

REVIEW OF THE LITERATURE



Paul Langerhans – insulin-producing
B-cells form the major endocrine
component of the islets



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Physician and scientist

REVIEW OF LITERATURE

OUTLINE OF THE CHAPTER		PAGE NO
1.	History of diabetes in ancient time	XXIII
2.	Prevalence of diabetes mellitus type 2	XXIV
3.	Pre diabetes symptom of diabetes mellitus type 2	XXV
4.	Risk factors of diabetes mellitus type 2	XXV
5.	Indian diabetic risk score	XXXIV
6.	Complication of diabetes mellitus type 2	XXXV
7.	diabetes mellitus type 2 care expenditure	XXXVIII

REVIEW OF LITERATURE

1. HISTORY OF DIABETES IN ANCIENT TIME

Diabetes in India has a long history since ancient time. The oldest reference of this disease dates back to more than 4500 years. The name of the disease found in “Devik Yuga” tell it has been known and treated by Indian long ago. It has been mentioned in (Chakradatta, Rasayana Chapter, Sloga 195) that Lord Shiva has dictated a formulation for the treatment of prameha to his son Lord Ganesha. Another view claims that Lord Ganesha was afflicted by prameha because of his eating and working habits like taking lots of sweets (modaka) and sitting in same place for which his father gave him the formulation named Shiva Gutika to rectify the disorder (Shah VK,2001).

1.1 Charaka Samhita (1500 BC)

The literary meaning of prameha is “Pra” means excess, “Meha” means urine, it has been classified into 20 types under which madhumeha (diabetes mellitus) is one of the classification, which means madhu-honey and meha-urine, in charaka samhita. Charaka Samhita has described the disease Prameha (pra-excess,meha-urine) in nidana sthana (chapter deals with aetiology, symptoms and pathogenesis) and chikitsa sthana (chapter deal with treatment aspects) , the period of this samhita is fixed by historians is about 1500 years BC. In charaka samhita prameha (urinary disorder) is classified into 20 types according to dosas involved, in which madhumeha (diabetes mellitus) one of the classification is characterised by excess urination, which is sweet and turbid in nature. It is said that all the 20 type of prameha if not treated will lead to madhumeha. The hereditary nature of the disease is also described in this samhita, which shows that Indians knew the disease and its management since ancient time.

1.2 Sushruta Samhita(10th century BC)

Sushruta samhita described 20 different diseased of urine called prameha, as described by Charaka (*SS-sushruta samhita*).After Charaka and Sushruta, many acharyas had written texts and commentary based on these two texts and other texts. Vagbhatta, the author of astanga hrdaya and Astanga sangraha has added new herbal

and herbo-mineral combination for the treatment of prameha and so there was a gradual growth in the system of medicine till the 16th century AD.

1.3 Prameha Nidanam (aetiology)

Prameha is mainly caused due to increase in kapha dosa that produces excess kleda (body fluid) in the body. The factors, which may increase kapha are considered as the causative factor for prameha. It is mentioned in AH, Nidanasthana, sloka 1b-3 that foods, drinks and activities that increase medas (fat), mutra (urine) and kapha are considered as the main causes. Thus intake of excess milk, curd, jiggery, sugar, and meat of animals from marshland, cereals that are less than a year old and recently distilled alcohol, laziness, excessive sleep, inactivity all these increase kapha in the body, which may lead to prameha. A study has proved the above-mentioned statement that People who enjoy the happiness of life with better living conditions with highly sedentary habits, excessive use of certain food items like curd, milk, etc. and lack of exercise are more prone to become victims of madhumeha (Incidence of Madhumeha, 1998).

1.4 Classification of Prameha in Ayurvedic

Two varieties of Prameha are described:

- (1) Sahaj (Genetic), which is a genetically transmitted disorder, carried on to next generation by defects in the sperm and ova.
- (2) Apathyannimitaja (Acquired), which arises as a result of improper diet and activity.

2. PREVALENCE OF DIABETES MELLITUS TYPE 2

Everyone knows someone who has diabetes mellitus type 2. Diabetes mellitus type 2 formerly known as non-insulin-dependent diabetes mellitus (NIDDM). Diabetes mellitus type 2 used to occur mainly in elders who were obese and older more than 40 years. Approximately 85 to 95% cases of all diabetes are diabetes mellitus type 2. (King H *et al*, 1998) reported that the impact of DMT2 will remain centred in the developing countries, since by the year 2025, 75% of all people with diabetes will be in the developing countries, as compared by 62% in 1995- a majority in the Indian subcontinent (59%) and china (68%).

