Chapter – III

Review of Literature
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REVIEW OF LITERATURE

Many studies have not been made on health management particularly with reference to diabetes mellitus. Evidently it is in embryonic stage of development. Research in this areas is scanty and issues are not yet formulated and adopted coherently. However, some studies available on the issue afford us initial insights with respect to a few characteristics and traits exhibited by diabetes in India. An attempt has been made in this chapter to make a review of the studies on health management with special reference to diabetes mellitus. It is to be noted that interest in this topic arose only very recently.

Ramachandran et al. in their article on "High Prevalence of Diabetes in an Urban Population in South India" revealed that the peak prevalence of diabetes was in the group aged 55-64. A family history of diabetes was present in half of the subjects with diabetes. Diabetes was significantly related to obesity in women but not in men. The plasma glucose concentration two hours after glucose loading was correlated to body mass index, age, and income in both sexes. The prevalence of diabetes was significantly higher in subjects whose income was above the mean.

Obesity, abdominal fat distribution, and physical inactivity act similarly and independently as risk factors for non insulin – dependent diabetes mellitus (NIDDM) and impaired glucose tolerance (IGT) in Hindu and Muslim Asian Indians has been analysed by Dowse. Univariate data and multiple logistic regression models indicated that age, family history of diabetes, body mass index (BMI), waist-hip-ratio (WHR), and physical inactivity conveyed similar risk for NIDDM (and IGT) in each ethnic group. After adjusting for all

other factors, Hindu ethnicity conferred additional risk for NIDDM (but not IGT) in men, but in women there were no clear ethnic differences. Although BMI and WHR were independently significant risk factors, WHR conveyed relatively stronger risk for NIDDM than BMI in women, whereas the converse was true in men.

Ramachandran and others have assessed in their article, the prevalence of diabetes and impaired glucose tolerance (IGT) in the urban and rural elderly population in South India. Positive family history of diabetes, body mass index (BMI) sub scapular – to – triceps ratio, and waist-to-hip ratio were significantly associated with diabetes in the urban population. Only age and BMI showed significant association with diabetes in the elderly rural population. None of the tested parameters, except age in the urban subjects, showed association with IGT. This study highlights the high prevalence of glucose intolerance in elderly south Indians having low mean BMI. Although there was a two fold higher prevalence of diabetes in the urban area, the occurrence of IGT was similar in urban and rural populations.

Students from nine schools and one college in Madras City, were screened for diabetes by oral glucose tolerance test. The criteria recommended by the World Health Organization was adopted to classify glucose tolerance. Among 3,515 students, between 5 and 19 years of age, participated in this survey, 1982 (56.4 per cent) were males and 1.533 were (43.6 per cent) females. Family history of diabetes was positive in 302 (8.6 per cent) students. There was no overt case of diabetes of any type. Three (0.09 per cent) males had renal glycosuria. It is therefore concluded that insulin-dependent diabetes, non-insulin dependent diabetes or any other type of diabetes in the young is rare in South India.

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Until recently, the standard clinical practice of treating patients with type 2 diabetes has been based on dietary control at diagnosis, which is changed to drug therapy as glucose intolerability increases and complications manifest. This approach has recently been challenged and the effectiveness and cost effectiveness of intensive therapy and early introduction of insulin have been studied. Given the importance of dietary advice, Franz et al.\textsuperscript{5} compared basic nutritional advice to advice based on formal guidelines. The cost effectiveness of this study was based on a trial that failed to show a statistical difference in the clinical outcomes that were assessed in terms of fasting glucose levels and glycosylated haemoglobin (HbA\textsubscript{1c}) levels. The insignificant difference in the clinical outcomes led to similar cost-effectiveness ratio. The authors suggested that the lack of any conclusive finding may have been a reflection of the short time period (6 months) considered.

Javitt and Aiello\textsuperscript{6} used an epidemiological model to extrapolate screening results into treatment effectiveness and subsequently into the cost per QALY. The results suggest that systematic screening alone as well as a combined screening and treatment programme are relatively cost effective.

Hendrickson and et al\textsuperscript{7} have analysed the direct medical costs for patients with type 2 disease in Sweden. The results showed that hospitalisation costs dominated treatment costs amounting to 42 per cent of the total. Drug costs were 27 per cent of total costs. Drug costs for insulin-treated individuals were twice as high as in those treated with oral antidiabetic agents. Complications had a varying impact on cost. For individuals with microvascular complications alone the annual cost was of the same order of

\textsuperscript{7} Henriksson F.Agrandh C., Berne C. et al.,"Direct Medical Costs for Patients with Type 2 Diabetes" in Sweden J. Intern med 2000; 248:387.1996.
magnitude as for those with no complications alone, the annual cost was approximately double the cost of those individuals without complication. Costs of individuals with both microvascular and macrovascular complications were approximately 3-fold higher than the costs in those without complications.

Panayiotopoulos et al\(^8\) showed that there was no statistically significant difference in surgical outcome between diabetic and non-diabetic patients, although the patients with diabetes tended to perform less well. In contrast, the diabetic population undergoing surgery had significantly higher costs compared with the non-diabetic population. Total cost for the diabetic population was $US12,823 (1999 values) compared with $US8,868 for the non-diabetic population. Regarding less severe diabetic foot infection, Eckman et al found little difference in the cost effectiveness across a range of strategies.

Wein\(^9\) has observed that an important part of the management of women with gestational diabetes (GD) is their subsequent follow-up after delivery. At this postnatal visit a glucose tolerance test (GTT) is essential. An analysis of the results of postnatal GTTs in 2957 women reveals that diabetes mellitus was diagnosed in 59 women (2.0 per cent) in the first 6 months after delivery. 31 of these 59 women may have had unrecognized prepregnancy diabetes mellitus. The significant independent predictors of postnatal diabetes mellitus on logistic regression analysis in these women were severity of GD, Asian origin and the 1-hour plasma glucose level during the antenatal GTT.

