DOES FASTING BLOOD SUGAR PREDICT RISK OF DEVELOPING DIABETES FOR NEXT 15 YEARS?

A COHORT STUDY

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT OF THE DR. M.G.R. MEDICAL UNIVERSITY FOR THE DEGREE OF M.D. BRANCH XV (COMMUNITY MEDICINE) EXAMINATION TO BE HELD IN MARCH – 2007

CERTIFICATE

This is to certify that "Does Fasting Blood Sugar Predict Risk Of DevelopingDiabetes For Next 15 Years.**" is a bona fide work of Dr. Sandhya.G.I in partial fulfillment of the requirements for the M.D. Community Medicine examination (Branch XV) of The Tamilnadu Dr. M.G.R. Medical University to be held in March 2007.**

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TABLE OF CONTENTS

TABLE OF CONTENTS

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1. INTRODUCTION

The last century has witnessed the epidemiologic transition among many populations, which has resulted in a decrease in infectious disease, with a concomitant increase in chronic noncommunicable diseases, such as cardiovascular disease, cancer, and diabetes.[3] At any given time, different countries in the world or even different regions within a country are at different stages of the epidemiologic transition. In developing countries like India, the increased incidence of noncommunicable diseases adds to the continuing burden of infectious, nutritional, and perinatal diseases, which has been termed the double-burden of diseases. [2]

Type 2 Diabetes, a global public health problem, is now emerging as a pandemic[2.] Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and to rise to 5.4% by the year 2025.[1] Much of this increase in diabetes will occur in developing countries, due to population growth, ageing, unhealthy diets, obesity and sedentary lifestyles. Thus, by the year 2025, 75% of people with diabetes will reside in developing countries, as compared with 62% in 1995[1]. In developed countries, most people with diabetes are above the age of retirement. In developing countries, those most frequently affected are in the middle, productive years of their lives, aged between 35 and 64.[1]

India has highest prevalence of diabetes among Asian countries.[1, 2] It is estimated that there are approximately 33 million adult currently with diabetes in India. This number is likely to increase to 57.2 million by the year 2025.[2] A large number of cross-

sectional studies are reported in different states of India[19, 31, 32] but there are no incidence studies done in India to estimate annual risk of new cases.

Many of the estimated numbers and percentages of people with diabetes in India were derived by applying diabetes prevalence estimates to the population[1]. Prevalence estimates are most useful for assessing the most general impact of a health condition and for estimating the medical and supportive care needs of people likely to be affected by it. The prevalence of a given condition will depend both on the rate of new cases and on how long people live with the condition. [4.] Survival with a health condition, in turn, depends on available treatments, the rate at which the disease progresses, whether treatments are appropriately applied, other health conditions a person may face and environmental supports. Because of these features, prevalence studies are not ideal for studying new occurrence of disease and its risk factor.

Gathering Informations based on incidence is the ideal method for studying disease occurrence because it involves collecting and analyzing all the relevant information on the source population, and we can get better information on when exposure and disease occurred. Because it is limited to new cases, differences in incidence between populations indicate differences in risk, and hence point to factors (i.e., differences between the populations) that lower or elevate risk. [4] Monitoring of national trends in the prevalence and incidence of NIDDM were needed so that the burden of diabetes can be assessed, the impact of risk factors can be described and interventions can be developed

The natural history of progression from normal glucose tolerance (NGT) to type 2 diabetes is not well defined.[26] Understanding the natural history of type 2 diabetes is essential for early detection of prediabetic hyperglycemia and for interrupting the progression from normal to abnormal glucose tolerance. A number of longitudinal studies

reported that people having pre diabetes are at a higher risk of developing diabetes and cardiovascular complications. [38] No longitudinal studies are available in India to estimate the risk of prediabetes stage in future diabetes.

This study is under taken as a follow up of a part of the ICMR-CMC study on CHD –prevalence and risk factors that was done in 1991-1993 to find out the whether baseline fasting blood sugar is a significant predictor of future diabetes or not.

