*Review*

# PANDEMIC TRENDS IN PREVALENCE OF DIABETES MELLITUS AND ASSOCIATED CORONARY HEART DISEASE IN INDIA – THEIR CAUSES AND PREVENTION.

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## ABSTRACT

The increasing trend of diabetes mellitus (DM) in India has become a major health problem. This is also true for the rising magnitude of associated coronary heart disease (CHD). In the last 25 years both have acquired pandemic forms, particularly in the urban areas. The comparative studies conducted in various regions of India till date have been reviewed and they support this trend. The studies on the migrant population of Indians to various countries show significant increase in the prevalence of diabetes as compared to the native or other migrant populations in the same country. The findings and importance of impaired glucose tolerance has been emphasized. The possible causes of the above increases have been described and India-specific factors have been mentioned. Particular emphasis has been laid on new and emerging risk factors for control of CHD in Indian diabetics. The role of modifiable and non-modifiable risk factors has been analyzed. To curb the future rise of the magnitude of these pandemics the preventive measures for both have been elaborately described.

**KEY WORDS:** Pandemic, Epidemic; Risk factors for diabetes and coronary heat disease.

## INTRODUCTION

It is well known that the prevalence of type 2 diabetes mellitus (DM) is rising globally but its impact is most marked in developing countries like India. Some of the important risk factors associated with diabetes are mostly similar in all countries but their expression and intensities vary widely between races, regions and countries. Asian Indians have a racial predisposition and other unique risk factors to develop DM to a greater extent. In India there is increasing urbanization and industrialization which has led to physical inactivity, sedentary lifestyle, psychosocial stress and obesity leading to progressive increase in prevalence of DM.

The current studies in India indicate that there is alarming rise in prevalence of diabetes which has gone beyond epidemic form to a pandemic one. To elaborate this situation we should understand the difference between epidemic and pandemic occurrence of a disease. Epidemic of a disease usually indicates an 'unusual' occurrence in a community or region of a disease which is clearly in excess of expected occurrence, while pandemic of a disease denotes an epidemic usually affecting large population, occurring over a wide geographic area, section, or entire nation (1). With this definition, DM in India has now acquired a pandemic form.

## PREVALENCE OF DM

The World Health Organization (WHO) (2,3) 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, very disturbing estimates have been reported by International Diabetes Federation and WHO, that in the year 2002, at least 177 million people are having DM worldwide, which indicates that previous estimate of 225 million by 2010 is an underestimate (4). As shown in Table 1 the greatest increase will

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be in India from 19.4 million to 57.2 million, while in China from 16 million to 37.6 million and USA from 13.9 million to 21.9 million during the same period, unless effective preventive measures are implemented to curb this enormous increase. Currently India has got the largest number of diabetics and is being called as diabetic capital of the world. In table–1 this number has been compared with the number of diabetics in other countries having large number of diabetics.

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. 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 1970' s, the methodology was somewhat standardized and the prevalence studies became more uniform. Most of these studies from 1938 to 1978 have been listed in Table 2 and studies from 1979 to 2001 in table 3.

**Table 1: Top Ten Countries for their Estimated Number of Adults with Daibetes (in Millions) (3)**

| | Country | Year 1995 | Country | Year 2025 |
|---|---|---|---|---|
| 1. | India | 19.4 | India | 57.2 |
| 2. | 4China | 16.0 | China | 37.6 |
| 3. | U.S.A | 13.9 | U.S.A | 21.9 |
| 4. | Russian Federation | 8.9 | Pakistan | 14.5 |
| 5. | Japan | 6.3 | Indonesia | 12.4 |
| 6. | Brazil | 4.9 | Russian Federation | 12.2 |
| 7. | Indonesia | 4.5 | Mexico | 11.7 |
| 8. | Pakistan | 4.3 | Brazil | 11.6 |
| 9. | Mexico | 3.8 | Egypt | 8.8 |
| 10. | Ukraine | 3.6 | Japan | 8.5 |
| All other Countries | | 49.7 | | 103.6 |
| Total | | 135.3 | | 300.0 |