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A study by Beischer\textsuperscript{10} investigated the prevalence of undiagnosed diabetes in women in the reproductive age group in a Victorian population by analysis of the results of glucose tolerance testing in 57,563 pregnancies. Gestational diabetes (GD) was diagnosed in 4,243 pregnancies and in 2,957 (69.7 per cent) of these, postnatal glucose tolerance testing was performed. Diabetes mellitus was diagnosed within 26 weeks of delivery in 59 women, 55 of whom were diagnosed by the postnatal glucose tolerance test (GTT). There were 4 women with GD who developed diabetic ketosis during pregnancy (3) or within 12 weeks of delivery (1). By consideration of the results of the antenatal and postnatal GTTs, it was deduced that 53 per cent (31 of 59) of the women with diabetes diagnosed after delivery may have had unrecognized pre pregnancy diabetes.

The motivation for diabetes prevention derives from the burden that diabetes places on individuals and communities. In addition to the human and social cost of diabetes, the economic cost of diabetes in the United States increased from approximately $1 billion per year in the 1970s to over $100 billion per year in the early 1990s. The prevalence and incidence of type 2 diabetes in adults has increased considerably over the last 25 years across the major race/ethnic groups of the United States and worldwide. King\textsuperscript{11} estimated that the number of adults with diabetes worldwide would rise from 135 million in 1995 to 300 million in 2025, including increases in both developed and developing countries. From the Behavioral Risk Surveillance System (BRSS) conducted in the United States, the prevalence of self-reported, physician-diagnosed diabetes increased by 33 per cent between 1990 and 1998, from 4.9 per cent to 6.5 per cent among individuals aged 18


years or older. At present, there are no formal, published recommendations for lifestyle approaches for prevention of type 2 diabetes. However, the American Diabetes Association has convened a technical review group to produce an evidence based review of medical nutrition therapy for diabetes. Two specific recommendations are made (i) All individuals should be encouraged to increase regular, moderate intensity physical activity to decrease the risk of developing type 2 diabetes. This is of benefit to them regardless of their BMI. (ii) Sustained weight loss through reduced calorie diet, with reduced intake of total and saturated fat, and increased physical activity may reduce the risk for type 2 diabetes.

Banz et al. analyzed the impact of the body weight gain in patients with type 2 diabetes had on the development of CHD. They used data from a clinical trial within a decision analytic approach to predict the rate of CHD in individuals with weight gain of less than 2 kg over a 10-year period and with weight gain greater than 2kg over the same period. The results predicted a significantly lower rate of CHD (30.0 per cent) in individuals with relatively stable body weight compared with those with a body weight gain greater than 2kg over the study period (CHD) rate was predicted to be 38.2 per cent). The study went on to compare first-line therapy use of glibenclamide, which has the adverse effect of increasing body-weight, with acarbose, which does not increase weight. Their findings suggest that, although acarbose is four times more expensive than glibenclamide in the environment studied (Germany), approximately one-third of this increase was offset by the lower CHD event rate associated with acarbose. The authors note that this is a tentative finding as all bodyweight changes were attributed to the drug therapy.

Singh\textsuperscript{13} has observed an overall increase in the prevalence of coronary disease, diabetes, hypertension, central obesity and associated disturbances with increasing insensitivity to insulin and the trend was more significant among urban than it was among rural subjects. Multivariate logistic regression analysis revealed a significant positive association of level of insulin insensitivity with the age – adjusted prevalences of coronary disease, hypertension, diabetes, hypertriglyceridemia, intolerance of glucose and central obesity among urban subjects. There has been a significant inverse association between insensitivity to insulin and physical activity both for rural and for urban subjects and between insensitivity to insulin and high density lipoprotein cholesterol level for urban subjects. For rural subjects there existed a significant association of sensitivity to insulin with coronary artery disease and intolerance of glucose without significant associations with other risk factors.

O'Brien et al\textsuperscript{14} used resource utilisation and unit costs from a wide variety of sources to derive their estimates. Resource use profiles were designed for a number of complications over a lifetime, with the first-year costs defined explicitly, subsequent years defined as static states such that subsequent years were allocated the same cost for each of the complications if this was applicable. This is obviously a simplification likely to lead to conservative estimate of costs since it assumes a constant rate of complication treatment cost over time. Five US state discharge databases were used to identify the prevalence of the complications based on primary diagnosis with diabetes recorded as a co morbidity. The event cost was dominated by the hospitalisation cost, apart from the case of ischemic stroke where hospitalisation cost represented a quarter of the event total cost. The formulation of the subsequent annual costs was based on treatment

\textsuperscript{13} Singh RB. et al, "Association of Central Obesity and Insulin Resistance with High Prevalence of Diabetes and Cardiovascular Disease in an Elderly Population with Low Fat Intake and Lower than Normal Prevalence of Obesity: The Indian Paradox" Coronary Artery Disease. 9(9) : 559-65, 1998.

guidelines due to inadequate published observational studies. The most obvious application of this analysis is in the population of the standard therapy arm of a cost-effectiveness model. The authors point out, however, that their approach has a number of limitations arising from the lack of observational studies on the treatment of type 2 diabetes and its complications, their assumption that the annual costs attributed to complications are constant over time, and that as treatment technology improves their estimates of cost will raise.

A Dutch study by Grijns \textsuperscript{15} considered the optimal timing of screening intervals using a simulation model to calculate the marginal cost of no screening versus screening once a year if diabetic retinopathy is diagnosed, twice a year if macular oedema is diagnosed and four times a year if proliferative diabetic retinopathy is diagnosed. Three further scenarios decreased the frequency of screening. Direct and indirect costs were considered for patients with type 1 diabetes as well as those with type 2 diabetes showed that the indirect costs were of little consequence, while the direct costs per year of realised sight gained were considered low compared with other interventions, with optimal initiation of screening associated with the youngest age cohort considered (35 year old). Generally, the results were similar to those gained by Javitt and Aiello and support the evidence that screening is cost effective relative to other interventions.