Huizinga M M *et al* (2006) reported that the prevalence of diabetes is rapidly rising all over the world at an alarming rate. Sadikot SM *et al* (2004) reported that there have been several studies from various parts of India, revealing a rising trend in the prevalence of diabetes mellitus type 2 in the urban population. Indian Council of Medical Research (ICMR) and Ahuja MM (1979) reported that the prevalence of diabetes to be 2.3% in the urban and 1.5% in the rural area. A series of studies of Ramachandran A (2002) showed that the percentage of adult urban subjects affected had increased from 5.2% in 1984 to 8.2% in 1989, 11.6% in 1995 and 13.9% in 2000 and Mohan V (2006) reported that which further increased to 14.3% in 2004. Ramachandran A (2001) and National Urban Survey in 2000 showed that the prevalence of diabetes in urban India was 12.1% in subject aged > 20years. Mohan V *et al* (2008) reported that In India, multicentric studies showed prevalence of diabetes as 5.4% urban and 3.4% rural in 2004.

The urban population exposed to a high fat, refined diet, sedentary habits, lack of physical exercise, obesity, addiction, and stressful behaviour, etc. These explain the high prevalence of diabetes. Abu SM *et al*(1997), Mbanya JC *et al*(1997) and Mohan V *et al* (2001) has studied that In developing countries, the prevalence of diabetes is lower among those with a low income than among more affluent groups . Mohan V *et al* (2001) has studied the impact of urbanization on the prevalence of diabetes in India is clearly shown in the CUPS study. The higher socioeconomic status (SES) group had two-fold higher prevalence of diabetes compared to the lower socioeconomic group.

Connolly N *et al* (2000) and Brancati FL *et al* (1996) studied that In the developed countries, most studies suggest that higher prevalence of type 2 diabetes, associated risk factors and diabetic complication rates vary inversely with socio-economic status i.e., in the lower SES population. Helmert U *et al* (1990) and Feinstein JS *et al* (1993) reported that the reason for the higher prevalence of type 2 diabetes among subjects with lower socio-economic status could be unhealthy life style, nutritional inadequacies and psychological stress. Malmstrom M *et al* (1999) studied that an increased rate of obesity, smoking and physical inactivity in socially deprived areas.

Hettihewa ML *et al* (2005) reported that early identification is an important tool for the management of diabetes, as insulin resistance or relative insulin deficiency may

lead to diverse complications of diabetes. Hoskote S *et al* (2008) studied that a better understanding about the cause of a predisposition of Indians to get T2DM is necessary for future planning of healthcare, policy and delivery in order to ensure that the burdens of disease are addressed.

Venkataraman K *et al* (2009) reported that over the past 30 years, the status of diabetes has changed from mild disorder to one of the major causes of morbidity and mortality affecting the youth and middle aged people in India leading to 109 thousand deaths in 2004, 1.157 million years of life lost in 2004. And ICMR (2006) reported that 2.263 million disability adjusted life years (DALYs) in India during 2004. Hoskote S *et al* (2008) studied that the impacts of T2DM are considerable as a lifelong disease; it increases morbidity and mortality and decreases the quality.

3. PRE DIABETIC SYMTOMS OF DIABETES MELLITUS TYPE 2

Some patients show no symptoms at all. Patients may feel very tired, thirsty, or nauseated and have to urinate often. Weight loss, blurred vision, frequent infections, and slow healing of wounds or sores are other symptoms. Some female have with vaginal yeast infection or burning on urination due to yeast infection.

Physical signs of insulin resistance include acanthosis nigricans, where the skin around the neck or in the armpits appears dark and thick. Female can have polycystic ovary syndrome with infrequent or absent periods, and excess hair and acne. Arslanian S (2002) mentioned that the peak age at which youth present with type 2 diabetes mellitus is in midpuberty about 13.5 year in youth. The genesis of syndrome X is in childhood as early as 8 years of age. Acanthosis nigricans a marker of insulin resistance is frequently associated finding in up to 90% of youth with type 2 diabetes mellitus.

4. RISK FACTORS OF DIABETES MELLITUS TYPE 2

Epidemiological studies conducted over the years have identified several risk factors associated with diabetes. These risk variables are similar across all countries but their expression and intensity vary widely among the population.

