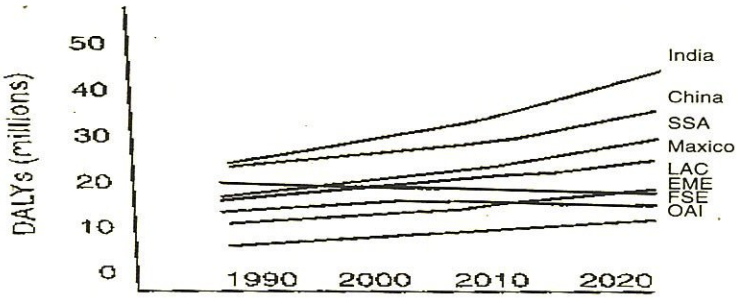
Alarming increase - Pandemic of CHD in India

Several reports indicate that during the past three decades there has been a substantial increase of CHD in developing countries particularly in India, while during the same period there has been a significant decline in CHD mortality in developed countries (25). At present, India has got the highest number of patients suffering from CHD. The current estimate of 25 million CHD patients is projected to increase to 40 million by the year 2020 as shown in Fig 1.

Table-7 illustrates the prevalence of CHD in India from 1960 onwards. Since then various studies on the prevalence of CHD in urban and rural population in India have been published. At that time, the prevalence of DM in India was not considered to be high and therefore these reports are about prevalence of CHD in general or selected population and not in diabetics.

As seen from above, the prevalence of CHD in urban population in India has progressively increased from 1.05% in 1960 (Agra) to 11.0% in 2001 (Chennai). In Jaipur Heart Watch (JHW) studies the prevalence of CHD was 7.59% in 1995 (JHW-1) and 7.30% in 2002 (JHW-2), indicating that there has not been significant difference in the prevalence of CHD in a comparatively short period of seven years in the same population (26, 27). However, in rural population there has been an increase in CHD prevalence

Fig. 1. Burden of CAD 1990 - 2020 (2)



SSA - Sub Saharan Africa
EME - Established Market Economics
OAI - Other Asia and Islands
LAC - Latin America and the Caribbean
FSE - Formerly Socialist Economics of Europe
DALY - Disability Adjusted Life Years

Fig 1: Projection of Prevalence of CHD in developing countries.

from 1.69% (1988) to 3.53% (1995) except for high prevalence reported in Kerala (7.43%).

CHD in Diabetes

So far we have discussed the prevalence of CHD in general settings but it is necessary to know the difference of prevalence of CHD in diabetic and non-diabetic population. This was first reported from Framingham study (see table-7) which indicated high prevalence of CHD in male diabetics as 39.1% as compared to non diabetics 19.1% while in female diabetics it was 27.2% as compared to 10.2% in non-diabetics (27).

Similar studies of prevalence of CHD in diabetics have been conducted in India as given in Table 9.

Table 7: Prevalence of CHD in Urban and Rural India

Author	Year	Age Group (years)	Place	Sample Size	CHD (% ±SD)
Urban Population					
Mathur KS	1960	30-70	Agra	1046	1.05±0.3
Padmavathi	1962	30-70	Delhi	1642	1.04±0.3
Sarvotham SG	1968	30-70	Chandigarh	2030	6.60+03
Gupta SP	1975	30-70	Rohtak	1407	3.63±0.5
Chaddha SL	1990	25.64	Delhi	13723	9.67±0.3
Reddy KS	1994	3564	New Delhi		10.9
Gupta R	1995	20-80	Jaipur	2212	7.59±0.6
Singh RB	1995	20-70	Morababad	152	8.55±2.3
Begom TR	1995	20-70	Trivandrum	506	12.65±1.5
Mohan V	2001	>20	Chennai	1262	11
Gupta R	2002	³20	Jaipur	1123	7.30
Rural Population					
Dhavan BD	1974	30-70	Haryana	1506	2.06±0.4
Jajoo UN	1988	30-70	Vidarbha	2433	1.69±0.3
Kutty VR	1993	25-65	Kerala	1130	7.43±0.8
Wander GS	1994	30-70	Punjab	1100	3.09±0.5
Gupta R	1994	20-80	Rajasthan	8148	3.53±0.3
Singh RB	1995	20-80	UP	162	3.09±1.4

The ICMR multicentric study was carried out in different hospitals in 1984–1987. Hence the figures are comparatively lower than the more recent studies in similar set up of patients. However, the PODIS (21) shows comparatively low figure of 4.5% of CHD because the study was conducted only in newly detected diabetics.

Ramachandran in 1998 (28) has reported prevalence of CHD 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* (29) at Chennai in 2001 found prevalence of 21.4%. Similarly in other studies Gupta PB *et al* have reported prevalence of CHD in diabetics as 19% (30) and Pathak SR (personal communication) as 23.2%, which are comparable to the reports of Mohan *et al*. Several studies have reported (31) higher incidence of diabetes and CHD 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 (32).

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).

Table 8: Average Annual incidence of Cardiovascular Disease per 1000 persons at risk (Adopted from Framingham Study)

Age	Men		Women	
	Diabetics	Non-Diabetics	Diabetics	Non-Diabetics
45–54	31.7	12.3	24.8	4.3
55–64	48.1	25.1	37.9	12.6
65–74	57.1	28.4	40.4	22.4
Total	39.1	19.1	27.2	10.2

Table 9: Prevalence of CHD in Diabetes in India

Author	Year	Place	Prevalence of CHD (%)
ICMR*	1984-87	Multicentric	Male 8.1% Female 4.7%
A. Ramachandran	1998	Chennai	14.2% (3.9 + 10.3%)
V. Mohan	2001	Chennai	21.4%
PODIS**	2001	Multicentric	4.5%
Gupta PB	2001	Surat	19%
Phatak SR	2002	Ahmedabad	Males 20.2% Females 26.1%

* ICMR = Indian Council of Medical Research

** Prevalence of Diabetes in India Study

However, this does not in any way reduce their importance in causation of CHD in Indians.