2. JUSTIFICATION

Type 2 Diabetes melitus is a chronic disease that affects the lives of millions of people. It is occurring in epidemic proportions worldwide.[2,3] The regions with the greatest potential increases are Asia and Africa, where diabetes rates could rise to 2 or 3 times those experienced today. [3] In Asia alone an estimated 85 million were affected; this continent had both the highest proportion of current cases and the greatest projected increases for the future. [1]

Very high levels of diabetes have been reported in urban areas of India,[29,31,32,33] but few data are available for rural regions where >70% of the population lives.[21] Data from a new large-scale survey done in 2005 suggest rural India may soon experience the same epidemic of diabetes. According to a cross-setional study in rural area of Andhra Pradesh on the basis of the finger-prick measurements, the prevalence of diabetes was 13.2% (95% CI 12.1–14.3), of which 6.4% (5.6–7.2) were known and 6.8% (5.9–7.6) were previously undiagnosed**.** [19]

Several cross sectional studies have been carried out in India[30, 31, 32, 33] about the prevalence of type 2diabetes but there are no longitudinal studies for incidence. Longitudinal studies involve lengthy periods of follow-up and many resources in terms of both time and funding, and it may be difficult to dofor practical reasons.

Why are these trends alarming? Once diabetes develops, the cost of caring for patients is prohibitive. Poorly managed diabetes leads to several complications (e.g., end-stage renal failure, blindness, amputation and heart disease) that many developing countries are ill equipped to tackle. In addition, the burden on individuals and on society extends past human suffering to include staggering economic costs, lost productivity, and

social capital.[45] So aggressive efforts must be directed toward primary prevention of diabetes in developing countries.

Development of type 2 diabetes is to some extent a predictable event. For prevention purposes, there is great interest in the identification of persons at high risk for developing diabetes. Several longitudinal and retrospective community-based studies have been conducted by independent researchers in different parts of world to estimate the incidence of type 2 diabetes and its predictors.[10, 26, 37, 38]The correlation of a risk factor(s) with development of diabetes is never 100%.

A commonly accepted entity and one of much concern is the prediabetes state[11] Epidermiological studies on the progression of disease have brought to light the importance of this state. American diabetes association (ADA) and World Health Organization (WHO) have recently introduced impaired fasting glucose (IFG; fasting plasma glucose level 6.1–6.9 mmol/l or 110-125mg/dl) as a category of intermediate glucose metabolism.[5, 6, 7] The relationships between impaired fasting glucose and type2 diabetes have never clearly investigated. A number of longitudinal studies from western countries reported different lower limit for impaired fasting glucose that can predict the future diabetes.[37,38] Still sufficient datas are lacking from Indian studies to identify the ideal lower limit of fasting blood sugar that predicts future diabetes.

This is a nonconcurrent cohort study on predictive validity of fasting blood glucose in future diabetes in a rural block in Tamil Nadu. In addition to estimating predictive validity of fasting glucose in future diabetes, other selected risk factors are also studied.

3. AIM AND OBJECTIVES

AIM

To estimate the predictive validity of fasting plasma glucose in risk of future type 2 diabetes in a rural south Indian population aged 30-60 years over time.

OBJECTIVES

. 1. To determine the risk`of progression from normoglycemia to type 2 diabetes based on the fasting plasma glucose (FPG) concentration among a cohort of rural people aged 30-60 years in Kaniyambadi block over a period of 15 years.

2. To measure association of selected risk factors and the probability of developing type 2 diabetes mellitus in Kaniyambadi block over a period of 15 years.

4. REVIEW OF LITERATURE

4.1 Introduction

Diabetes is a chronic condition that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin, it produces. Hyperglycaemia and other related disturbances in the body's metabolism can lead to serious damage to many of the body's systems, especially the nerves and blood vessels.[18]

There are two basic forms of diabetes:

- Type 1: people with this type of diabetes produce very little or no insulin. People with type 1 diabetes require daily injections of insulin to survive.
- Type 2: people with this type of diabetes cannot use insulin effectively. People with type 2 diabetes can sometimes manage their condition with lifestyle measures alone, but oral drugs are often required, and less frequently insulin, in order to achieve good metabolic control.

Most people with diabetes have type 2. Many of them have no symptoms and are only diagnosed after many years of onset. [18]

4.2 Complications associated with diabetes mellitus[18]

Cardiovascular disease is responsible for between 50% and 80% of deaths in people with diabetes.

Risk factors for heart disease in people with diabetes include high blood pressure, high serum cholesterol, obesity and smoking. Recognition and management of these conditions may delay or prevent heart disease in people with diabetes.

- Diabetic neuropathy is probably the most common complication. Studies suggest that up to 50% of people with diabetes are affected to some degree. Major risk factors of this condition are the level and duration of elevated blood glucose. Neuropathy can lead

to sensory loss and damage to the limbs. It is also a major cause of impotence in diabetic men.