Gadsby R (2002) has reported different risk factors involve type 2 diabetes. Those are increased of age, gender, country and place of residence, ethnicity, socioeconomic status, lifestyle (physical inactivity & diet) and obesity. Kumar and Clark *et al* (2005) studied that diet and physical exercise have a marked effect in deferring the onset of type2 diabetes. Kumar C *et al* (2005) studied that the four major determinants for development of typt-2 diabetes mellitus are increase in age, obesity, ethnicity and family history. Permutt MA *et al* (2005) reported that it occurs when impaired insulin effectiveness (insulin resistance) is accompanied by the failure to produce sufficient - cell insulin. Deo S *et al* (2006), Sadikot S *et al* (2004) and Ramchandran A *et al* (2003) are studied that there was no significant gender difference in prevalence of diabetes. Park K *et al* (2007) studied that Diabetes Mellitus is multifactorial disease main risk factors include modifiable variables like Body Mass Index (BMI), physical inactivity, diet, infections and non-modifiable variables like age, family history of Diabetes Mellitus. Gupta R *et al* (2008) also reported that its pathogenesis appears to involve complex interactions between genetic and environmental factors.

Gupta R *et al* (2008) studied that T2DM is a non-autoimmune, complex, heterogeneous and polygenic metabolic disease condition in which the body fails to produce enough insulin, characterized by abnormal glucose homeostasis. Ripsin C *et al* (2009) reported that the incidence of diabetes type 2 increases with increasing age, obesity and lifestyle.

4.1 Obesity risk factor

Berger M (1992) reported that the synchrony of obesity and type 2 diabetes is so obvious that a term ‘diabesity’ has been coined that suggests a striking interrelationship between the two diseases.

Singh KD *et al* (2000) proposed that BMI not 25 kg/m² but 22.3 kg/m² should be applied as a cut off for defining obesity as a risk for developing NIDDM in Punjabi. The percentage of individuals above BMI 22.3 kg/m² in the present study is 76%, thus indicating that majority of the Punjabi patients having NIDDM are obese. Punjabi female diabetics are highly obese with a higher waist circumference indicating high levels of visceral obesity and the cause whether is genetic, environmental or habitual is yet to be discovered.

Ramachandran A *et al* (2002) reported that there is also a probable indication that there is a preferential abdominal adiposity in Indians irrespective of the degree of general adiposity.

Ganong W (2005) reported that obesity is the most common nutritional problem is measured with the indicator of body mass index (BMI). As body weight increases, insulin resistance also increases, which decreases the ability of insulin to move glucose into fat and muscle and to shut off glucose release from the liver and weight reduction decreases insulin resistance.

Khan SE *et al* (2006) reported that in obese individuals, adipose tissue releases increased amounts of non-stratified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of insulin resistance.

Shai I *et al* (2006) reported that obesity is also considered a key risk factor for T2DM. The association between increasing body mass index (BMI) and greater weight gain and risk of diabetes is most pronounced among Asians, suggesting that lower cut off BMI values are needed to identify Asians at a higher risk of diabetes.

David G *et al* (2011) reported that Excess body fat is associated with 30% of cases of diabetes in those of Chinese and Japanese descent, 60-80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders.

4.2 BMI risk factor

Ramchandran A *et al* (2003, 2008) studies reported independent predictor nature of BMI for development of diabetes. Block JP *et al* (2004) and Ogden CL *et al* (2006) studied that According to World Health Organization estimates, ≈ 1.6 billion adults worldwide were overweight (body mass index [BMI] ≥ 25 kg/m²) and at least 400 million were obese (BMI ≥ 30 kg/m²) in 2005. These numbers are expected to reach 2.3 billion and 700 million, respectively, by 2015. The percentage of overweight and obese adults increased markedly from 47% and 15% in 1976 to 1980 to $>66\%$ and 33% in 2005 to 2006, with the greatest proportion of increase seen among the individuals studied.

Ganong *et al* (2005) had reported that BMI is normal from 18.5 to 24.9kg/m², more than 25kg/m² is called overweight and above 30kg/m² is called obese.

Mohan V *et al* (2007) studied that BMI cut point for Indians for any cardio metabolic risk factors is 23 kg/m² in both sexes.

Sumanth MM *et al* (2012) study also reported significantly lower age of onset among those with higher BMI.