Gupta *at al* has reported that there is high prevalence of various conventional risk factors in his Jaipur Heart Watch – 2 studies. 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 (26). The high rates of CHD in Indians worldwide are accompanied by paradoxically low rates of conventional risk factors. Indians, however have a higher prevalence of emerging and new risk factors, which render the conventional risk factors doubly dangerous (25).

Table 10: Conventional Risk Factors for CHD

- Positive family history of premature vascular disease
- Advancing age
- Male gender and postmenopausal state in women
- Diabetes
- Insulin resistance/hyperinsulinemia
- Dyslipidemia:elevated LDL-C and low HDL-C.
- Smoking
- Hypertension
- Obesity/Central obesity
- Sedentary lifestyle

What are the causes of the increase of CHD in India?

Epidemiological Transitions (ET) as Risk Factors for DM & CHD

The studies of the morbidity and mortality patterns of various diseases reveal that over decades and centuries the shifts in the DM and CHD continue to occur throughout the world. This shift is termed as epidemiological transition. In developed economies, decades ago communicable diseases were quite prevalent. After their control, now the noncommunicable diseases have become more prevalent. During the phase of transition from developing to developed country, similar disease pattern is likely to evolve. This transition occurs in combination with economic development (increase in personal and community wealth) along with social and demographic transformation (increase in population). This occurs at different rates in various countries of the world. So far as India is concerned we are in a phase of economic, social and demographic transformation. Hence, the rate of CHD, DM, obesity, hypertension and cancer is increasing as a consequence of consumption of calorie-rich diet, physical inactivity and psychosocial stress. This may be the result of increased urbanization and industrialisation. We are considered to be in the second phase of E.T. and perhaps urban areas are in the third phase (33).

Out of the emerging risk factors the insulin resistance, lipoprotein (a), [Lp (a)] and hyperhomocysteinemia seem to be acquiring great importance in causation of CHD in Indians.

Relevance of CHD Risk Factors in Diabetes

Type-2 diabetes predisposes the comparatively young persons to the acceleration, dissemination and severity of atherosclerotic process in coronary arteries leading to CHD. Hence CHD has become the commonest cause of morbidity and mortality in type-2 diabetes.

Out of the various risk factors mentioned above for practical purpose it would be desirable to discuss them under the modifiable and non-modifiable subgroups given below.

Non-modifiable Risk Factors

The population growth and demographic transition : These factors seem to be unlikely to explain the diabetes pandemic in India. China's population is higher (1.3 billion) than India (1.0 billion) in 2003 but India has the largest number of diabetics (35.5 million) while China had only 23.8 million. Similarly, for India the expectation of life at birth in 1951 was 41 years while in 2000 it is 64 years. Looking to the number of diabetics in each decade in both groups, this is also not likely to explain the large increase of diabetics. The Indians have higher genetic predisposition to diabetes as evidenced by–

1. More number of patients having positive family history for DM as compared to Europeans, if one or both parents are diabetic.
2. Higher prevalence of abnormal glucose tolerance in off springs if both parents are diabetic;
3. More insulin resistance than Europeans, demonstrated by glucose-insulin clamp studies;
4. Development of diabetes at a younger age; and
5. For a given BMI Indians have higher body fat, intra-abdominal fat and lower BMI threshold for developing diabetes.

The prevalence of DM in persons doing less physical activity (17.0%) is higher as compared to those with moderate (9.7%) and heavy exercise (5.6%). The persons with positive family history and leading sedentary life style are running 3 times high risk of development of DM as compared to normal.

1. Genetic

Indians are genetically prone not only for development of diabetes but also for coronary heart disease. Various studies notably the Chennai Urban Population Study (CUPS No.5) has demonstrated higher prevalence of CHD in diabetics (21.4%) as compared to nondiabetics (9.1%) (29).

Some genes have been incriminated amongst Indian diabetics like PCI-K121Q Polymorphism, PPAR-Y gene: PRO 12ALA Polymorphism, PGC-1 α gene : Thr 394 Thr (G A) Polymorphism (34).

2. Age at Onset

Diabetes as well as IGT are seen about a decade earlier in Indians. As we know that vascular complications are related to duration of uncontrolled

hyperglycaemia, Indians developing IGT/ DM at earlier age (35) are therefore, exposed to hyperglycaemia from relatively younger age.

3. *Gender*

Commonly women are considered at lower risk of CHD morbidity and mortality than men. It is widely believed that diabetes erases this female advantage and increases the risk of CHD to a greater extent than in men. The meta-analysis of ten international studies, having sufficient data adjusted for other cardiac risk factors, shows that the relative risk of coronary death from diabetes was 2.58 for women and 1.85 for men (36). Premenopausal women with diabetes face a similar risk of developing CHD as nondiabetic men of the same age. Following an acute myocardial infarction, diabetic women have double the rate of recurrence and shorter survival than men.