- Diabetic retinopathy is a leading cause of blindness and visual disability. Research findings suggest that, after 15 years of diabetes, approximately 2% of people become blind, while about 10% develop severe visual handicap.
- Diabetes is among the leading causes of kidney failure, but its frequency varies between populations and is also related to the severity and duration of the disease.
- Diabetic foot disease, due to changes in blood vessels and nerves, often leads to ulceration and subsequent limb amputation. Diabetes is the most common cause of non-traumatic amputation of the lower limb.

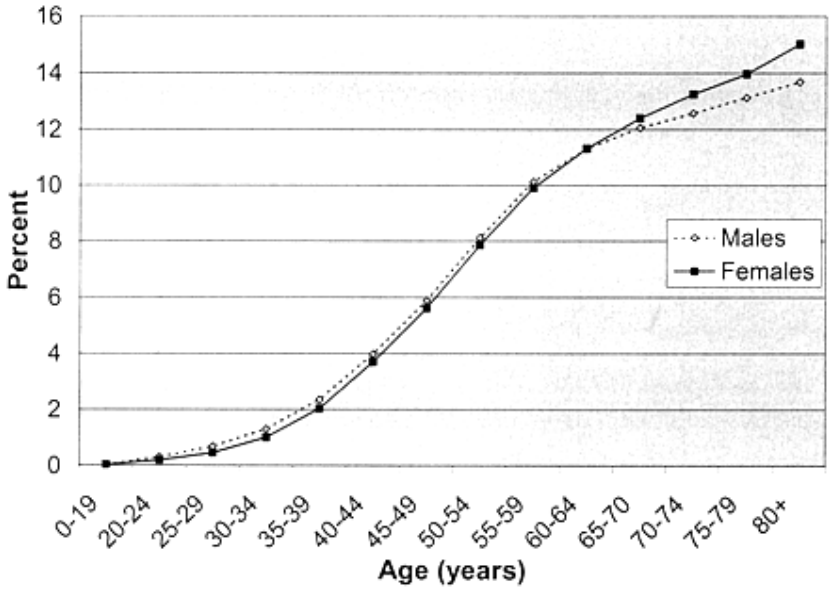
4.3 Pathology of diabetes[18]

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the ß-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects iinsulin action frequently coexist in the same patient, and it is often unclear which abnormality is the primary cause of the hyperglycaemia

4.4 Global burden of type 2 diabetes

Figure 4.1

Global diabetes prevalence by age and sex for 2000



Source: Global Prevalence of Diabetes Estimates for the year 2000 and projections for 2030

Diabetes Care 27:1047-1053, 2004

A diabetes epidemic is underway. Between 1995 and 2025 there will be a 35% increase in the worldwide prevalence of diabetes, from 4.0 to 5.4%.[1] Prevalence is higher in developed than in developing countries and will remain so in 2025. [1] In developed countries, the increase in prevalence will be 27%, from 6.0 to 7.6%. In developing countries, the increase will be 48%, from 3.3 to 4.9% between 1995 and 2025. The highest increases in prevalence will be for China (68%) and India (59%). [1]Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources.

The age structure of the diabetic populations of developed and developing countries are markedly different. For the developed countries, the oldest age group has

the largest number of people with diabetes in 1995 and will experience the greatest increase in numbers by the year 2025. [1] However, for the developing countries, the 45- to 64-year-old age group contained the largest number of people with diabetes in 1995, and this tendency will be further accentuated by the year 2025. The age structure of the world total follows the trend for developing countries.

4.5 Male/female diabetes ratio

For 1995 for the world as a whole, there were more women than men with diabetes (73 vs. 62 million[1]. The female excess is pronounced in the developed countries (31 vs. 20 million), but in the developing countries, there are equal numbers of men and women with diabetes (42 million in each case). By the year 2025, the worldwide female/male excess is estimated to be reduced somewhat (to 159 vs. 141 million).[1]

4.6 Urban rural difference

For developing countries as a whole, the urban/rural ratio in diabetes frequency is predicted to rise from 1.6 in 1995 to 3.3 in 2025[1].By 2025, there will be a considerable excess of diabetes in the urban areas.