**Table 2: Studies of Prevalence of DM in India from 1938 to 1978.**

| YEAR | AUTOHOR | PLACE | AGE (YEARS) | TEST USED | PREVALENCE RATE(%) |
|---|---|---|---|---|---|
| 1938 | Chakravarty | Calcutta | > 5 | U | 0.73 |
| 1959 | Patel et al | Mumbai | All ages | B | 0.98 |
| 1963 | Patel et al | Mumbai | All ages | | 2.36 |
| 1964 | Ganguli et al | Lucknow | > 20 | B | 2.3 |
| 1964 | Vaishnava et al | Vellore | All ages | B | 2.56 |
| 1965 | Ramadwar D.K | Nagpur | > 20 | B | 2.4 |
| 1966 | Berry et al | Chandigarh | > 15 | U | 1.53 |
| 1966 | Sainani et al | Mumbai | All ages | B | 2.24 |
| 1966 | Saroj kumari | New Delhi | - | U | 2.26 |
| 1966 | Satyanarayan | Hyderabad | > 20 | U | 4.12 |
| 1966 | Shanker et al | Hubli | All ages | U | 2.20 |
| 1966 | Ahuja et al | Delhi | All ages | U | 9.4 |
| 1966 | Vishwanathan | Madras | > 20 | U | 11.3 |
| 1966 | Misra et al | Jabalpur | All ages | B | 1.70 |
| 1966 | Pai et al | Trivandrum | > 20 | U | 8.7 |
| 1966 | Gour K.N. | Varanasi | > 10 | U | 2.7 |
| 1966 | Datta et al | Pondichery | All ages | U | 0.70 |
| 1968 | Ajgoankar S.S | Mumbai | > 15 | B | 2.5 |
| 1970 | Gupta et al | | > 15 | B & U | 1.67 |
| 1970 | Moses | Ahmedabad | Adults | B & U | 3.8 |
| 1970 | Tripathi et al | Madras | > 15 | U | 12.67 |
| 1971 | Tripathi et al | Cuttack | > 10 | B | 1.2 (Ur) |
| 1972 | Ahuja et al | Cuttack | > 15 | B | 2.3 (Ur) |
| 1972 | Jaya Rao | New Delhi | > 20 | B & U | 2.4 |
| 1973 | Mukherjee A.B. | Hyderabad | All ages | GTT | 0.7 |
| 1973 | Parmoshware | Calcutta | > 5 | B | 0.81 |
| 1975 | Gupta O.P. | Bangalore | > 15 | U | 2.16 |
| 1975 | Mutallik | Ahmedabad | > 15 | B & U | 1.48 |
| 1975 | Pai et al | Poona | > 15 | B & U | 1.81 |
| 1975 | Tripathi B B | Trivandrum | > 15 | B & U | 1.40 |
| 1975 | Chhetri et al | Cuttack | > 15 | B & U | 1.63 |
| 1978 | Gupta et al | Calcutta | > 15 | B & U | 3.8 (Ur) |
| | | Ahmedabad | | B & U | 1.93 (R) |

*B- blood glucose; U-urine glucose; GTT- Glucose tolerance test; Ur-Urban; R-rural*

The above studies were conducted in urban or in rural and urban populations of one particular region, which did not reflect true prevalence for the entire country. In 1978 ICMR organized a multicentric urban and rural diabetes prevalence study on a computerized, centrally designed uniform proforma in six cities located in different regions of the country. In 2001, Ramachandran et al reported a similar study, also in six cities located in different regions of the country. These two studies have been compared in Table 4.

**Table 3: Studies of Prevalence of DM in India from 1979 till 2001.**

| YEAR | AUTHOR | PLACE | PREVALENCE RATE(%) |
|---|---|---|---|
| 1979 | Johnson et al | Madurai | 0.5 (U) |
| 1984 | Murthy et al | Tenali | 4.7 (U) |
| 1986 | Patel J.C. | Bhadran | 3.8 (R) |
| 1988 | Ramachandran et al | Kudremukh | 5.0 (U) |
| 1989 | Kodali et al | Gangarathi | 2.2 (R) |
| 1989 | Rao et al | Eluru | 1.6 (R) |
| 1991 | Ahuja et al | New Delhi | 6.7 (R) |
| 1992 | Ramachandran et al | Madras | 8.2 (U) |
| 1997 | Ramachandran et al | Madras | 2.4 (R) |
| 1999 | Ashabai et al | Chennai | 11.6 (U) |
| 2000 | Ramachandran et al (DESI) | National | 17.4 (U)<br>12.1 (U) |
| 2001 | Misra et al | Northern India | 10.3<br>15.2 (IFG) |