Modifiable/Preventable Risk Factors:

1) *Hyperglycaemia and IGT:* Impaired glucose tolerance and diabetes have been recognized as risk factors for CHD for many years but the relationship between different degrees of hyperglycaemia and CHD risk was not clear. Until recently, relatively little data was available examining whether higher levels of glucose predicted progressively higher risk of CHD. Several recent prospective epidemiologic studies have clearly demonstrated that glucose is a continuous CHD risk factor in people with both type 1 and type 2 DM (37, 38). Hence DM is being considered as CHD equivalent these days. The data from these studies suggest that the risk of CHD rises by about 10 to 30% for every 1% increase in HbA1C The United Kingdom Prospective Diabetes Study (UKPDS) data also indicate that with each 1% rise in HbA1C the incidence of MI rose by about 14%. Moreover, recent data suggest that people with even IGT have increased risk of CHD (39-44). The clock of CHD actually starts ticking before the onset of actual clinical diabetes (45). These observations support the hypothesis that lowering the glucose to within the normal range may prevent/ postpone CHD.

Table 11: New and Emerging Risk Factors for CHD in Indians (25).

- Hyperhomocysteinemia.
- Hyperfibrinogenemia.
- Small dense LDL phenotype.
- Hypertriglyceridemia and increased IDL.
- Elevated lipoprotein (a): Lp(a).
- Insulin resistance.
- Inflammation and infectious agents.
- Psychosocial factors.
- Non-lipid related gene polymorphisms.
- Miscellaneous: Oxidation susceptibility and antioxidant intake.
- WBC count and Haemostatic/fibrinogen abnormalities, Iron overload.

2) *Dyslipidemia:* The important lipoprotein abnormalities in Indian diabetics are described as raised level of triglycerides, VLDL, small dense LDL, Lp(a) and decreased level of HDL-C. Mohan *et al* have reported higher levels of triglycerides, LDL, and total cholesterol in persons with CHD as compared to persons without CHD (29).

In the study of complications in newly diagnosed diabetics in India (CINDI) 34% patients had triglycerides more than 200 mg%, 36% had total cholesterol more than 200 mg %, 23% had LDL-C more than 130 mg% , while HDL-C was lower than 35 mg % in 15% of the cases. Gupta A *et al* in diabetic population in an urban Indian study carried out in Jaipur, have reported high cholesterol in 47.1% men, 48.5% women; high LDL-C in 45.7% men, 46.9% women; high triglyceride in 44.3% men, 40.6% women and low HDL-C in 60% men and 57.8% women. Taking the criteria recommended by ADA 1998, Udawat *et al* (46) have reported dyslipidemia in 89% of diabetic patients, raised LDL-C (> 100 mg%) in 76%, low HDL-C (< 35 mg%) in 58% and hypertriglyceridemia (> 200 mg) in 22% patients. The incidence of dyslipidemia in his study was higher in diabetic group than in nondiabetic group.

3) *Hypertension:* Hypertension occurs about twice as frequently in people with diabetes than in general population. Hypertension and diabetes together considerably accelerate the development of CHD along with other macrovascular and microvascular complications. Amongst the Indian studies Singh R.B *et al* have reported prevalence of hypertension in diabetics as 51.9% in urban and 29.4% in rural as compared to non diabetics who had 21.9% in urban and 16.9% in rural population (47). Similarly Ramachandran *et al* have reported the prevalence of hypertension in diabetics as 29.3% as compared to non diabetics 24.4% (48).The study of Gupta A also shows higher prevalence of hypertension in diabetics (73.1%) as compared to non diabetics (32.4%). However in freshly detected diabetics, CINDI study the prevalence of hypertension was reported as 20.18%, which is lower than the other studies because the study included only newly detected diabetics.

4) *Microalbuminuria and Diabetic Nephropathy:* Several prospective epidemiologic studies have demonstrated that microalbuminuria is an important risk factor for CHD in patients with DM. In a recent meta-analysis of these studies, it was shown that the presence of microalbuminuria doubles the CHD mortality and morbidity (49). The clinical proteinuria consistent with diabetic nephropathy increases the CHD risk greater than twofold (50, 51).

5) *Lipoprotein (a) [Lp(a)]* : Lp(a) is a form of low density lipoprotein (LDL) and has an apoprotein (a) [apo (a)]

molecule covalently linked to apoprotein (B) [apo B 100]. Lp (a) is genetically determined and has structural homology similar to plasminogen. Mohan *et al* have reported higher Lp(a) levels in cases of type 2 DM with CHD (24.6 mg/dl), as compared to type 2 DM without CHD (15.1 mg/dl). Several studies done outside India have reported higher Lp(a) levels in Asian Indians as compared to native population (25). These studies include (i) Coronary Artery Disease in Indians (CADI) (30 mg/dl) (52) (ii) Study of Health Assessment and Risk Factors in Ethnic groups (SHARE) (39.1 mg/dl) (53) and (iii) Study from Singapore (2 times higher in Indians than Malays and Chinese) (54).

6) *Apolipoprotein – B:* Apolipoprotein B (Apo B) is the principal protein moiety of lipoproteins of low density, intermediate density and very low density (LDL, IDL and VLDL). Its concentrations are a good estimate of the total mass of these atherogenic particles. Association of high Apo B concentration with increased CHD incidence is demonstrated in white populations. Snehalatha and Ramachandran *et al* have shown that the apolipoprotein B and A1 provide better information regarding the risk of CHD. Diabetes per se enhances Apo B concentrations and this could probably be one of the mechanisms of accelerated CHD in diabetes (55).