In the second study undertaken by Brown et al. \textsuperscript{16} 10709 patients were identified and incremental costs over and above a matched control population were calculated for the differing stages of treatment for cardiovascular and renal complications. The estimates were based on regression analysis. Patients with type 2 diabetes without complications had an average annual treatment cost of $US2263. The incremental cost for cardiovascular disease


(CVD) was approximately $US8235 if a major cardiovascular event was experienced. Patients with type 2 diabetes with renal disease were estimated to have annual total treatment costs of $US3750, $US4428 and $US17445 (all 1999 values) for early onset, advanced renal dysfunction and end-stage renal failure, respectively. These were higher estimates than earlier studies had reported, which according to the authors was due to a better representation of incremental costs through the modeling approach than reliance purely on observational data, since observational studies only attribute costs after clinical identification of the complication. The modeling approach, according to the authors, is able to identify better the increased costs incurred prior to clinical (or labelled) identification as a model provides more accurate estimates across the full term of treatment.

A similar method is used in two related studies that are based on observational data. The first study by Brown et al\(^\text{17}\) considers 8 years of follow-up of newly diagnosed type 2 diabetes patients from a Health Maintenance Organisation (HMO) matched with a control cohort. Observational data were based on clinical records and limited to the HMO scheme. As outpatient and other ancillary service use were not directly recorded, resource utilisation of these services was estimated through a regression model. Broadly speaking, the annual costs of the diabetic population were approximately double those of the matched case controls. After years 1 and 2, costs fell to their lowest level and then increased steadily over the remaining study period by 65 per cent at the end of the study compared with the initial year. Costs were dominated by inpatient treatment (46 per cent of the total). Cardiac and cerebrovascular complications were 23 per cent of total incremental costs where the increment was defined as costs attributable to the diabetic population over and above matched control costs. An interesting finding was that hospital admissions that were unrelated to diabetes accounted for more than half of the incremental cost over the study period and consequently for most of the growth in these costs over time. The

\(^{17}\) Brown J, Nichols G, Glauber H; et al. Type 2 Diabetes: Incremental Medical Care Costs During the First 8 Years After Diagnosis. Diabetes Care 1999; 1116-24.
authors concluded that the more costly stages of treatment for diabetes complications occur after an 8-year lead time. The authors also note that their costs are lower than other reported estimates and attribute this to the use of costs rather than charges and the use of cost-effective strategies utilised by this particular HMO.

Prevalence of type 2 diabetes and impaired glucose tolerance in the Kashmir Valley of the Indian subcontinent has been surveyed by Zargar and others. This cross-sectional population survey was undertaken to determine the prevalence of type 2 diabetes and impaired glucose tolerance in subjects aged 40 years or more in Kashmir valley, India. The study was carried out in two phases. In phase one, 6091 randomly selected subjects, 40 years or older, from all six districts of the valley were surveyed for prevalence of known diabetes mellitus. In phase two, 5083 subjects, 40 years or older, were screened with oral glucose tolerance test for prevalence of undiagnosed (asymptomatic) diabetes mellitus and impaired glucose tolerance. Abnormalities of carbohydrate intolerance were determined as recommended by WHO. The study revealed the prevalence of IGT as well as of diabetes was significantly more in females as compared to males. Subjects who had family history of diabetes had a significantly higher prevalence of abnormal GTT. Prevalence of known diabetes as well as that of abnormal GTT steadily increased with age, with a highest prevalence in the age group of > or = 70 years. Obese subjects had a significantly higher basal as well as 2 hrs blood glucose in males as well as in females. Subjects with diabetes on GTT had a higher waist/hip ratio. Overall the prevalence of diabetes as well as IGT was significantly higher in the urban population. In subjects greater than 40 years of age having a family history of diabetes, obesity, higher age (50 years or above), female sex and urban origin have more chance of developing abnormal glucose tolerance.

Type 2 Diabetes in Southern Kerala by Kutty\textsuperscript{19} et.al, have analysed the variation in prevalence among geographic divisions within a region. Their findings are that the overall crude prevalence rate of type 2 diabetes was 5.9 per cent. It was highest in the urban, followed by midland, highland and coastal regions. Ageing was associated with greater prevalence of type 2 diabetes in all regions and both sexes. Women showed a higher prevalence in the highland and coastal areas and men in the urban and midland areas. When compared to a population with standard age structure suggested by the World Health Organisation for international comparisons, prevalence in the age group 30-64 years was found to be 16.9 per cent in the urban, 10.1 per cent in the midland, 6.8 per cent in the highland and 3.6 per cent in the coastal regions, respectively. Overall age – adjusted prevalence of type 2 diabetes in 30-64 year olds in Neyyattinkara was 9.2 per cent among men, 7.4 per cent among women, and 8.2 per cent for all persons.

The study undertaken by Viswanathan\textsuperscript{20} and others has assessed the adverse effects of diabetic nephropathy on cardiovascular autonomic neuropathy (CAN) in South Indian Type 2 diabetes patients. The study showed that the presence of nephropathy was associated with the risk of cardiac autonomic neuropathy in Type 2 diabetes patients and it probably had an earlier onset also in them.

The prevalence of multiple diabetes related complications has been reviewed by Morgan and others\textsuperscript{21}. The study says that all complications were related to both age and duration of diabetes but duration was particularly apparent for the microvascular complications (retinopathy and nephropathy).


\textsuperscript{20} Viswanathan V et al, "High Prevalence and Early Onset of Cardiac Autonomic Neuropathy among South Indian Type 2 Diabetic Patients with Neuropathy" Diabetic Research & Clinical Practice. 48 (3) : 211-6, June 2000.

Macrovascular complications in the Type 2 diabetic population appear advanced in onset compared with Type 1. Multiple complications are apparent in almost one fifth of patients with diabetes. Macrovascular morbidity in Type 2 diabetes of early onset indicates that a targeted approach to treatment may prove most beneficial in both patient and health service terms.