*U = Urban, R = Rural, IFG = Impaired Fasting Glucose, DESI = Diabetes Epidemic Study in India.*

**Table 4: Increasing Trend of Prevalence of DM in India : Comparison between ICMR Study (1978 – Urban Only (5)) and National Urban Diabetes Survey 2001-NUDS (6).**

| City | Region | Prevalence (%) Year 1978 | Year 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 |

From the above table it will be seen that the prevalence rate of diabetes in urban population of four major regions of India has increased from 0.9 - 3.8% in 1978 to 9.5 – 13.5% in 2001. This indicates enormous increase in prevalence rate in urban areas within 23 years in different regions of India. However, the reports in 2001 from prevalence of diabetes in India study (PODIS–(7) unpublished data) indicate comparatively low prevalence of diabetes in different regions. The results of this study given below are at variance as compared to other studies up to this period Table 5.

**Table 5: Showing the Prevalence of Diabetes in India Study and Impaired Fasting Glucose (IFG) in Different Regions of India (7).***

| | DM | | | IFG | | |
|---|---|---|---|---|---|---|
| Region | Urban | Rural | Total | Urban | Rural | Total |
| West | 5.91 | 2.48 | 4.28 | 6.12 | 2.87 | 4.62 |
| South | 5.67 | 2.08 | 4.11 | 6.90 | 2.81 | 4.94 |
| East | 3.36 | 1.53 | 2.51 | 3.01 | 1.87 | 2.47 |
| North | 4.84 | 1.58 | 3.27 | 4.82 | 2.87 | 3.86 |
| Central | 3.20 | 152 | 2.39 | 2.89 | 1.19 | 2.07 |
| All India | 4.75 | 1.87 | 3.37 | 4.89 | 2.37 | 3.68 |

**All values in percentages.*

## 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. As mentioned in Table 6, in United Kingdom (U.K), Asian Indian men had four times higher prevalence of diabetes than their British counterparts (8). 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 (8, 9). The possible (DESI) explanation could be the effects of environmental factors like psychological stress, lifestyle changes, acquired obesity and thrifty phenotype situation.

**Table 6 : Studies on Prevalence in Migrant Indians in Different Countries**

| Country | Year | Age | Prevalence | Population Screened |
|---|---|---|---|---|
| UK | 1990 | > 20 | M/F 11.2 /8.9 | Asians (Mostly Punjabi) |
| | | | | Europeans |
| | | | 2.8 / 4.3 | Bhatia Community |
| 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 | Malays |
| | | | 10.1 | Chinese |
| | | | 7.7 | |
| South Africa | 1994 | > 25 | 9.1 | Bhatia Community |
| USA | 1991 | > 15 | 9.1 | Bhatia Community |

## Prevalence in Migrant Indians in Different Countries

*Impaired Glucose Tolerance*

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 (10). 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 (11). 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 (6).

Laying emphasis on impaired fasting glucose (IFG), in another study, Misra et al have reported higher prevalence of IFG as 15.2% than that of DM (10.3%) in the same population (12).

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 7 and 8.

**Table 7: Global Major Risk Factors for Type 2 DM (American Diabetes Association) (13).**

- Family history of DM (Parents or siblings with DM).
- Race, ethnicity.
- Obesity (20% over desired bodyweight or body mass index > 24 ($kg/m^2$).
- 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

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**Table 8: Additional Indicators for High Risk of Type 2 DM in India (14).**

- 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 atherosclerosis.
- Stress hyperglycemia.
- 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).

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 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 fast foods. As emphasized earlier, there has also been progressive urbanization, industrialization and modernization. It has been reported that increase in stress is accompanied by

the various changes mentioned above which lead to burden the neuro-endocrine system, increasing the risk for developing type 2 DM. These factors affect Indian population comparatively at younger age, particularly so in males.

## 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 (17). 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 millions by the year 2020 as shown in Fig 1.