7) *Fibrinogen Levels:* Fibrinogen has been reported to be an independent risk factor for myocardial infarction and CHD mortality, (56) due to strong association of fibrinogen with blood viscosity and thrombus formation. Furthermore, polymorphism of the fibrinogen gene has been shown to be associated with CHD in type 2 diabetic patients (57). Deepa *et al* in South Indian males reported higher levels of fibrinogen in patients with CHD (both with and without diabetes) (58). This study also showed an inverse correlation of fibrinogen levels with HDL cholesterol.

8) *Hyperhomocysteinemia:* Homocystein, a product of methionine metabolism, has been found to be elevated in Asian Indians. The levels of homocystein are influenced by age, genetics and nutritional factors particularly deficiency of folate, vitamin B6 and vitamin B12. According to the present reports hyperhomocysteinemia is considered to be an independent risk factor for CHD. It is also reported to increase the mortality risk after acute myocardial infarction. However, all the prospective studies have not supported relationship of plasma homocystein levels and CHD. Deepa *et al* have also not found an association between elevated homocystein levels and CHD in south Indian males with or without diabetes (59). Similarly Baxi H *et al.* have also not found any relationship between homocystein levels and CHD in western part of India in patients

with or without diabetes. They have explained this normal value due to deficiency of folate, vitamin B6 and B12 in Indian population. Further, in diabetics with nephropathy there is excretion of these vitamins in the urine. Hence, normohomocysteinemia does not reduce the chances of developing CHD in diabetics.

9) *Carotid Intima Media Thickness:* The Study of Second Manifestations of Arterial Disease (SMART) (60) had suggested that carotid intimae media thickness (IMT) and arterial stiffness are clear markers of CHD risk. The study of Japanese subjects had also supported this new hypothesis (61). Ravikumar *et al* in the Chennai Urban Population Study (CUPS – 9) have demonstrated that diabetic patients have decreased flow mediated dilatation (FMD) and increased arterial stiffness compared with age and sex matched nondiabetic subjects (62) hence these are considered as risk factors for the development of CHD.

How can we contain the increase of DM and CHD?

Prevention of Diabetes

Diabetes is preventable if we catch it early. As mentioned earlier, the number of people with diabetes in India will increase more than two-fold by the year 2025, if preventive measures are not taken during this period. Hence prevention of diabetes acquires tremendous significance for the individual, family and community at large. For primary prevention two approaches are described (1) Population based approach (2) High risk group based approach. Usually combination of both approaches is more successful. The population-based approach prevents diabetes both in high risk and low risk individuals (63). It also helps to reduce the risk of CHD, hypertension and comorbid conditions. However, implementation of this approach may be difficult in view of large area, enormous population and high rate of illiteracy in our country.

Under the circumstances attention should be focused on high risk individuals like population at greatest risk of developing type 2 DM ; such as (1) Overweight persons, BMI > 26 kg/m or waist circumference > 90 cm for men, > 85 cm for women. (2) Persons with IGT (3) Women with a past history of gestational diabetes and delivering babies more than 4 kg and less than 2.5 kg.

There are many screening methods adopted as Framingham score, Finnish score, Danish Diabetes score etc. which are not suitable for India. As selective screening of the population is necessary, it should be done effectively. Mohan *et al* from their Chennai Urban Rural Epidemiology Study (CURES) cohort have attempted to develop (64) a simple user friendly and cost-effective Indian Diabetes Risk Score (DRS) which is given below.

Particulars	Score
Age (years)	
< 35 (reference)	0
35 – 49	20
≥ 50	30
Abdominal obesity	
Waist <80 cm (female), <90 cm (male) [reference]	0
Waist ≥80 – 89 cm (female), ≥90 – 99 cm (male)	10
Waist ≥90 m (female), ≥100 cm (male)	20
Physical activity	
Exercise (regular) + strenuous work (reference)	0
Exercise (regular) or strenuous work	20
No exercise and sedentary work	30
Family history	
No family history (reference)	0
Either parent	10
Both parents	20
Minimum score	0
Maximum score	100

Based on the above table if the score is ≥60, the person is considered to be having very high risk of developing DM. Such person should undergo oral glucose tolerance test. If the score is between 30-35, risk of having DM is moderate and if score is <30 these persons are considered low risk for developing DM. Individuals with score ≥30 should be recommended lifestyle modification to reduce the score.

Primary Prevention in High Risk Individuals

The evidence, accumulated from various studies notably the Diabetes Prevention Program (DPP) (65, 66) shows that risk of developing type 2 DM can be reduced by : (1) Participating in 150 minutes of moderate physical activity such as brisk walking per week. (2) Consuming a diet with less than 30% of energy as fat and less than 10% energy as saturated fat. (3) Consuming a diet of low energy density with a wide range of carbohydrate foods rich in dietary fiber and of low glycemic index (cereals, vegetables, legumes and fruits).

Primary Prevention in Population as a Whole

Under this programme as mentioned above it is recommended: (1) to avoid excessive consumption of foods containing saturated fat and simple carbohydrates. (2) Doing regular physical exercise. (3) Avoiding or managing stress (67).

What Can the Government do to Prevent Type 2 Diabetes Pandemic?

Make healthy foods (vegetables, fruits, legumes, cereals etc.) cheaper and easily available while unhealthy foods (fast foods etc) expensive and difficult to buy. (2) Ban or restrict advertising of unhealthy foods, or allow them to advertise with a word of caution as is done for tobacco products. (3) Ensure that there are open spaces in our cities for sports and outdoor activities and that our streets/ roads are safe to walk. (4) Encourage exercise and healthy food programmes in schools, universities and at workplaces.