4.7 Type2 diabetes –major health problem in India

Epidemiological studies among migrant Asian Indians in many countries showed higher prevalence of type 2 diabetes compared with the host populations and other migrant ethnic group[34]

India is facing an epidemic of type 2 diabetes,[2,3,24,55] with high prevalence in urban areas [29] .One fourth of the adult population in India is either already diabetic or ready to get it anytime (World Diabetes Foundation). By 2025, there will be three fold excess in urban areas. Male/female diabetes ratio in India is 1.3 (11 vs. 8 million). By 2025 male excess will, decrease in India. [2] Previous studies shows that South-Asian

ethnicity is associated with multiple risk factors for type 2 diabetes and CVD [51] Epidemiological studies among migrant Asian Indians in many countries showed higher prevalence of type 2 diabetes compared with the host populations and other migrant ethnic groups 2

4.8 Trends and burden in urban India

Studies conducted in India in the last decade have highlighted that not only isthe prevalence of type 2 diabetes high, but also that it is increasing rapidly in the urban population (Fig4.2)

Survey conducted in 1988-1989, in the city of Madras, south India, showed that the prevalence of diabetes mellitus in adults was 8.2% and prevalence of impaired glucose tolerance (IGT) was 8.7%.[31]. Another cross-sectional study conducted 5 years later in the same urban area age-standardized prevalence of diabetes had increased to11.6% from 8.2% in 1989 and IGT was 9.1%, similar to 8.7% in 1989[31]. In the peri urban study group, the age-standardized prevalence of Type 2 diabetes was 5.9%, which

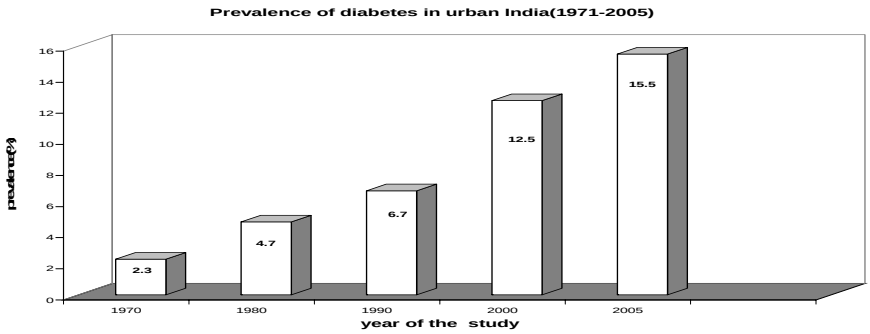


fig 4.2

Year	1970's	1980's	1990's	2000	2005
Study/Place	ICMR	Tenali	New Delhi	NUDS	CURES
Author	Ahuja	Murthy	Ahuja	Ramachandran	Mohan

was intermediate to that in the urban (11.6%) and rural (2.4%) populations.

4 .9 Burden in rural area

India has nearly 33 million diabetic subjects today. A wide urban-rural difference in the rates of prevalence of diabetes was evident in the last decade (a four-fold difference). Now,the impact of urbanisation is being felt in the rural population, which has also resulted in changes in their lifestyle. As a consequence there is an increase in the prevalence of diabetes in the rural population, too (from 2.2 per cent to 6.4 percent[44] There is also an increasing incidence of impaired glucose tolerance (IGT) in both the rural and urban population.

. A cross-sectional population survey was undertaken to determine the prevalence of diabetes mellitus (DM) and impaired glucose tolerance (IGT) in subjects aged 25 years and above in India.[59]The standardized prevalence rate for DM in the total Indian, urban and rural populations was 4.3, 5.9 and 2.7%, respectively. The corresponding IGT rates in the three populations were 5.2, 6.3 and 3.7%, respectively. The scenario is changing rapidly due to socio-economic transition occurring in the rural areas

Since most of the prevalence, studies of India were concentrated in urban areas, sufficient data is lacking from the rural areas**.** A study on the prevalence and management of diabetes in rural India, found 13 per cent of adults aged 30 or older have the disease, with a further 16 per cent exhibiting features of pre-diabetes. The study sampled more

than 4,500 people in rural areas of Andhra Pradesh[19]. The findings reflect the rapidly changing nature of health problems across India, even in remote rural aeas. Another major concern is since majority of Indian population is living in rural areas even small increase in prevalence in rural area will create significant burden on Indian health system.

4.10. Economic costs of diabetes

Because of its chronic nature, the severity of its complications and the means required to control them, diabetes is a costly disease, not only for affected individuals and their families, but also for the health systems.