Sumanth MM *et al* (2012), Snehalatha C *et al* (2003), Zargar A *et al* (2000) and Sayeed M *et al* (1995) study also supported the evidence that among Asians, even at lower BMI, there was higher odds of diabetes (adjusted OR 2.2). Hence early identification of high BMI, would give opportunity for primary prevention and early diagnosis of the diabetes. Also, it would suggest that Indians, especially, have to maintain lower BMI to prevent diabetes. Sumanth MM *et al* (2012) studied showed that BMI is a significant independent predictor of development of diabetes.

This signifies the importance of surveillance for those with higher BMI. Several explanations have been given related to obesity and diabetes.

4.3 Physical activities

Burchfiel CM *et al* (1995) and Wei M (1999) reported that Physical inactivity has emerged in epidemiological studies as an independent risk factor for type 2 diabetes. Observational studies and intervention trials have shown a beneficial effect of regular exercise on both insulin resistance and glucose intolerance.

Hu FB *et al* (2001) reported that the majority of cases of type 2 diabetes could be prevented by weight loss, regular exercise, modification of diet, abstinence from smoking, and the consumption of limited amounts of alcohol. Weight control would appear to offer the greatest benefit.

Tuomilehto J *et al* (2001) reported that the changes in lifestyle was not only improved glucose tolerance but also reduced the magnitude of several other cardiovascular risk factors. It may prevent or postpone the onset of type 2 diabetes and the complications related to the disease.

Ramachandran A *et al* (2003), Ramachandran A *et al* (2008) and Kokiwar P *et al* (2007) studied showed similar findings of significance of association of DM with physical activity.

Villegas R *et al* (2006) reported that physical activity, either from leisure-time exercise or daily activity reduces the risk of type 2 diabetes in women, supporting the current health promotion efforts encouraging both exercise and non-exercise activity levels.

Sumanth MM *et al* (2012) study also reported prevalence of diabetes decreased significantly as the physical activity level increased.

4.4 Age risk factor

Rosenbloom AL *et al* (1999), Dabelea D *et al* (1998) and Kitagawa T *et al* (1998) has studied that Type 2 diabetes mellitus not been considered a paediatric disease. However there has been an emerging epidemic of type 2 diabetes mellitus in children specifically adolescents who are obese and from minority population. The diabetes epidemic is accelerating in the developing world, with an increasing proportion of affected people in younger age groups. Recent reports describe type 2 diabetes be diagnose in the children and adolescents.

4.5 Genetics of diabetes mellitus type 2

Indians have a high risk for diabetes. Strong family history of the disease has been noted in the Indians and also in other Asian population. In India, nearly 75% of type 2 diabetic patients have first-degree family history of diabetes. The prevalence of diabetes increases with increasing family history of diabetes. The risk of the offspring developing diabetes with a parental history increases above 50% and it is around 40% if the patients have a diabetic sibling. Viswanathan M *et al* (1996) and Mohan V *et al* (1986) reported that Family history of diabetes with a high prevalence among first-degree relative and it seen through more than two generations is commonly seen in Asian Indians.

Mohan V *et al* (2007) studied that Genome wide association studies has catalogued around 20 genes (like TCF7L2, HHEX, CDKAL1, SLC30A8 etc) showing a strong association with T2DM.

4.6 Family history as a risk factor

Meigs J *et al* (2000) and Viswanathan M *et al* (1996) Studies also reported relatively higher risk with maternal history of diabetes. Velho G *et al* (2001) studied that Family

history could act through environmental as well as genetic mechanism. Environmentally there is a possibility of being exposed to similar diet, stress, physical activity, socio economic status etc. Genetic mechanism acts through specific genetic expressions. Sumanth MM *et al* (2012) studied also reported maternal history of diabetes to be stronger risk compared to paternal history of diabetes. Sumanth MM *et al* (2012) studied showed that odds of diabetes among those who had family history of diabetes (in terms of history of parental compared to paternal. When both parents were diabetic, the risk increased synergistically diabetes) were at 3.8-times compared those without family history of diabetes.

This would also infer that family history of diabetes could be important public health tool in predicting development of diabetes and hence could help in prevention of diabetes.

4.7 Sedentary lifestyle

Abate N *et al* (2001) studied that Changes in work patterns from heavy labour to sedentary, the increase in computerization and mechanization, and improved transport are just a few of the changes that have had an impact on human metabolism associated with it. Hu FB *et al* (2001, 2003) mentioned that a sedentary lifestyle (defined as hours of television watching and or having a sedentary occupation) was associated with a higher risk of type 2 diabetes in the Nurses' Health Study and the Health Professional Follow-up Study.