Prevention of CHD in Diabetics in Indians

As discussed above, the major risk factors responsible for pandemic of CHD

in India include hypertension, DM or IGT, dyslipidemia, high fat diet, lack of physical activity and increased tobacco use. The new and emerging risk factors like raised lipoprotein (a) [Lp (a)], homocystein etc also play significant role. Since adverse effect of these factors is greater in Indians, the benefits of modifying them are also correspondingly greater.

Individual Based Prevention Strategy for CHD

This involves identifying individuals with markedly elevated risk factors and targeting them for interventions. The interventions in these individuals include low intake of saturated fat, regular exercise, tobacco abstinence and maintenance of optimum body weight and waist circumference. Drug therapy is used when these measures fail to produce desirable results.

Maintaining tight glycemic control has been shown to reduce risk of CHD in diabetics (68, 69). Systolic blood pressure reduction by 5 to 10 mm Hg results in 20 – 30 % risk reduction in CHD events in diabetics (70) especially when drugs like angiotensin converting enzyme (ACE) inhibitors, diuretics, beta blockers or calcium channel blockers (CCB) are used. Some (71 - 73) but not all (74,75) large trials suggest that ACE inhibitors may be superior to CCB for treatment of hypertension in diabetics. Moreover the addition of ACE inhibitors to other effective therapies to treat hypertension reduces the risk of CV events by 25% in high-risk people with diabetes (76). Elevated levels of LDL-C have been universally accepted as major risk factor for CHD in general population and more so in diabetics. The subgroup analysis of the available trials suggest that in patients with DM and modestly elevated LDL-C levels, therapy with statin class of agents reduces the CHD risk by 20 to 30% (77-80). Collaborative Atorvastatin Diabetes Study (CARDS) showed that in patients with type 2 DM, Atorvastatin 10 mg reduced the risk of major CV events by 37%. Similarly fibrates by reducing triglyceride and increasing HDL levels also reduce the risk of CHD events. (81-83). Although Aspirin therapy has shown CV risk reduction in nondiabetic patients, none of the studies including Primary Prevention Project (PPP) showed any significant CV risk reduction in diabetic subgroup (84).

Since data on lowering Lp(a) and its impact on CHD risk reduction is not available, the current emphasis should be on lowering LDL-C levels to < 80 mg/dl (rather than < 100 mg/dl) in persons with elevated Lp(a) levels as the later has been shown to render elevated LDL concentrations doubly dangerous. Recently (2006), Hope-2 (85) study showed no CV risk reduction with Vitamin B12 and folic acid despite of effective reduction of homocystine levels.

Population Based Strategy for Prevention

The population based approach aims to lower risk factors in the population

through both government and community actions. Since there is a continuum of risk associated with most of the CHD risk factors, more people making small changes will result in large benefits to the society as opposed to large changes in small number of high-risk patients. People should be advised to restrict the consumption of saturated fat and cholesterol. Emphasis should be on eating foods with adequate starch and fiber. Tobacco use in any form should be avoided and alcohol intake if at all, should be only in moderate amount. Importance of daily physical exercise such as walking should be encouraged. As Yoga lifestyle intervention program (86) has been found to have favourable effects on angina as well as risk factors of CHD (body weight, lipid levels etc) it can also be suggested as an additional measure for prevention of CHD.

Several major trials have been conducted for prevention of diabetes, which include Diabetes Prevention Programme (DPP) where lifestyle modification was compared with oral metformin, where risk reduction was 31% with metformin and 58% with lifestyle changes. The Finnish Diabetes Prevention study done in 1993 also showed 58% risk reduction with lifestyle modification.

The IDRS has a sensitivity of 72.5% and specificity of 60.1% and is derived on the largest population based study on diabetics in India CURES (64). The advantage of IDRS are its simplicity, low cost and is easily applicable for mass screening programmes Physical activity and waist circumference are risk factors for both diabetes and CHD, if these modifiable risk factors are altered, the risk score can be considerably reduced. Subjects with high IDRS regardless of their blood sugar status are ideal candidates for life style modification as these are risk factors for not only diabetes but also for CHD.

Conclusion

Currently India has the largest number of patients of diabetes mellitus and coronary heart disease in the world. The present estimates indicate alarming increase upto 2025. India as a developing nation is passing through epidemiological transition of the occurrence of various noncommunicable diseases, which is intertwined with economic (wealth), social (food and physical activity) and demographic (population) upheavals. The global and India – specific factors for their pandemic increase have been critically examined. It is essential to contain the alaming increase, hence simple, cost effective and practical suggestions have been described for implementation at individual, community and national levels by the people and governments. Finally, it is appealed that the nation should demonstrate courage and determination to do the hard work to curb the menace of increase of the prevalence of these diseases.