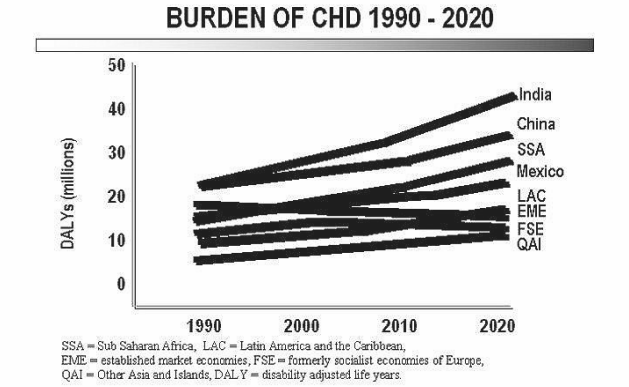


**Fig 1 : Projection of Prevalence of CHD in Developing Contries**

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Since 1960, 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 populations and not in diabetics. Table 9 illustrates the prevalence of CHD in India from 1960 onwards.

As seen from table 9, 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 (18, 19). However, in rural population there has been increase in CHD prevalence from 1.69% (1988) to 3.53% (1995) except for high prevalence reported in Kerala (7.43%).

**Table 9: Prevalence of CHD in Urban and Rural India.**

| Urban Population | | | | | |
|---|---|---|---|---|---|
| **Author** | **Year** | **Age Group (Years)** | **Place** | **Sample size** | **CHD(%±SD)** |
| 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 ± 0.6 |
| 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 | 35-64 | New Delhi | | 10.9 |
| Gupta R | 1995 | 20-80 | Jaipur | 2212 | 7.59 ± 0.6 |
| Singh RB | 1995 | 20-70 | Morabadad | 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 | ≥20 | Jaipur | 1123 | 7.30 |
| **Rural Population** | | | | | |
| **Author** | **Year** | **Age Group (Years)** | **Place** | **Sample size** | **CHD(%±SD)** |
| Dewan 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 | U.P | 162 | 3.09 ± 1.4 |

## 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 nondiabetic population. This was first reported from Framingham study (see table 10, Figures are per 1000) which indicated higher prevalence of CHD in male diabetics (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 (19).

**Table 10: 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 |

Similar studies of prevalence of CHD in diabetics have been conducted in India as given in Table 11.

**Table 11: Prevalence of CHD in Diabetes in India**

| Author | Year | Place | Prevalence of CHD (%) |
|---|---|---|---|
| I C M R * | 1984-87 | Multicentric | Male 8.1% Female 4.7% |
| A. Ramchandran | 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 | 20.2%Males 26.1%Females |

*I C M R * : Indian Council for Medical Research: P O D I S **: Prevalence of Diabetes in Indian Study*

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 shows comparatively low figure of 4.5% of CHD because the study was conducted only in newly detected diabetics (7).

Ramachandran in 1998 (20) 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 (21) 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% (22) and Phatak SR (personal communication) as 23.2% which are comparable to the reports of Mohan et al. Several studies have reported (15) 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 (16).

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 CHD in Indians.

Gupta R. (unpublished work) has reported that there is high prevalence of various conventional risk factors in his Jaipur Heart Watch – 2 study. 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 (18). 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 (17).

**Table 12: Conventional Risk Factors for CHD (23).**

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

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 to the acceleration 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 will be desirable to discuss them

under the modifiable and non modifiable subgroups given below.

### *Non Modifiable Risk Factors*

*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%) (21).

*2. Age at Onset*

Diabetes as well as IGT is seen about a decade earlier in Indians. As we know that vascular complications are related to duration of uncontrolled hyperglycemia. Indians developing IGT/DM at earlier age (25) are therefore, exposed to hyperglycemia 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 (26). Premenopausal women with diabetes face a similar risk of developing CHD as nondiabetic men of the same age. Following an myocardial infarction (MI), diabetic women have double the rate of recurrence and shorter survival than men (26).