Similarly, the study by Evans et al.\textsuperscript{22} used a patient register in a region of Scotland to identify patients with both type 1 and 2 diabetes. Using extrapolation, the authors suggest that patients with diabetes account for approximately 8 per cent of the UK drugs budget, and of this, 90 per cent of the expenditure is attributable to patients with type 2 diabetes. The relative risk of drug usage was higher for type 1 diabetes (1.70 for type 2, 2.07 for type 1 compared with the non-diabetes population); however, given the lower prevalence of type 1 diabetes, the budget impact was greater for type 2 diabetes.

Recently, interest has turned to the analysis of treatment of patients with diabetes who are at risk of coronary heart disease (CHD). This interest stems not only from the high risk of CHD in the diabetic population, but also from the subgroup analysis of the diabetic population undertaken within the Scandinavian Simvastatin Survival Study. In this analysis, three sub-groups were identified; those individuals with normal fasting glucose, those with impaired fasting glucose, and those with diabetes. Each group was analysed comparing a simvastatin arm to a placebo with direct healthcare resource utilisation defining the outcome measure. While the study did not differentiate between patients with type 1 and type 2 diabetic population, the study reports that cardiovascular hospitalisations were reduced by 30 per cent in the simvastatin group compared with placebo (comparable reduction was 23 per cent in the normal fasting glucose group). On an average, the impaired fasting glucose group showed a decrease in hospital costs of $US4600 (1999

values), which offset 74 per cent of the cost of simvastatin. Indeed, there was a net cost saving for the diabetic subgroup in this respect.

The incidence of type 1 diabetes in young children has increased in recent years. In addition, the incidence of type 2 diabetes has been increasingly recognized in older children and adolescents, often in association with obesity. Large numbers of children are currently affected by diabetes, and many more will be affected by diabetes in the future. Diabetes imposes considerable demands on children and their families. Because they are coping with normal developmental challenges, the additional burden of diabetes may be difficult for many children to deal with effectively. Especially burdensome may be the demands of intensive management. With children as patients, families play a significant role in diabetes management and are instrumental in the implementation of interventions. Diabetes can adversely affect both psychosocial and neurocognitive functioning, thus potentially affecting the quality of life of the child and the entire family. Psychosocial factors can also influence regimen adherence and glycemic control. Therefore, psychosocial factors are very important to consider in the management of children and adolescents with diabetes.

Asha Bai and others in their paper have attempted to determine prevalence of known diabetes among those who are more than 20 years of age in Chennai City. The prevalence was significantly high in females. The prevalence of known diabetes was low in total population but increased in those aged > 20 and further increased in those aged > or = 40 years.

One thousand four hundred and twenty five type 2 diabetes patients attending a diabetes centre in South India were interviewed for finding the

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prevalence of known diabetes. Urinary albumin concentration was measured by immunotubodimetric assay. Microalbuminuria was diagnosed if the urinary albumin excretion was > 30 mg/g of creatinine. Overall prevalence of microalbuminuria was 36.3 per cent. The prevalence of microalbuminuria increased with the increase in duration of diabetes. Multivariate regression analysis revealed age, diastolic blood pressure, glycated hemoglobin, fasting plasma glucose, and duration of diabetes to be associated with microalbuminuria.

A study on “High Prevalence of Diabetes, Obesity and Dyslipidemia in Urban Slum Population in Northern India” has been undertaken by Misra, Pandey, Devi and Others. In this study, Diabetes mellitus was recorded in 11.2 per cent of males and 9.9 per cent of females, the overall prevalence being 10.3 per cent. Based on body mass index (BMI) obesity was more prevalent in females than in males. On the other hand, classifying obesity based on percentage body fat, 10.6 per cent of males and 40.2 per cent of females were obese. High waist-hip ratio was observed in 9.4 per cent of males and 51.1 per cent of the females. All individual skin folds and sum of skinfolds were significantly higher in females. In both males and females above 30 years of age, there was a steep increase in the prevalence of high waist hip ratio and in females percentage body fat was very high. Further more, total cholesterol and low – density lipoprotein cholesterol were high in both males and females. Appreciable prevalence of obesity, dyslipidemia, diabetes mellitus, substantial increase in body fat, generalized and regional obesity in middle age, particularly in females, need immediate attention in terms of prevention and health education in such economically deprived populations.


Diabetes Epidemiology Study Group in India (DESI)\textsuperscript{27} has conducted a national urban diabetes survey. It has pointed out that there has been no reported national survey of diabetes in India, in the last three decades, although several regional studies show a rising prevalence of diabetes. The study has found out that age standardized prevalence of diabetes and impaired glucose tolerance were 21.1 per cent and 14.0 per cent respectively, with no gender difference. Diabetes and impaired glucose tolerance showed increasing trend with age. Subjects under 40 years of age had a higher prevalence of impaired glucose tolerance than diabetes. Diabetes showed a positive and independent association with age, BMI, WHR, family history of diabetes, monthly income and sedentary physical activity. Age, BMI and family history of diabetes showed associations with impaired glucose tolerance. This national study shows that the prevalence of diabetes is high in urban India. There is a large pool of subjects with impaired glucose tolerance at a high risk of conversion to diabetes.

A study has been carried out by Zargar\textsuperscript{28} to determine the prevalence of gestational diabetes mellitus (GDM) in Kashmiri women and to assess the effect of various demographic factors. The study proves that women with obesity, hypertension, osmotic symptoms, proteinuria or hydramnios had a higher prevalence of GDM.

The Epidemiological survey\textsuperscript{29} of chronic vascular complications of type 2 diabetic in-patients in four municipalities including Beijing, Shanghai, Tianjin, and Chongqing revealed the prevalence of diabetic retinopathy 31.5 per cent.