References :

1. Gupta OP and Pathak S (2003). Pandemic trends in prevalence of diabetes mellitus and associated coronary heart disease in India-their causes and prevention. *Int J Diab Dev Countries* **23:**37-50.
2. Enas EA and Jacob S (1998). Coronary artery disease in Indians in the USA. In: Coronary artery disease in Indians. *A Global perspective.* Sethi KK (ed) *Mumbai: Cardiological society of India,* 32-43.
3. Murray CJ and Lopez AD (1997). Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study: *Lancet* **349:**1498-1504.
4. Gupta R, Prakash H, Mazumdar S, Sharma S and Gupta VP (1995). Prevalence of coronary heart disease and coronary risk factors in urban population of Rajasthan. *Indian Heart J* **47:** 331-8.
5. Gupta R, Gupta VP, Sarna M, Bhatnagar S, Thanvi J, Sharma V *et al.* (2002). Prevalence of coronary heart disease and coronary risk factors in urban Indian population: Jaipur Heart Watch-2. *Indian Heart J* **54:** 59-66.
6. Elizabeth Barrett-Connor and Pyorala K (2001). Long Term Complications: Diabetes and coronary heart disease. The epidemiology of Diabetes Mellitus. An International perspective edited by Jean Marie Ekoe, Paul Zimmet and Rhys (eds) Williams: John Wiley& Sons Ltd **21A:** 301-17.
7. Stamler J, Vaccaro O, Neaton JD and Wentworth D (1993). For the Multiple Risk Factor Intervention Trial Research Group. Diabetes, other risk factors, and 12 year cardiovascular mortality for men screened in the MRFIT. *Diabetes Care* **16:**434-44.
8. Seaman T, deLeon CM, Berkman L and Ostfeld A (1993). Risk factors for coronary heart disease among older men and women: a prospective study of elderly community dwelling . *Am J Epidemiol* **138:** 1037-49.
9. Manson JE, Colditz GA, Stampfer MJ *et al* (1991). A prospective study of maturity onset diabetes and risk of coronary heart disease and stroke in women, *Arch Intern Med* **151:** 1141-7.
10. Collins VR, Dowse GK, Cabealawa S, Ram P and Zimmet PZ (1996). High mortality from cardiovascular disease and analysis of risk factors in Indian and Melanesians Fijians. *Int J Epidemiol* **25:** 59-69.
11. Kennel W B and McGee DI (1997). Diabetes and glucose tolerance as risk factor for cardiovascular disease: The Framingham study. *Diabetes Care* 120-31.
12. Haffner SM, Lehto S, Ronnemaa T *et al* (1998). Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. *N Engl J Med* **339:** 229-34.
13. Malmberg K, Yusuf S, Gerstein HC *et al* (2000). Impact of diabetes on long term prognosis in patients with unstable angina and non-q wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) registry. *Circulation* **102:** 1014-9.
14. Reddy KS and Yusuf S (1998). Emerging epidemic of cardiovascular disease in

developing countries. *Circulation* **97:** 596-601.

15. King H, Aubert RE and Herman WH (1998). Global burden of diabetes, 1995-2025, prevalence, numerical estimates and projection. *Diabetes care* **21:** 1414-31.
16. King H and Rewers, M (2002). WHO ad hoc diabetes reporting group, global estimates for prevalence of diabetes and IGT in adults, Diabetes Care 1993; 16: 157–77. 4. Cosgrove P, Engelgau M, Islam I. Cost effective approaches to diabetes care and prevention. Diabetes *Voice* **47:** 13–6.
17. IDF Report – Diabetes Atlas – 2003
18. Mohan V, Deepa M and Deepa R (2006). Secular trends in the prevalence of diabetes and IGT in urban south India-The Chennai Urban Rural Epidemiology Study (CURES-17). *Diabetologia* **49:** 1175-1178.
19. Gupta OP *et al* (1978). Advances in metabolic disorders. R. Levine and R Luft (eds) **9:** 147–65.
20. Ramchandran A, Snehalatha C, Anil Kapur *et al* (2001). High Prevalence of diabetes and impaired glucose tolerance in India- National Urban Diabetes Survey. *Diabetologia* **44:** 1094–101.
21. Sadikot SM, NigamA, Das S *et al.* (2004). The burden of diabetes and impaired glucose tolerance in India using the WHO 1999 criteria: prevalence of diabetes in India study (PODIS). *Diab Res Clin Pract* **66:** 301-7.
22. Basavanagowdappa FS, Prabhakar, AK, Prasanna P *et al.* (2006). Study of prevalence of diabetes mellitus and impaired fasting glucose in rural population, *Int J Diab Dev Countries* **25:**98-101.
23. American Diabetes Association Position statement: screening for type 2 diabetes. (1998). *Diabetes Care* **22 (supp. 1) S:** 20–S 24.
24. Hazra DK (1999). Proceedings Novo Nordisk Diabetes Update Publication, 25-33.
25. Enas EA and Jacob S (1998). Coronary artery disease in Indians in the USA. *In*: Coronary Artery Disease in Indians. A Global Perspective. Mumbai: Sethi KK *(ed) Cardiological Society of India* 32–43.
26. Gupta R, Prakash H, Mazumdar S, Sharma S and Gupta VP (1995). Prevalence of coronary heart disease and coronary risk factors in urban population of Rajasthan, *Indian Heart J* **47:** 331–8.
27. Kannel WB and McGee DI (1997). Diabetes and Glucose Tolerance as risk factor for cardiovascular disease: The Framingham study. *Diabetes care* **20:** 120–31.
28. Ramchandran A (1999). Epidemiology of vascular complications in type 2 diabetes in Indians. *Novo Nordisk Diabetes Update proceedings* 101–5.
29. Mohan V, Deepa R, Shanthirani S and Premlatha G (2001). Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India (CUPS No. 5 – Chennai Urban population study). *J Am Coll Cardiol* **38:** 687–97.
30. Gupta PB, Bhatt P and Thakker K. (2002). Vascular Complications of type 2 diabetes mellitus. *Gujarat Med J* **59:** 9–12.
31. Fall CHD, Yagnik CS, Rao S and Coyaji KI (1999). The effect of maternal body composition before pregnancy on fetal growth; The Pune Maternal Nutrition

Study *In*: Fetal programming influences on development and disease in later life. Shaugan PM, O'Brien, Wheeler T and Barker DJP (*eds*) RCOG London **21:** 231-45.