Life style intervention has shown effective significant changes over control in body weight and improving insulin sensitivity and that causes prevention of diabetes (American diabetes association 2005).

4.8 Hypertension

Gillow JT (1999) studied that In the UKPDS (United Kingdom Prospective Diabetes Study) 38% of the newly diagnosed patients with Type 2 diabetes had hypertension and in the years after diagnosis of type 2 diabetes, the prevalence of hypertension was higher than in the age matched general population. Deepa R *et al* (2003) mentioned about the Overall prevalence of hypertension in the non-diabetic Population was 16.7%, while diabetic subjects had a 3 Times higher prevalence of hypertension i.e. 46.7%.

4.9 Cardiovascular disease

Barba C *et al* concluded that Asians generally have a higher percentage of body fat than white people of the same age, sex, and BMI. Also, the proportion of Asian people with risk factors for type 2 diabetes mellitus and cardiovascular disease is substantial even below the existing WHO BMI cut-off point of 25 kg/m².

Bell DS *et al* (1994) reported that the people with diabetes have a 2-fold increased risk of stroke. Morrish NJ *et al* (2001) has studied that the age-adjusted mortality, mostly due to coronary heart disease (CHD) in many but not all populations, is 2-4 times higher than in the non-diabetic population. Saxena KK, (2002) reported that Framingham heart study (1974) demonstrated a direct association between diabetes and heart failure.

Surekha rani H *et al* (2005) Indians being more susceptible to coronary heart disease than any other ethnic group makes it necessary to implement measures for the management of dual epidemics. It is also necessary to initiate primary preventive measures like reduction in serum lipids, avoiding smoking, increasing the intake of fruits and vegetables, physical activity, maintenance of healthy body weight and secondary preventive measures like control of hyperglycaemia and hypertension to mitigate the devastating consequences of diabetes leading to CHD.

4.10 Diabetes mellitus and thyroid diseases

Zeidler A *et al* (1982) and Johnson JL *et al* (2002) reported that High prevalence rates of T2D and hypothyroidism have been reported in different populations, but the full impact of the development of these two metabolic abnormalities appears to be evolving.

Engler H *et al* (1992) reported Patients with T2D commonly display the symptoms of hypothyroidism, and symptoms of hyperthyroidism have been documented in patients with type 1 diabetes. Since there may be a link between diabetes and thyroid diseases, the American Diabetes Association (ADA) has proposed that people with diabetes be checked for thyroid disorders.

Patricia Wu *et al* (2000) reported that the female predominance of developing T2D and thyroid dysfunction simultaneously is 78.95% (30 out of 38). This finding

supports the higher-than-normal prevalence of these two major metabolic disorders at the same time in the female population.

Hanukoglu A *et al* (2003) studied diabetes and thyroid disorders have a propensity to appear together in patients.

Satish R *et al* (2003) reported that Diabetes mellitus and thyroid diseases are the two most common endocrinopathies seen in the adult population. Excess or deficiency of either insulin or thyroid hormones can result in functional abnormalities of one another, as both of them are closely involved in cellular metabolism.

Brix TH *et al* (2005) studied that thyroid autoimmunity is common in T2D female patients.

Thakkar NV *et al* (2011) observed a high prevalence of both disorders together in the female population of Gujarat. Hypothyroidism was the more commonly observed thyroid dysfunction in HT+DM patients; hyperthyroidism developed in only one patient with T2D.

4.11 Poly cystic ovary disease

Legro RS *et al* (1999) studied that PCOS women are at significantly increased risk for IGT and type 2 diabetes mellitus at all weights and at a young age; PCOS may be a more important risk factor than ethnicity or race for glucose intolerance in young women. The prevalence rates of glucose intolerance are similar in ethnically diverse populations of PCOS women. Although obesity and age substantially increase risk, IGT and diabetes can occur in young, non obese PCOS women. Fasting glucose levels are poor predictors of diabetes in PCOS women.

Dunaif A (1992), Franks S (1995), Knochenhauer ES (1998) reported that the Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of premenopausal Women. Dunaif A (1989) reported that PCOS women have profound insulin resistance independent of obesity.

Dunaif A (1992) reported that is secondary to a unique, apparently genetic, disorder of insulin action. Warram JH (1990) suggested that Insulin resistance is now recognized as a major risk factor for the development of type 2 diabetes mellitus.