Studies in India estimate that, for a low-income Indian family with an adult with diabetes, as much as 25% of family income may be devoted to diabetes care. Diabetic epidemic in India likely to trim approximately 1 per cent from the country's gross domestic product.. However, the full burden of diabetes is hard to measureas as death records often fail to reflect the role of diabetes in diagnosis.of cause of death.

4.11 Diagnositic criteria for type 2 diabetes [5,6,7,8,9]

In 1997, an International Expert Committee[5] was convened to re examine the classification and diagnostic criteria of diabetes, which were based on the 1979 publication of the National Diabetes Data Group and subsequent WHO study grou Because of its deliberations, the Committee recommended several changes to the diagnostic criteria for diabetes and for lesser degrees of impaired glucose regulation (IFG/IGT) [7] .The following were the major changes or issues addressed. The major change recommended in the diagnostic criteria for diabetes mellitus were[5]

1. The use of fasting plasma glucose (FPG) test for the diagnosis of diabetes.

2. Lowering of the diagnostic value of the fasting plasma glucose concentration to 7.0 mmol l^{-1} (126 mg dl^{-1}) and above from the former level of 7.8 mmol l^{-1} (140 mg dl^{-1}) and

above.

For whole blood the proposed new level is 6.1 mmol l^{-1} (110 mg dl^{-1}) and above, [12] from the former 6.7 mmol l^{8}(120 mg dl^{-1}). The WHO adopted this lower cut off point for FPG in 1999. The WHO-1999 criteria differ from the ADA criteria by still taking into account the post load glucose levels. Because the ADA criteria are based on fasting plasma glucose (FPG) values only, and the cut off point for the diagnosis of diabetes has been lowered to 126 mg/dL (7.0 mmol/L) (the cut off point of the WHO-1985 criteria is 140 mg/dL [7.8 mmol/L]),it is of importance to know how this affects the incidence of diabetes.

4.12 Rationale for the revised criteria for diagnosing diabetes

The revised criteria for diagnosing diabetes are based primarily on longitudinal studies demonstrating the presence of micro vascular and macro vascular complications at these lower glucose concentrations [61] In addition, the 1985 WHO diagnostic criterion for diabetes based on fasting plasma glucose level 140mg/dl represents a greater degree of hyperglycaemia than the criterion based on plasma glucose level two hours after a 75 g glucose load 200mg/dl.[8] A fasting plasma glucose level of>=126mg/dl accords more closely with this 2 h post-glucose.of hyperglycaemia than did the cut point of 2-h PG ≥ 200 mg/dl (11.1 mmol/l[27]

Table 4.1 new WHO criteria for diagnosis of diabetes mellitus

GLUCOSE CONCENTRATION, MMOL L/1 (MG DL/1)				
		Whole blood	Whole blood	Plasma*
		Venous	Capillary	Venous
Diabetes Mellitus:				
	Fasting	>=6.1 (>=110)	>=6.1 (>=110)	>=7.0 (>=126)

	or			
	2-h post glucose load	>=10.0 (>=180)	>=11.1 (>=200)	>=11.1 (>=200)
	or both			
Impaired Glucose Tolerance (IGT):				
	Fasting (if measured)	<6.1 (<110)	<6.1 (<110)	<7.0 (<126)
	and			
	2-h post glucose load	>=6.7 (>=120) and	>=7.8 (>=140) and	>=7.8 (>=140) and
		<10.0 (<180)	<11.1 (<200)	<11.1 (<200)
Impaired Fasting Glycaemia (IFG):				
	Fasting	>=5.6 (>=100) and	>=5.6 (>=100) and	>=6.1 (>=110) and
		<6.1 (<110)	<6.1 (<110)	<7.0 (<126)
	and (if measured)			
	2-h post glucose load	<6.7 (<120)	<7.8 (<140)	<7.8 (<140)

Source WHO: definition, diagnosis and classification of diabetes mellitus andits complication. Report of a WHO consultation part 1 diagnosis and classification of diabetes mellitus Geneva, world h1999