32. Yagnik CS (2000). The origin of metabolic syndrome in Indians In: The metabolic syndrome. Sood OP and Ratan A (*eds.) Ranbaxy Science Foundation* 17–29.
33. Miahall Gaziano and Braunwalts (2005). Text Book of Heart Disease. Global Burden of cardio vascular disease, Zipes, DP, Libby P and Braunward E (eds). Elsevier Sanders Saunders, 7th edition, 1-26.
34. Mohan V, Gokulakrishnan K, Deepa R, Shantirani CS and Datta M (2005). Association of physical inactivity with components of metabolic syndrome and coronary artery disease-the Chennai Urban Population Study (CUPS no.15). *Diabet Med* **22:**1206-11.
35. Raheja BS and Kapur A (2001). Diabcare Asia Study, India Study Group, JAPI, 717–22.
36. Enas EA, Santhilkumar A, Juturu V and Gupta R (2001). Coronary Artery Disease in women, *Indian Heart J* **53:** 282–92.
37. Wel M, Gaskill SP, Haffner SM and Stern MP (1998). Effect of diabetes and level of glycemia on all-cause and cardiovascular mortality. The San Antonio Heart Study. *Diabetes care* **21:** 1167-72.
38. Letho S, Ronnemaa T, Pyorala K and Laakse M (1999). Poor glycemic control predicts coronary heart disease events in patients with type 1 diabetes without nephropathy. *Arterioscler Thromb Vasc Biol* **13:** 1014-9.
39. Coutinhe M, Gerstein HC, Wang Y and Yusuf S (1999). The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* **22:** 233-40.
40. Gerstein HC, Pais P, Pogus J and Yusuf S (1999). Relationship of glucose and insulin levels to the risk of myocardial infarction: a case-control study. *J Am Coll Cardiol* **33:** 612-9.
41. Gerstein HC and Yusuf S (1996). Dysglycaemia and risk of cardiovascular disease. *Lancet* **347:** 949-56.
42. Balkau B, Shipley M, Jarrett RJ *et al* (1998). High blood glucose concentrations is a risk factor for mortality in middle-aged nondiabetic men. *Diabetes Care* **21:** 360-7.
43. Bjornholt JV, Erikssen G, Asser EJ *et al.* (1999). Fasting blood glucose: an underestimated risk factor for cardiovascular death. Results from a 22-year follow- up of healthy nondiabetic men. *Diabetes Care* **22:** 45-9.
44. Haffner SM (1998). The importance of hyperglycemia in the nonfasting state to the development of cardiovascular disease. *Endocr Rev* **19:** 583-92.
45. Haffner SM, Storn MP, Hazuda HP *et al.* (1990). Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock of coronary heart disease start ticking before the onset of clinical diabetes? *JAMA* **263:** 2893-8.
46. Udawat H, Goyal RK and Maheshwari S (2001). Coronary risk and dyslipidemia in type 2 diabetic patients. *J Assoc Physicians India* **49:** 970-3.

47. Singh RB, Bajaj S, Niaz MA, Rastogi SS and Moshiri M (1998). Prevalence of type 2 diabetes mellitus and risk of hypertension and coronary artery disease in rural and urban population with low rates of obesity. *International Journal of Cardiology* **66:** 65–72.

48. Ramchandran A, Snehlatha C, Latha E, Satyawani K and Vijay V (1998). Clustering of cardiovascular risk factors in urban Asian Indians. *Diabetes Care* **21:** 967–71.

49. Dinneen SF and Gerstein HC (1997). The association of microalbuminuria and mortality in non-insulin dependent diabetes mellitus. *Arch Intern Med* **157:** 1413–8.

50. Gall MA, Borch Johnsen K, Hougaard P *et al.* (1995). Albuminuria and poor glycemic control predict mortality in N I DDM. *Diabetes* **44:** 1303–9.

51. Agewall SW, Kstrand J, Ljungman S and Fagerberg B (1997). Risk factor intervention study group. Usefulness of micro albuminuria in predicting cardiovascular mortality in treated hypertensive men with and without diabetes mellitus. *Am J Cardiol* **80:** 164–9.

52. Enas EA, Garg A, Davidson MA, Nair VM, Huet B and Yusuf S (1996). Coronary Heart disease and its risk factors in first generation immigrant Asian Indian to the United States of America. *Indian Heart J* **48:** 343–54.

53. Anand S, Yusuf S and Vuskan V (2000). Differences in risk factors, atherosclerosis and cardiovascular disease between ethnic groups in Canada. Study of Health Assessment and Risk in Ethnic groups (SHARE). *Lancet* **356:** 279–84.

54. Hughes K, Awe TC, Kuperan P and Choo M (1997). Central Obesity, Insulin resistance, syndrome X, Lipoprotein (a) and cardiovascular risk in Indians, Malays and Chinese in Singapore. *J Epidemiol community Health* **51:** 394–9.

55. Snehalatha C, Ramchandran A, Sivasankari S *et al.* (2002). Is increased Apolipoprotein B – A major factor enhancing the risk of coronary artery disease in type 2 diabetes? *JAPI* **50:** 1036–8.

56. Swahn E, von Schenck H and Wallentin L (1989). Plasma fibrinogen in unstable coronary artery disease. *Scand J Clin Lab Invest* **49:** 49–54.