Lillioja S *et al* (1993) reported that pancreatic b-cell dysfunction is a second important risk factor. And this abnormality is also found in PCOS. PCOS women would thus be predicted to be at an increased risk for type 2 diabetes mellitus.

5. INDIAN DIABETES RISK SCORE

V Mohan *et al* (2005) provided a simplified Indian Diabetes Risk Score for identifying undiagnosed diabetic subjects in India. The information for these risk factors can be obtained based on four simple questions and one anthropometric measurement namely waist circumference. The four questions are:

1. What is your age?
2. Do you have a family history of diabetes? If yes, does your father or mother or both have diabetes?
3. Do you exercise regularly?
4. How physically demanding is your work [occupation]?

Table 1 : shows Indian Diabetes Risk Score [IDRS]

Particulars	Score
Age (year) - <35	0
Age (year) - 35-49	20
Age (year) - ≥ 50	30
Abdominal obesity	
Waist <80 cm [female] , <90 [male]	0
Waist $\geq 80 - 89$ cm [female], $\geq 90 - 99$ cm[male]	10
Waist ≥ 90 cm [female] , ≥ 100 cm [male]	20
Physical activity	
Exercise [regular] + strenuous work	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

6. COMPLICATIONS OF DIABETES MELLITUS TYPE 2

Permutt MA *et al* (2005) studied that the burden of diabetes is to a large extent the consequence of macrovascular (coronary artery disease, peripheral vascular disease, and atherosclerosis) and microvascular (like retinopathy, neuropathy and nephropathy) complications of the disease.

6.1 Retinopathy

Kohner EM *et al* (1998) reported that Diabetic retinopathy can be present at the time of diagnosis of Type 2 diabetes mellitus due to insidious onset of the disease as shown in the United Kingdom Prospective Diabetes Study (UKPDS), which revealed that 39% of the men and 35% of women were having retinopathy at the time of diagnosis of diabetes. Kuzuya T *et al* (1994) reported that in developed countries, diabetes is one of the leading causes of visual impairment and blindness. Rema M *et al* (1996) studied that Type 2 diabetes mellitus patients and the study had shown that 34.1% diabetic subjects had evidence of retinopathy, this included 30.8% with non-proliferative diabetic retinopathy (NPDR) and 3.4% with proliferative diabetic retinopathy (PDR). Diabetic retinopathy can be present at the time of diagnosis of Type 2 diabetes mellitus due to insidious onset of the disease as shown in the United Kingdom Prospective Diabetes Study (UKPDS), which revealed that 39% of the men and 35% of women were having retinopathy at the time of diagnosis of diabetes. A distinctly lower prevalence rate of diabetic retinopathy is seen among south Indians as compared to the western population.

6.2 Nephropathy

American Diabetes Association (2002) reported that Diabetes is the leading cause of end stage renal failure in many populations in both developed and developing countries.

The Studied of John L *et al* (1991) show from the Vellore that the prevalence of nephropathy was 8.9% and the Chennai studied of Ramachandran A *et al* (1999) show the prevalence of nephropathy was 5.5%. which was very less when compared with studied of Samanta *et al* (1991) shows the prevalence of 22.3% in Asian Indians in the UK.

6.3 Coronary heart disease

Ramachandran A *et al* (1998) reported that the prevalence of CHD in Indians may be as high as in the migrant Indians. The prevalence of CHD indicated by major Q wave changes was found to be 3.9% which was similar to the prevalence in the Asian Indians in UK (4%) as shown by Mckeique *et al* (1991). Another 10.3% had other abnormal ECG changes. A similar prevalence of major Q waves changes was shown by Mohan *et al* 2001(2.1%), Chadha *et al* 1990(3.2%) and Gupta R *et al* 1998(2.8%). Prevalence of peripheral vascular disease (PVD) in Asian Indians was comparatively low in Indian patients shown by Mohan *et al* (overall 3.2%, 6.3% in diabetes) and also in our study (4.0%) compared to the white population which is probably due to younger age of our type 2 diabetic patients.

6.4 Foot ulcer (wood)

Diabetic foot infections are a major problem and a common cause for hospital admission of diabetic patients in India (Vijay V, 1999). Although the prevalence of PVD is low, neuropathy is very common and is an associated risk factor for foot infections, which often tend to recur.