4.13 Advantages of fasting plasma glucose over oral glucose tolerance test

1. Reproducibility –a property for, which the FPG appears to be preferable.[40] When OGTT were repeated in adults during a 2 to 6 week interval, the intra-individual coefficients of variation were 6.4% for the FPG and 16.7% for the 2-h PG. [19] For the men in the Paris Prospective study[38] in whom diabetes was diagnosed at baseline, 58% diagnosed by FPG were still considered diabetic after 30 months of follow-up, Therefore, as expected, diabetes diagnosed by FPG was more stable[40]. The San Antonio group reported that patients diagnosed with diabetes exclusively based on the 2-hr PG were five

times more likely to revert to non diabetic status after 7–8 years of follow-up than those meeting the 126 mg/dl FPG diagnostic criteria

2. The measurement of FPG is less expensive and less intrusive than the 2-hr PG. Although both tests require overnight fasting for at least 8 h, the 2-h PG frequently results in an extended office visit for the patient, potentially resulting in more lost wages or an inability to engage in other desired activities

3. A minority of patients cannot tolerate the glucose challenge drink, making the results of the test uninterruptible because the full glucose load was not ingested.

4.14 Disadvantages of FPG

Some patients will not have actually fasted, potentially resulting in a falsely elevated FPG, whereas the impact of non fasting on the 2-h PG value may be less.

4.15 Prediabetes [11]

The term 'prediabetes' has been used to describe the condition in which blood glucose levels are higher than normal but not yet diabetic and includes the two abnormalities, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)**4.16**

Impaired fasting glucose[7] (IFG)

This stage includes individuals with fasting glucose levels ≥110 mg/dl (6.1 mmol/l) but <126 mg/dl (7.0 mmol/l) (IFG). In 1997 and 1999, American Diabetes Association and the WHO respectively added the term impaired fasting glucose

4.17 Impaired glucose tolerance. [7](IGT)

People whose FPG was <126 mg/dl but whose 2-h PG after a 75-g oral glucose challenge was 140–199 mg/dl. The FPG and 2-h PG are both single point-in-time measures of glycaemia. Both are associated with adverse outcomes that result from chronic hyperglycaemia. Although they are not interchangeable, since the FPG alone does

not always detect people with IGT and the 2-h PG does not always detect people with IFG, both tests are useful in terms of their ability to detect hyperglycaemia and the consequences of disordered glucose metabolism.

4.18 Pathophysiology of Prediabetes [11]

Normal control of FG depends on the ability to maintain adequate basal insulin secretion, and on appropriate levels of insulin sensitivity in the liver to control hepatic glucose output. Abnormalities of these metabolic functions characterise IFG. Defects of insulin secretion are often evident in IFG, whereas impaired insulin sensitivity may be more apparent in IGT. Individuals with isolated IFG and isolated IGT showed similar impairments in insulin action, but those with isolated IFG have a more pronounced defect in early insulin secretion and, in addition, increased endogenous glucose output. More severe metabolic abnormalities are present in individuals with combined IFG and IGT. Data from the RIAD study demonstrated that isolated IFG and isolated IGT show differences in the degree of insulin resistance and anomalies of insulin secretion: subjects with IGT exhibit a deficit in the early and late phases of insulin secretion, but this study is limited by its cross-sectional design.

4.19 Importance of Impaired fasting glucose

The category IFG was introduced to designate the zone between the upper limit of normal FPG and the lower limit of diabetic FPG,[5] much as IGT designates the zone between the upper limit of normal 2-h PG and the lower limit of diabetic 2-h PG.IGT and IFG are not clinical entities in their own right, but rather risk categories for future diabetes and cardiovascular disease[63, 64, 65]. Such subjects, like those with IGT, have increased risks of progressing to diabetes and macro vascular disease. Although prospective data are sparse and early available data suggest a lower risk of progression than IGT, although a similar CVD risk factor profile has been shown in subjects impaired

fasting glucose (IFG; fasting plasma glucose level 6.1–6.9 mmol/l) can predict future type 2 diabetes as accurately as does impaired glucose tolerance is still not clear. Some of the longitudinal population-based studies demonstrate the higher sensitivity of IGT over IFG for predicting progression to type 2 diabetes. Screening by the criteria for IFG alone would identify fewer people who subsequently progress to type 2 diabetes than would the oral glucose tolerance test.[38, 66, 67] Data from theHoorn study showed that the risk of diabetes does increase markedly at FPG concentrations above ~100 mg/dl. [63]

The Paris Prospective study[38] reported that the risk of developing diabetes over three years was greater among middle aged men with fasting blood glucose>6.1than it was for a lower FPG.