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\item \textsuperscript{29} Zhang B. et al, "Epidemiological Survey of Chronic Vascular Complications of Type 2 Diabetic in-patients in four Municipalities" Chung-Kuo I Hsueh Ko Hsueh Yuan Hseuh Pao Acta Academiae Medicinae Sinicae. 24(5) : 452 – 6, October 2002.
\end{itemize}
diabetic nephropathy 39.7 per cent, diabetic neuropathy 51.1 per cent, hypertension 41.8 per cent coronary heart disease (CHD 25.1 per cent) cerebral vascular disease (CVD) 17.3 per cent and vessel complication of lower limbs 9.3 per cent. Multivariate logistic regression analysis shows that diabetes family history, duration of diabetes (> 5 years), and systolic blood pressure (>125 mmHg) are the risk factors for diabetic retinopathy; duration of diabetes (>5 years), systolic blood pressure (>125 mmHg), LDL-C (>3.12 mmol/L) and triglyceride (>1.70 mmol/L) are the risk factors for diabetic nephropathy; age (>45 years), duration of diabetes (> 5 years), and systolic blood pressure (>125 mmHg)/ LDL-C (>3.12 mmol/L), are the risk factors for CHD; age (>45 years), duration of diabetes (> 5 years), and systolic blood pressure (>125 mmHg), and triglyceride (1.70 mmol/L) are the risk factors for CVD. In order to improve patients' outcome, multiple metabolic controls in type 2 diabetes patients are urgently needed, which include decreasing glycemia, reducing hypertension and improving lipid levels.

Idriss-Kanoun and Kanoun 30 have evaluated the frequency of micro and macro vascular complications among a cohort of diabetic out-patients without proteinuria. Prevalence of diabetic micro angiopathy was one of the most frequent in the world. Diabetic peripheral neuropathy and retinopathy were the most frequent complications found in patients. Prevalence rates of vascular complications of diabetes were correlated with age, duration and type of diabetes. Prevention of diabetes complications needs early screening of glucose tolerance abnormalities, better glycemic control, reduction of associated vascular risk factors and identification of genetic factors predisposing to a higher cardiovascular risk.

There has been a significant trend for a higher incidence of neuropathy, overt nephropathy, and coronary artery disease with lower use of specialist care. Multivariate analyses controlling for diabetes duration, demographic characteristics, health care practices, and physiological risk

factors demonstrated that higher past use of specialist care was found to be significantly protective against the development of overt nephropathy and neuropathy against coronary artery diseases. A higher proportion of diabetes duration spent in specialists care may result in delayed development of certain diabetes complications independent of other risk factors. This study thus supports the concept that the benefits of specialist care should be available to all patients with type 1 diabetes.\textsuperscript{31}

Goday\textsuperscript{32} has analysed the non—coronary complications of diabetes. Diabetes mellitus is among the diseases with great impact on health and society, not only for its high prevalence but also fit its chronic complications and high mortality. The most precise method to investigate the prevalence of diabetes is by oral glucose tolerance testing. In Spain, the prevalence of diabetes in the 30-65 year old population is estimated to be 6.5 per cent among 60-65 year old, and 10.3 per cent among the 30-89 year old population. The ratio of known to unknown diabetes ranges from 1:3 to 2:3. The incidence of diabetes mellitus type 2 in Spain is 8/1000 persons per year, and the incidence of type 1 is 11 to 12 cases per 100,000 persons per year. The prevalence of chronic complications varies according to type of diabetes, time since onset and degree of metabolic control: neuropathy 25 per cent, retinopathy 32 per cent and nephropathy 23 per cent. Diabetes is one of the most important causes of death in Spain, occupying third place for women and seventh for men.

The study on "Clinical Predictors for a High Risk for the Development of Diabetes Mellitus in the Early Puerperium in Women with Recent


Gestational Diabetes Mellitus" by Schaefer -Graf\textsuperscript{33} concluded that no maternal demographic or neonatal parameters were significantly associated with diabetes mellitus. During pregnancy, the highest fasting glucose level, followed by the severity of glucose intolerance, and earlier gestational diabetes mellitus diagnosis were the best predictors for postpartum diabetes mellitus. Diabetes education should begin during pregnancy, especially for women who are identified to be at a high risk when they are highly motivated and under medical care.

Pradeepa and Mohan\textsuperscript{34} in their study on "The Changing Scenario of the Diabetes Epidemic: Implications for India" have shown that diabetes mellitus is one of the main threats to human health in the 21\textsuperscript{st} century. The prevalence of diabetes ranges from nearly 0 per cent in New Guinea to 50 per cent in the Pima Indians. The past two decades have seen an explosive increase in the number of people diagnosed with diabetes world – wide. The World Health Organization estimated that there were 135 million diabetics in 1995 and this number would increase to 300 million by the year 2025. India leads the world today with the largest number of diabetics in any given country. In the 1970s, the prevalence of diabetes among urban Indians was reported to be 2.1 per cent and this has now risen to 12.1 per cent. Moreover, there is an equally large pool of individuals with impaired glucose tolerance, many of whom will develop type 2 diabetes mellitus in the future. Diabetes can affect nearly every organ system in the body. The Chennai Urban Population Study (CUPS) showed that prevalence of diabetic retinopathy, nephropathy and neuropathy is not very different in urban south Indians compared to that reported among Europeans. However, coronary artery disease (CAD) occurs with increased prevalence and at a younger age (premature CAD), while peripheral vascular disease showed the opposite trend, with lower prevalence.


compared to that reported in Europeans. There is an urgent need for lifestyle intervention, with the incorporation of a healthy diet, an increased physical activity and weight reduction as a means of preventing diabetes in those who are in the prediabetic stage and thus prevent the diabetes epidemic, which is looming large in our country.

Epidemiology of type 2 diabetes in Indians have been analysed by Ramachandran\textsuperscript{35}. Prevalence of diabetes is increasing globally. India have the maximum increase during the last two years. Type 2 diabetes mellitus is the commonest form of diabetes. The prevalence of type 2 diabetes mellitus is 2.4 per cent in rural population and 11.6 per cent in urban population. Subjects under 40 years of age have a higher prevalence of impaired glucose tolerance than diabetes. The important risk factors for high prevalence of diabetes include: High familial aggregation, obesity specially central one, insulin resistance and lifestyle changes due to rapid urbanization.