Kapur A *et al* (1997) mentioned how clinical interactions between the doctor and patient can unwittingly create barriers to insulin. The authors of this study mention that patients often spoke of health care providers using insulin as a threat to promote behavioural changes, or as a punishment for failure to comply or as a bargaining tool in promising its withdrawal as a reward for behavioural change.

6.5 Hyperglycaemia

Kumar C *et al* (2005) reported that Duration and degree of hyperglycemia play a major role in production of complications.

Sinha S *et al* (2004) reported that Impairment of pulmonary diffusion Capacity for carbon monoxide was common in DM2 Asian Indian patients having microangiopathy. Pathophysiologically, it could be related to glycaemic control or dyslipidaemia. Srivastava BK *et al* (2005) reported that Hyperglycaemia along with hypertension increases the Risk of micro as well as macro vascular complications of Diabetes in Type 2 diabetic subjects. With judicious use of currently available anti-

hypertensive agents, it is quite possible to achieve normotensive levels in diabetic Subjects. Thus by the control of both of these risk factors, the complication of diabetes can be definitely minimized.

Statton IM *et al* (2000) suggested that even a modest reduction in glycaemia has the potential to prevent deaths from complications related to diabetes as cardiovascular and cerebrovascular disease account for 50-60% of all mortality in this and other diabetic populations. Individuals with very high concentrations of glycaemia would be most likely to benefit from reduction of glycaemia as they are particularly at risk from the complications of type 2 diabetes, but the data suggest that any improvement in glycaemia control across the diabetic range is likely to reduce the risk of diabetic complications.

6.6 Hypoglycaemia

The effect of intensive treatment of diabetes on the development and progression of the risk is three times greater in the group undertaking intensive therapy, in which the glucose targets were close to normal. The effect of intensive treatment of diabetes on the development and progression of it is apparent that impaired awareness of hypoglycaemia is a major risk factor for severe hypoglycaemia. In the DCCT, 36% of all episodes of severe hypoglycaemia occurred with no warning symptoms in patients who were awake. Impaired awareness of hypoglycaemia is common in people treated with insulin. While the chronic form of this acquired condition mainly affects those with type 1 diabetes, the risk also increases in people with progressive beta cell failure (insulin treated type- 2 diabetes). Vignesh JP *et al* (2004) reported that frequent Hypoglycemia in Type 2 diabetes, caused either by inappropriate treatment and or impaired counter-regulation, rapidly induces loss of symptoms and blunts the release of counter-regulatory hormones in response to hypoglycaemia. Asymptomatic hypoglycaemia can be diagnosed by routine Blood glucose monitoring and should alert the patient and Clinician to the possibility of developing impaired awareness of hypoglycaemia. Burge MR *et al* (1998) reported Fasting was well tolerated among these elderly patients with type 2 diabetes treated with sulfonylurea. Older age should not be considered a contraindication to sulfonylurea treatment for diabetes. Stimulation of epinephrine secretion at normal or elevated plasma glucose levels appears to be the primary mechanism of protection against hypoglycaemia in this

study. Pramming S *et al* (1991) has studied that the rates of hypoglycaemia rose as the duration and number of people treated with insulin therapy increased, with almost 50% of patients experiencing hypoglycaemia without warning symptoms after 25 years or more of treatment.

7. DIABETES MELLITUS TYPE 2 CARES EXPENDITURE

Kapur A *et al* (2001) reported that the economic loss due to lost man-days or lost economic opportunity.

Kapur A *et al* (2001), Zimmer P *et al* (2003) mentioned that mainly due to the high costs related with management of diabetes associated complications.

Rao MV *et al* (2002) studied that India has worked continuously to improve its health care system in recent decades and efforts have been made to expand the public health system and reduce the burden of disease, there remains no universal coverage.

Zimmer P *et al* (2003) reported that diabetic individuals compared to non diabetic individuals are more than twice as costly to treat.

V Mohan (2004) had conducted a study in families having type 2 diabetes in Chennai reported that a median figure of Rs. 4510 (US\$ 100) was spent annually for diabetes by the families and the median percentage of annual income spent on diabetes treatment was 22% for the entire group (59% - low SES group, 32% - middle SES group, 18% - upper middle income group and 12% - high-income group). The above estimates highlight the large differences in diabetes care expenditure between developing and developed countries.

Thus diabetes affecting the earning or active member of the family, affects not only that individual but might often have significant effect on the family.