4.20. Impact of lowering impaired fasting glucose from 110 mg/dl to 100mg/dl

The Expert Committee on Diagnosis and Classification of Diabetes Mellitus recently recommended that the normal fasting glucose level should be adjusted downward from 110 to 100 mg/dl. The advantages of this change as reported by the committee have been questioned. [62,65]by a number of other studies.

4.21 Risk factors for diabetes [66]

Specific population subgroups have a much higher prevalence of diabetes than the population as a whole. These subgroups have certain attributes or risk factors that either directly cause diabetes or are associated. Several of the risk factors associated with diabetes are potentially modifiable

Most of the risk factors of diabetes are explained in terms of metabolic syndrome.[67]The metabolic syndrome is a cluster of the most dangerous heart attack risk factors: diabetes and prediabetes, abdominal obesity, high cholesterol and high blood

pressure According to the The International Diabetes Federation (IDF)), a person has the metabolic syndrome if they have central obesity (waist circumference > 94cm for Europid men and > 80cm for Europid women) plus any 2 of the following factors: increased triglyceride concentrations, reduced HDL cholesterol levels, increased blood pressure (systolic >130mmHg or diastolic >85mmHg), and increased fasting plasma glucose (>100mg/dL [5.6mmol/L]) or previously diagnosed type 2 diabetes. Definitions of obesity based on gender and ethnicity are provided(South Asians Male ≥ 90 cmFemale ≥ 80 cm) It also increases the risk of developing type 2 diabetes, if not already present, fivefold.[67]

Table 1— Risk factors for type 2 diabetes[66]

AGE ≥45 YEARS
OVERWEIGHT (BMI ≥25 KG/M2*)
FAMILY HISTORY OF DIABETES (I.E., PARENTS OR SIBLINGS WITH DIABETES
HABITUAL PHYSICAL INACTIVITY
RACE/ETHNICITY (E.G., AFRICAN-AMERICANS, HISPANIC-AMERICANS, NATIVE AMERICANS, ASIAN-AMERICANS, AND PACIFIC ISLANDERS
PREVIOUSLY IDENTIFIED IFG OR IGT
HISTORY OF GDM OR DELIVERY OF A BABY WEIGHING >9 LBS
HDL CHOLESTEROL ≤35 MG/DL (0.90 MMOL/L) AND/OR A TRIGLYCERIDE LEVEL ≥250 MG/DL (2.82 MMOL/L)
POLYCYSTIC OVARY SYNDROME

Source ADA position statements on screening for diabetes type 2 diabetes care volume27suppliment 1 January 2004

4.22 Risk factors for type2 diabetes mellitus – Indian population[29]

India is facing an epidemic of type 2 diabetes, with high prevalence in urban areas. Urbanization and associated life style changes adversely affect the risk factors for

diabetes unmasking the high genetic tendency existing in the population.[28]Various epidemiological studies in Indians have shown that the increasing prevalence of diabetes could be attributed to a high genetic risk and lower risk thresholds for acquired risk factors such as age, obesity,abdominal adiposity and a high percentage of body fat.

The risk of diabetes increases with a body mass index (BMI) of >23 kg/m(2) and waist circumference of 85 cm for men and 80 cm for women in Asian Indians.[29] For a given BMI, Asian Indians have higher central adiposity. However, the strong association between the BMI and diabetes indicated that even minor changes in BMI had adverse effects in the population Studies from India shows risk of diabetes in Indians increases at a lower BMI than western countries[50] Because Indian urban populations have a modest increase in overweight and low rates of obesity in association with the rapid emergence of diabetes and cardiovascular risk, a body mass index of 21 kg/m2 should be considered safe, with a range of 19-23 kg/m2 acceptable; > 23 kg/m2 should be considered overweight, and > 25 kg/m2 should be taken to indicate obesity. A waist: hip ratio > 0.88 in males and > 0.85 in females should be considered to indicate central obesity [57]

Increasing age, obesity, positive family history of diabetes, abnormal sub scapular triceps skin fold ratio were all found to be associated with increased risk of DM[49]Indians have an increased susceptibility to type 2 diabetes and insulin resistance compared with Europeans Recent studies indicate a rising prevalence of diabetes and insulin resistance. Prevalence of diabetes was found to be lower in the low socio-economic group living in urban areas compared with the high-income group.