Viswanathan\textsuperscript{36} and others in their article on "Prevalence of Pathogens in Diabetic Foot Infection in South India Type 2 Diabetes Patients" have highlighted that a group of 654 (M:F, 433:221) type 2 diabetes patients with foot ulcers was studied. Specimens like pus, wound exudates and tissue were processed for smear for Gram's staining, aerobic and anaerobic culture, and biochemical identifications. In 728 diabetes patients, 654 pathogens were isolated. Aerobic pathogens were isolated in 437 (66.8 per cent) patients and anaerobic pathogens were isolated in 217 (33.2 per cent). As Wagner's grading increased, the prevalence of anaerobic pathogens also increased, Neuropathy was common in diabetes patients infected with both aerobic and anaerobic pathogens, Ulcers infected with anaerobic pathogens showed a longer healing time than ulcers infected with aerobic pathogens. There was no


\textsuperscript{36} Viswanathan V. et al, "Prevalence of Pathogens in Diabetic Foot Infection in South Indian Type 2 Diabetic Patients" Journal of the Association of Physicians of India. 50 : 1013-6, Aug 2002.
significant difference in peripheral vascular disease (PVD) in patients selected for the study.

One thousand consecutive type 2 diabetes patients attending a diabetes centre in South India were interviewed for analysing the prevalence of neuropathy\textsuperscript{37}. Biothesimetry studies were performed by a single observer using a biothesimeter. Neuropathy was diagnosed if the vibratory threshold of the great toe exceeded twenty five. Overall, 19.1 per cent of the patients had evidence of neuropathy. The prevalence of neuropathy increased with increase in age and duration of diabetes.

An analysis about diabetes in old age by Kesavadev, and Nair\textsuperscript{38} reveals that diabetes in elderly is emerging as one of the most important public health problems of the 21\textsuperscript{st} century. In developing countries, the majority of people with diabetes are in the age range of 45-64 years. A better understanding on the pathogenesis of diabetes in the ageing population is required to successfully treat and prevent its devastating complications. Changes in body composition with accumulation of fat in the abdomen are a key factor in the causation of diabetes in the aging population. The size and strength of skeletal muscle, a major tissue involved in glucose metabolism, also declines leading to muscle weakness and a reduction in physical activity. These changes lead to marked reduction in energy expenditure and abdominal fat accumulation causing insulin resistance. Recent evidence suggests that four months of aerobic exercise can improve muscle oxidative capacity similarly in younger and older people, but that insulin sensitivity is less likely to improve in older people. It appears that older people need to exercise more frequently to improve their insulin sensitivity. Diagnosis and management of diabetes in the elderly requires special attention since age, genetics, body composition and lifestyle factors all interact. Increasing

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\item \textsuperscript{37} Ashok S. et al, "Prevalence of Neuropathy in Type 2 Diabetic Patients Attending a Diabetes Centre in South India" Journal of the Association of Physicians of India. 50:546-50, Apr 2002.
\item \textsuperscript{38} Kesavadev JD and other, "Diabetes in Old Age: An Emerging Epidemic", Journal of the Association of Physicians of India.51:1083-94, Nov 2003.
\end{itemize}
evidence suggests that postprandial hyperglycemia is more sensitive to diagnose diabetes in elderly people than in the young. Age related changes in body function and cognition demand special caution in the selection of hypoglycemia drugs in the elderly. Targets of diabetes therapy in the elderly have to be individualized, considering the age of the patient, remaining life-expectancy and severity of co-morbid conditions. Short acting insulin secretagogues are preferred to avoid prolonged and frequent hypoglycemia. Judicious choice of insulin sensitizers, timely introduction of insulin, meticulous control of hypertension and hyperlipidemia are critical to prevent complications.

Prevalence of diabetes, impaired fasting glucose and insulin resistance syndrome in an urban Indian population has been analysed by Gupta and Gupta\(^{39}\). Diabetes was present in 70 men (13.2 per cent) and 64 women (11.5 per cent). Age-adjusted prevalence of diabetes was 9.3 per cent in men, 8.1 per cent in women and 8.6 per cent overall (CI 6.9 – 10.3). IFG was present in 28 men (5.3 per cent) and 29 women (5.2 per cent). IRS was present in 52 men (9.8 per cent) and 114 women (20.4 per cent) with age-adjusted prevalence of 7.9 per cent in men (CI 6.7-9.1) and 17.5 per cent in women (CI 14.4 – 20.6) with an overall prevalence of 12.8 per cent (CI 10.8 - 14.8). Other metabolic abnormalities of IRS in men and women were high triglycerides in 32.1 and 28.6 per cent, low HDL cholesterol in 54.9 and 90.2 per cent; central obesity in 21.8 and 44.0 per cent, and high normal blood pressure or hypertension in 35.5 and 32.4 per cent.

The epidemiology of cardiovascular complications in type 2 diabetes has been analysed by Meigs.\(^{40}\) Type 2 diabetes is increasing in epidemic proportions worldwide, and is strongly associated with atherosclerotic cardiovascular diseases (CVD). Hyperglycemia increase risk of CVD, but

\begin{itemize}
  \item Meighs JB., "Epidemiology of Cardiovascular Complications in Type 2 Diabetes Mellitus" Acta Diabetologica. 40 Suppl 2 : S358-61, December 2003.
\end{itemize}
glycaemic control does not substantially reduced CVD risk. There are several potential explanations for this apparent paradox, including the roles of the metabolic syndrome and post-load hyperglycemia in the association of type 2 diabetes and CVD.

The study on "Prevalence Rates of Hypertension and Chronic Diabetic Complications of in-patients with Diabetes" reveals the prevalence rates of chronic diabetes complications and related macro-vascular diseases on in-patients with diabetes mellitus were much higher than those of non-diabetes, and was close to the levels seen in the western countries. Hypertension, especially high systolic blood pressure was the most important risk factor of chronic diabetes complications and the related macro-vascular diseases.