57. Thomas AE, Green FR, Kelleher CH *et al.* (1991). Variation in the promoter region of the β-fibrinogen is associated with plasma fibrinogen levels in smokers and nonsmokers. *Thromb Haemost* **65:** 487-490.

58. Deepa R, Velmurugan K, Saravanan G *et al.* (2002). Relationship of tissue plasminogen activator, plasminogen activator inhibitor-1 and fibrinogen with coronary artery disease in South Indian male subjects. *J Assoc Physicians India* **50:** 901-906.

59. Deepa R, Velmurugan K, Saravanan G, Karkuzhali K, Dwarkanath V and Mohan V (2001). Absence of association between serum homocystein levels and coronary artery disease in south Indian males. *Ind Heart J* **53:** 44–7.

60. Simons PC, Algra A, Bots ML, *et al.* (1999). Common carotid intima media thickness and arterial stiffness:

Indicators of carotid vascular risk in high risk patients. The SMART study. *Circulation* **100:** 951-7.

61. Taniwaki H, Kawagishi T, Emoto M *et al.* (1999). Correlation between the intimal media thickness of the carotid artery and aortic pulse wave velocity in patients with type 2 diabetes. *Diabetes Care* **22:** 1851-7.
62. Ravikumar R, Deepa R, Shanthirani S and Mohan V (2001). Comparison of carotid intima media thickness, arterial stiffness and brachial artery flow mediated dilatation in diabetic and nondiabetic subjects. (The Chennai Urban Population Study (CUPS-9). *Am J Cardiol* **90:** 702-7.
63. Siemen D, Voyle J, Swinvurn V and O'Dea K (1997). Community based approaches for the primary prevention of non-insulin dependent diabetes mellitus. *Diabetic Medicine* **14:** 519–26.
64. Mohan V, Deepa R, Deepa M *et al* (2005). A Simplified Indian Diabetes Risk Sore for Screening for Undiagnosed Diabetic Subjects. *J Assoc Physicians India* **53:** 755-63.
65. DPP Research Group (2002). The Diabetes Prevention Program. Reduction in incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* **346:** 393–403.
66. Ruth C (2002). Is type 2 diabetes preventable? What the evidence based guidelines say. *Diabetes Voice* **47:** 18–20.
67. Edwards CL, William P and Lane J D (2002). Stress management improves long term glycemic control in type 2 diabetes. *Diabetes Care* **25:** 30–4.
68. UK Prospective Diabetes Study (UKPDS) Group (1998). Intensive blood glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* **352:** 837–53.
69. UK Prospective Diabetes Study (UKPDS) Group (1998). Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UK PDS 34). *Lancet* **352:** 854 65.
70. UK Prospective Diabetes Study (UKPDS) Group (1998). Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes. (UKPDS 38). *BMJ* **317:** 703–13.
71. Estacle RO, Jeffers BW, Hiatt WR *et al.* (1998). The effect of nislodipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin dependent diabetes and hypertension. *N Eng J Med* **338:** 645–52.
72. Tatti P, Pahor M, Byington RP *et al.* (1998). Outcome results of the Fosinopril versus Amlodipine Cardiovascular Events Trial (FACET) in patients with hypertension and NIDDM. *Diabetes Care* **21:** 597–603.
73. Hansson L, Lindholm LH, Niskanen L *et al.* (1999). Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPP) randomized trial. *Lancet* **353:** 11–6.
74. UK Prospective Diabetes Study (UKPDS) Group (1998). Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular

complications in Type 2 diabetes: UKPDS 39. *BMJ* **317:** 713– 20.

75. Hansson L, Lindholm LH, Ekbom T *et al* (1999). Randomized trial of old and new antihypertensive drug in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet* **354:** 1751–6.
76. Heart Outcome Prevention Evaluation (HOPE) study investigators (2000). Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO HOPE substudy. *Lancet* **255:** 253–9.
77. Pyorala K, Pederson TR, Kjekshus J *et al* (1997). Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. *Diabetes Care* **20:** 614–20.
78. Sacks FM, Pfeffer MA, Moye LA *et al* (1996). The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* **335:** 1001-9.
79. Goldberg RB, Mellies MJ, Sacks FM *et al* (1998). Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent (CARE) trial. The Care investigators. *Circulation* **98:** 2513–9.
80. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group (1998). Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* **339:** 1349–57.
81. Koskinen P, Manttari M, Manninen V *et al* (1992). Coronary heart disease incidence in NIDDM patients in the Helsinki Heart Study. *Diabetes Care* **15:** 820–5.
82. Rubins HB, Robins SJ, Collins D *et al.* (1999). Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High- Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med* **341:** 4108–11.
83. Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: the Bezafibrate Infarction Prevention (BIP) study (2000). *Circulation.* **102:** 21–7.
84. Sacco M, Pellegrini F, Roncaglioni MC *et al* (2003). Primary prevention of cardiovascular events with low-dose aspirin and vitamin E in type 2 diabetic patients: results of the Primary Prevention Project (PPP) Trial. Di*abetes Care* **26:** 3264-3272.
85. Lonn E, Yusuf S, Arnold MJ *et al* (2006). Homocystein lowering with folic acid and B vitamins in vascular disease, The Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators. *New Eng J Med* **354:**1567-1577.
86. Manchanda SC, Narang R, Reddy KS *et al* (1998). Coronary atherosclerotic reversal potential of yoga lifestyle intervention. *In:* Coronary Artery Disease in Indians. Sethi K*K* (ed). 177–187.