CHAPTER - I

INTRODUCTION
An epidemic of diabetes mellitus (DM) is underway in both developed and developing countries. There is a comparatively higher rate amongst the non-Europeans and Indians are no exception. The number of people expected to suffer from diabetes mellitus is predicted to be about 150 million in 2010 and 300 million in 2025. In India the number is expected to reach about 72 million by then.(1) Type-2 diabetes mellitus is the predominant from of diabetes worldwide and it has become one of the most hazardous public health problems, resulting in significant expenditure as regards treatment and management of complications. In India several studies have been carried out that clearly bring to light the fact that Asian Indians have a high prevalence of insulin resistance syndrome that may underlie their greater than normal tendency to develop diabetes mellitus and atherosclerosis. Apart from the very large number of known diabetics, which looks like the tip of the iceberg, underneath lies the group of innumerable number of individuals who are first degree relatives to the existing diabetics and in fact are markedly prone to become diabetic in the coming time. This group requires keen attention and screening to get identified and can be subjected to prevention strategies which will ultimately be reducing the economic burden on the developing country like ours.

Type-2 diabetes mellitus is characterized by disorders of insulin action and insulin secretion, either of which may be predominant feature and both of which are usually present by the time the disease is clinically manifested. It is a heterogeneous group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, action or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs especially the eyes,
kidneys, nerves, heart and the blood vessels.

The growing prevalence of type-2 diabetes and obesity in societies worldwide is widely recognized as among the greatest threats to global health in the coming century. Nevertheless, we remain far from a comprehensive understanding of the molecular pathogenesis of this condition. This makes it impossible to identify optimal strategies for intervention and treatment that will provide effective remedies to the projected increase in morbidity and mortality. Diabetes mellitus has now assumed epidemic proportions in many countries of the world. With the present population of 19.4 million diabetics and thereby leading to approximately 60 million by the year 2025, India would rank first in sharing the global burden of diabetes. Against this backdrop of epidemiological transitions other environmental factors like maternal and foetal malnutrition, early childhood over nutrition and unhygienic semi-urban and urban milieu have lately been incriminated in either initiating or unmasking the problem of insulin resistance and diabetes. Genetic predisposition to central (visceral) adiposity, insulin resistance and diabetes are thought to be important determinants.

Revised diagnostic criteria have clearly defined categories of impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and frank diabetes. Recognition of IFG and IGT is important as they are harbingers of future development of diabetes. More importantly, they have greater predilection for cardiovascular complications. They have emerged as the most important target for primary prevention with lifestyle modification and pharmacological agents like metformin and insulin sensitizers. Insulin resistance and hyperinsulinemia occupy the central stage of the metabolic syndrome. The later includes clustering of several risk factors like
central adiposity, hypertension, dyslipidemia, hyperuricemia and procoagulant states.

From an epidemiologic standpoint, type-2 DM is not due to any of the other specific etiologic types of the disease. The extent to which type-2 DM represents a single disease is uncertain. The disease has a distinctive epidemiology, with much of the variation in frequency accounted for by known risk factors. Furthermore, consistent relationship with known risk factors prevails within populations, suggesting that the most cases share a similar pathogenetic basis. Much of the information on the risk factors and knowledge of the pathogenesis has been derived from studies of high frequency populations, such as Pima Indians and Mexican Americans, but similar patterns have been confirmed in other racial groups and on other continents.

Type-2 DM is often asymptomatic, so many cases remain undiagnosed. Even in countries with well developed care systems, such as United States, there is typically one undiagnosed case in the population. In less developed countries, undiagnosed cases usually outnumber diagnosed ones. Consequently, population based studies in which all people in representative samples of the population are tested are necessary for a clear understanding of the epidemiology of the disease.

The relation between development of complications and levels of blood sugar wasn’t very clear until we received definite direction from the large studies like UKPDS and DCCT. Both studies have clearly stated that intensive control of blood sugar leads to delay in development of complications. Thus close to the end of year 2000, worldwide focus has been on intensive control of blood sugar levels to obtain better results. Now the studies are directed towards searching individuals at risk of
developing diabetes and to implement strategies of prevention upon them. It is indeed very important and practical to identify individuals at risk in community and to follow them up in a country like India, which is on verge of an epidemic, thus needing such study most.

Prevalence of diabetes is very rapidly increasing as various studies have reported all over the world, and India is being considered a country at the edge of an epidemic of diabetes expected to be having large number of diabetes patients in the world by year 2025. Diabetes along with its complications is a great economic burden on governments and on individuals. So present studies are directed to identify such individuals who are at risk of developing diabetes so that early intervention may result in control of development of diabetes or its complications. In this regard, most of the countries have launched a multicentric evaluation of their population to detect diabetic individuals or individuals at the risk of developing diabetes (utilizing glucose tolerance test to detect impaired glucose tolerance, impaired fasting glucose and frank diabetes) and along with this evaluation, the efforts are being carried to initiate prevention programs at primary and secondary levels.

As it is well known that a strong genetic predisposition is observed in family of diabetics, those closely related to a diabetic individual are at greater risk of developing diabetes. Amongst those at risk, maximum incidence is likely to be observed in first degree relatives of the patients themselves (Type-2 diabetes individuals). Interestingly, though this is a well known entity, very little work is done all over the globe to identify those first degree relatives who are at the maximum risk of developing diabetes. Community surveys to identify the diabetic
population are very sparsely done in our country. Few such studies are reported from
Southern India, which only report about the prevalence of diabetes, rather than
population at risk. In other words, these studies have not mentioned the risk of
development of diabetes in first degree relatives of diabetic individuals detected
during these surveys.

Thus by observing all the work done in India, either to look for prevalence or
identification of high risk individuals as like first degree relatives is not representing
the incidence of diabetes in general for the country as the studies are available from
one cross sectional area only. There is no study so far all over the country to detect
incidence of diabetes in first degree relatives.

The present work satisfies many urgent needs and necessities required in the
field of diabetes. It offers detection of diabetics and abnormal glucose tolerance in
most susceptible individuals who are on the way to develop diabetes with increasing
rate. An effort is also being put forth to measure fasting insulin levels and lipid profile
to observe early metabolic abnormalities in these high risk individuals which may be
used further on as indicators for prediction of development of diabetes. Observing
increasing importance being imported to adipocyte functions in relation to insulin
resistance and diabetic complications, we also measured leptin and adiponectin in
study population of first degree relatives and correlation of these with other
established parameters. If all these indicators are detected early, efficient prevention
program may also be started early to help community to sustain against the impending
diabetes epidemic looming large over this country.