Mohan and others in their paper on "Glucose Intolerance (Diabetes and IGT) in a Selected South Indian Population with Special Reference to Family History, Obesity and Lifestyle Factors – The Chennai Urban Population Study" have assessed the impact of family history of diabetes, obesity and lifestyle factors particularly physical activity on glucose intolerance in a selected South Indian population. The overall prevalence of diabetes in the study population was 12.0 per cent, which included 7.2 per cent of known diabetic subjects and 4.8 per cent undiagnosed diabetic subjects, while the prevalence of impaired glucose tolerance was 5.9 per cent. The prevalence of glucose intolerance was significantly higher among subjects with both parents diabetic compared to those with one parent diabetic.


Sumi Patel and Nicholas\textsuperscript{43} in their paper on “Prevalence of Type 2 Diabetes Mellitus Among the Asian Indian Population” have analysed that type 2 diabetes mellitus is an epidemic that afflicts more than 16 million people in the United States, and has numerous devastating complications. Much discussion has focused on the ethnic groups in this country that are hard hit by the disease, but little has been written about a fast-growing ethnic group in which diabetes is a major problem, not only in this country but in the group’s native land. The group is Asian Indians. One factor Asian Indians have in common with Native Americans, blacks, and Hispanics is a genetic disposition to diabetes. In addition, Asian Indians (and other Asians) are also largely sedentary. While Asian Indians generally are not obese, the body distribution of fat plays a role in triggering the disease. It has focused on the Asian Indian community and the cultural, genetic, and environmental differences that contribute to the prevalence of diabetes in the rapidly growing population. An important aspect of diabetes in the Asian Indian population is that India currently has the largest number of diabetes patients in the world: 19.4 million persons are afflicted. This number is expected to increase to almost 57.2 million in just 22 years.

A recent study by ‘Diabetes India’ group\textsuperscript{44} had estimated the prevalence of diabetes in urban and rural areas in India. An overall diabetes prevalence of 4.3 per cent was reported, the prevalence in urban and rural areas being 5.6 per cent and 2.7 per cent respectively. Total prevalence of IGT was 5.2 per cent, urban being 6.3 per cent and rural 3.7 per cent.

The rural Indian population is undergoing lifestyle transition due to socio-economic growth. This study was done to determine the temporal changes in prevalence of diabetes and IGT that could have occurred in a rural population in India as a result of the lifestyle transition. Nearly a three-fold

\textsuperscript{43} Sumi Patel and Nicholas G. Poporich, “Prevalence of Type 2 Diabetes Mellitus Among the Asian Indian Population” Search, Vol. No. 28, Nov 2003.

increase in age- and sex-adjusted prevalence of diabetes (from 2.20 per cent to 6.36 per cent) was seen in 2003 when compared with a similar study done 14 years before. Prevalence of IGT did not change significantly (7.44 per cent in 1989 vs 7.18 per cent in 2003)\(^45\). Improvement in living conditions had occurred during the period, occupational changes were seen, the number of manual labourers had decreased and economic conditions had improved. BMI and waist circumference had increased. After correcting for age, sex and differences in time periods, waist circumference and physical inactivity showed significant associations with the increased prevalence of diabetes. Demographic transition due to improved living conditions in rural India was associated with a three - fold increase in the prevalence of diabetes. Increased upper body adiposity and physical inactivity showed significant association with this phenomenon.

The main crux of the study by Kanta Barman\(^46\) is to determine the prevalence of diabetes – related complications in subjects with fibro calculus pancreatic diabetes (FCPD) and compare them with subjects with type 2 diabetes mellitus matched for age, sex, and duration of diabetes. FCPD patients had lower body mass index (BMI) \(P<.001\), systolic blood pressure, diastolic blood pressure, serum cholesterol, serum triglyceride, and serum creatinine but higher glycosylated hemoglobin levels compared to patients with type 2 diabetes. Prevalence of CAD was significantly higher among type 2 diabetic patients (11.9 per cent) compared to FCPD patients (5.1 per cent). There was no significant difference in the prevalence of other diabetic complications between the two study groups. The prevalence of retinopathy, nephropathy, neuropathy, and PCD was similar among FCPD patients and

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type 2 diabetes patients, but the prevalence of CAD was lower among FCPD patients.

The presence of at least one complication was found in 49 persons (26.5 per cent), two complications – in 14 patients (7.57 per cent) and three complications in 4 patients (2.16 per cent). The conventional therapy duration was twice longer in patients with retinopathy. The significant influence of the age, the age of diabetes onset and duration was found in those patients. Comparing the groups of patients treated conventionally less than 3.5 years and more than 3.5 years it was found that patients in the first group were older, fell ill later and they had longer diabetes duration than patients in the second group. The risk of retinopathy increases from 4.2 per cent to 8.9 per cent inpatients treated conventionally more than 3.5 years. The risk of diabetic cataract is 5 times higher in that group. Chronic complications of diabetes occur in 26.5 per cent patients with a diabetes duration of at least 5 years. CIT is the risk factor of the eye complications in diabetes, particularly when applied longer than 3.5 years. The prolongation of CIT over 3.5 years increases the risk of retinopathy twice and the risk of cataract 5 times in patients with type 1 diabetes. So the early intensification of insulin therapy reduces the risk of the retinopathy and cataract development in later course of the diseases\textsuperscript{47}.