### *Modifiable/Preventable Risk Factors:*

*1) Hyperglycemia 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 hyperglycemia 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 (27-33). 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 $HbA_1c$. The United Kingdom Prospective Diabetes Study (UKPDS) data also indicate that with each 1% rise in $HbA_1c$, the incidence of MI rose by about 14%. Moreover, recent data suggest that people with even IGT have increased risk of CHD (34-39). The clock of CHD actually starts ticking before the onset of actual clinical diabetes (85). These observations support the hypothesis that lowering the glucose to levels within the normal range may prevent/postpone CHD.

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 (21).

**Table 13: New and Emerging Risk Factors for CHD in Indians (23).**

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

In the study of complications in newly diagnosed diabetics in India (CINDI - unpublished data) 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 (unpublished work) 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 (40) 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 (41). Similarly Ramachandran et al have reported the prevalence of hypertension in diabetics as 29.3% as compared to non diabetics 24.4% (42).The study of (Gupta A. unpublished work) also shows higher prevalence of hypertension in diabetics (73.1%) as compared to non diabetics (32.4%). However in freshly detected diabetics, CINDI study (unpublished data) 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 risk of CHD mortality or morbidity (43). The clinical proteinuria consistent with diabetic nephropathy increases the CHD risk greater than twofold (44, 45).

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 (46) 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 have reported higher Lp(a) levels in Asian Indians as compared to native population(17). These studies include (i) Coronary Artery Disease in Indians (CADI) (30 mg/dl) (47) (ii) Study of Health Assessment and Risk Factors in Ethnic groups (SHARE) (39.1 mg/dl) (48) and (iii) Study from Singapore (2 times higher in Indians than Malays and Chinese) (24).

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 (49).

7) *Fibrinogen Levels:* Fibrinogen has been reported to be an independent risk factor for myocardial infarction and CHD mortality, (50) 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 (51). Deepa et al in South Indian males reported higher levels of fibrinogen in patients with CHD (both with and without diabetes) (52). 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 R and Mohan V have also not found an association between elevated homocystein levels and CHD in south Indian males with or without diabetes (53). Similarly Baxi H et al. (Personal communication) have also not found any relationship between homocystein levels and CHD in western part of India in patients with and 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) (82) had suggested that carotid intima media thickness (IMT) and arterial stiffness are clear markers of CHD risk. The study of Japanese subjects had also supported this new hypothesis (83). Ravikumar and Mohan 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 (84) hence these are considered as risk factors for the development of CHD.

## PREVENTION OF DIABETES

As mentioned earlier, the number of people with diabetes in India will increase threefold 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 (54). It also helps to reduce the risk of CHD, hypertension and comorbid conditions. However, implementation of this approach in our country may not be feasible in view of large area, enormous population and high rate of illiteracy. It is suggested that as diabetes is a familial disease, marriages between two diabetics or having strong family history of diabetes should be discouraged.

Under the circumstances attention should be focused on high risk individuals as like population at greatest risk of developing type 2 DM ; such as (1) Overweight persons, B M I > 26 $kg/m^2$ or waist circumference > 90 cm for men > 85 cm for women. (2) Persons with IGT (3) Women with a past history of gestational diabetes.

## Primary Prevention in High Risk Individuals

The evidence, accumulated from various studies notably the Diabetes Prevention Program (DPP) (55, 56) 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 program 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 (57).

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

(1) Make healthy foods (vegetables, fruits, legumes, cereals) 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 with tobacco products. (3) Ensure that there are open spaces in our cities for sports and outdoor activities and that our streets 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 intake, 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 are 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 (58, 59). Systolic blood pressure reduction by 5 to 10 mm Hg results in 20 – 30 % risk reduction in CHD events in diabetics (60-65) especially when drugs like angiotensin converting enzyme (ACE) inhibitors, diuretics, beta blockers or calcium channel blockers (CCB) are used. Some (66-68) but not all (69, 70) 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 (71). Elevated levels of LDL-C have been universally accepted as major risk factor for CHD in general population and more so in diabetics. Although trials conducted specifically in patients with diabetes are lacking, yet 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% (72-75). Similarly "fibrates" by reducing triglyceride and increasing HDL levels also reduce the risk of CHD events. (76-78). Moreover, aspirin therapy (75 to 325 mg/day) is also shown to reduce the risk of these events in high

risk people with DM (79, 80). 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 (17).

## 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 (81) has been found to have favorable 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.

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