The study\textsuperscript{48} has aimed to determine the prevalence of chronic complications and associated factors in type 2 diabetes in 500 diabetes patients. Of the 500 diabetes patients examined (160 males, 340 females, mean age 55.2, 10.6 years), retinopathy was seen in 43 per cent, neuropathy in 39.6 per cent and foot ulcers in 4 per cent. Nephropathy was found in 20.2 per cent, and was significantly associated with hypertension. The prevalence


of microvascular complications was higher in the group of patients with HbA1c>8 per cent and was significantly related in duration of diabetes, hypertension and obesity. Hypertension was manifest in 64.6 per cent patients, 61 per cent had raised Body Mass Index and Waist Hip Ratio was more than normal in 88 per cent subjects. Macrovascular complications were encountered in 102 diabetes patients, with angina in 85 (17 per cent), heart attack in 25 (5 per cent) and stroke in 13 (2.6 per cent). The prevalence of diabetic microvascular complications was higher in people with poor glycaemic control, longer duration of diabetes and associated hypertension and obesity.

The burden of diabetes and impaired glucose tolerance in India has been analysed by Murthy\textsuperscript{49}. A random multistage cross-sectional population survey was undertaken to determine the prevalence of diabetes mellitus (DM) and impaired glucose tolerance in subjects aged 25 years and above in India. The study identified the urban prevalence of DM and IGT to be significantly greater than in the rural population (\(P<0.001\) in both instances). The prevalence of DM was significantly more than that of IGT (\(P<0.001\)) within both the rural and urban population. Type 2 diabetes is a major health problem in India.

Rema and others\textsuperscript{50} in their study on the "Prevalence of Diabetic Retinopathy in Urban India" have assessed the prevalence of diabetic retinopathy (DR) in type 2 diabetes subjects in urban India. The overall prevalence of DR in the population was 17.6 per cent which included 20.8 per cent known diabetes subjects and 5.1 per cent in subjects with newly detected diabetes. The prevalence of DR was significantly higher in men than in women and among subjects with proteinuria. Logistic regression analysis showed that for every 5-year increase in the duration of diabetes, the risk for DR increased 1.89-fold. For every 2 per cent elevation of glycated


hemoglobin, the risk for DR increased by a factor of 1.7 per cent. This study shows that the prevalence of diabetic retinopathy is lower in urban South Indians than in other ethnic groups. However, due to the large number of diabetic subjects, DR is likely to pose a public health burden in India; hence, routine retinal examination is mandatory to detect DR in the early stages.

At the other end of the treatment spectrum is the evaluation of insulin therapy in the type 2 diabetes population. The Kumamoto clinical study\textsuperscript{51} examined whether intensive glycaemic control based on multiple insulin injections (MIT) reduces the frequency or severity of microvascular complications compared with conventional insulin therapy (CIT) in this population. On entry patients were classified into a primary prevention group who had no evidence of retinopathy or microalbuminuria and to a secondary prevention group with mild retinopathy and miroalbuminuria. Over a 6-years period the cumulative percentages of the development and progression of retinopathy and nephropathy were 7.7 per cent for the MIT group and 32 per cent for the CIT group in the primary prevention sub-population, and 19.2 per cent for the MIT group and 44 per cent for the CIT group in the secondary prevention sub-population. The population was subsequently followed-up to a total of 10 years. Generally, the clinical trial results were maintained over time. MIT prolonged the number of years free of diabetes complications, for example, 22 years for progression of retinopathy and 2.2 years for progression of clinical neuropathy. Associated total treatment costs over the 10-year period were also calculated and the MIT cost was shown to be $US1233 (1999 values) less expensive than the CIT therapy due to the greater cost offsets achieved. On this basis, the authors conclude that intensive treatment appears to be justified.

Socio-economic inequalities in the prevalence of Type 2 diabetes, cardiovascular risk factors and chronic diabetes complications in the Basque

\textsuperscript{51} Rema, et al Ibid.
Country, Spain have been analysed by Larranaga\textsuperscript{52}. The prevalence of known Type 2 diabetes was higher in patients of lower socio-economic status, especially among women. In Type 2 diabetes patients, obesity, sedentary lifestyle, and abnormal levels of low-density lipoprotein cholesterol an HbA were more prevalent among those from lower socio-economic status. Macroangiopathy was inversely associated with socio-economic status after adjustment for clinical and demographic variables. Patients of lower socio-economic status more frequently visited primary care services than those of higher status. This study shows an association between deprivation and Type 2 diabetes patients. Despite a greater use of health services by less wealthy patients, they showed worse glycaemic control and more chronic complications. Besides clinical variables, socio-economic status and environmental information need to be considered in the assessment of risk profile of diabetes patients by health professionals and by health service planners.

Van Hecke and others\textsuperscript{53} have analysed the complications of diabetes. After 7 to 9 years of follow-up, 64 patients had died and 128 patients had incident CVD. The age-and sex-adjusted hazard ratios (HRs) of all-cause mortality were 1.45 and 4.16 in patients with nonproliferative and proliferative retinopathy at baseline, respectively. Adjustments for cardiovascular risk factors completely obliterated the association with nonproliferative retinopathy, whereas the association with proliferative retinopathy remained twofold increased, although nonsignificant. The age-and sex-adjusted HRs of incident CVD were 1.73 and 2.05 in patients with nonproliferative and proliferative retinopathy, respectively. After adjustments for cardiovascular risk factors, both associations were attenuated and lost statistical significance. This study shows that type 1 diabetes patients with nonproliferative or


\textsuperscript{53} Van Hecke MV. et al," Diabetic Retinopathy is Associated with Mortality and Cardiovascular Disease Incidence: The EURODIAB Prospective Complications Study" Diabetes Care. 28(6): 1383-9, June 2005.

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proliferative retinopathy have an increased risk for all-cause of mortality and incident CVD. The presence of cardiovascular risk factors explained the associations to a large extent, except for the associations with proliferative retinopathy, which suggests that other shared mechanisms may be involved.

The problem of diabetes mellitus is not only a national problem, but also an international problem. A large number of studies conducted so far point out the large scale prevalence of diabetes mellitus in both developed and developing countries including India. It is high time that there should be more intensive study of the problem. From the above review of literature, it is clear that though a good amount of research has been done with a focus on different dimensions of health, studies on the management of diabetes mellitus are limited. To fill this gap, the present study has been undertaken.