Clustering of cardiovascular risk factor

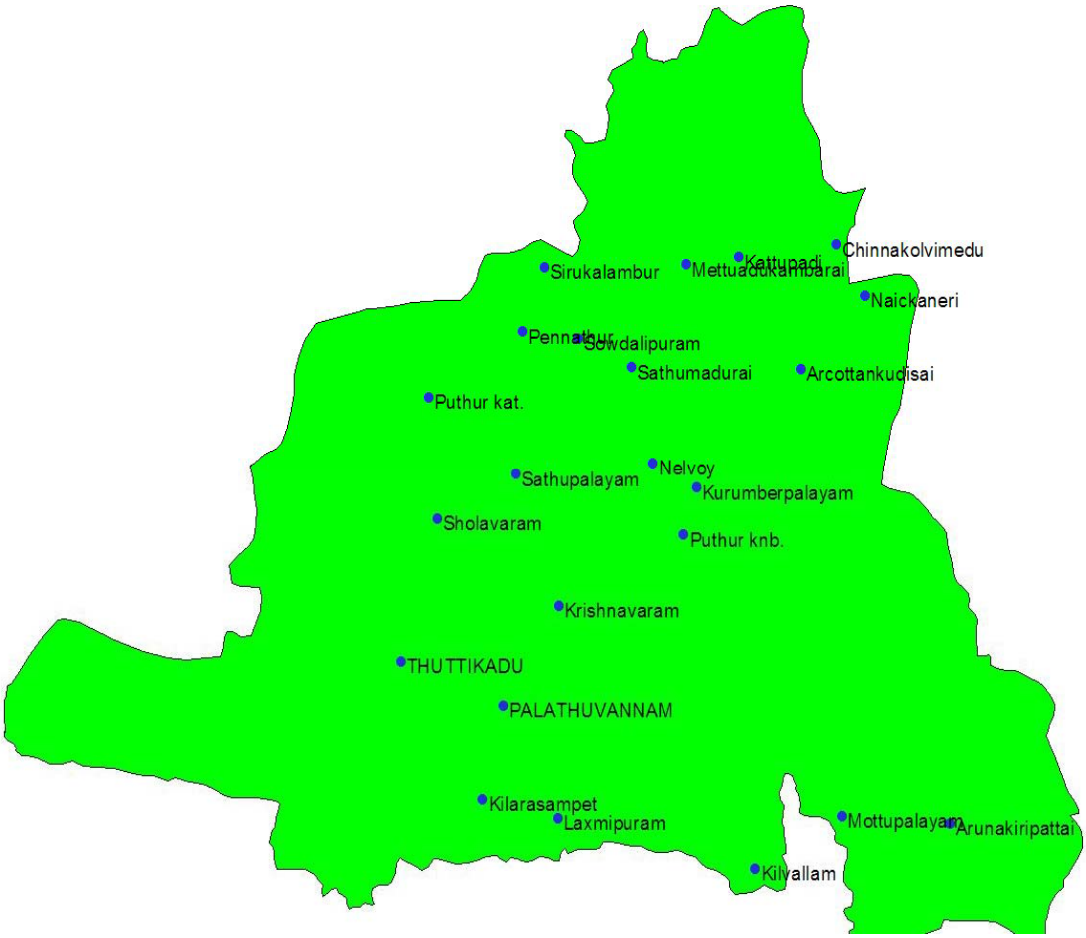
Clustering of cardiovascular risk factors (or syndrome ‘X’) namely central adiposity, obesity, hyperinsulinaemia, dyslipidaemia, hypertension and glucose intolerance has been

noted in urban Indians in studies by Ramachandran *et al.* by Mohan *et al* and by Mishra *et al.*

Prevention of type 2 diabetes

Epidemiological data suggest that lifestyle changes involving increased physical activity and reduced energy intake will at least partially prevent type 2 diabetes. It is only very recently that prospective intervention studies have clearly confirmed the efficacy of such measures[68,69] The American , and Finnish prevention studies, illustrate the benefits in a developed country. Participants in both studies were people who already had IGT and were overweight or obese (thus a very high-risk group). With a mean follow-up of about 3 years, the two studies had remarkably concordant outcomes, with a 58% reduction in incidence of type 2 diabetes, resulting from a reduction in energy intake targeted to achieve weight reductions of 7% and 5%, respectively, and an exercise regimen targeted to achieve moderate levels of exercise for 150 and 210 minutes per week, respectively.

KANIYAMBADI BLOCK
STUDY AREA



5. MATERIALS AND METHODS

5.1. Study area

The study was conducted in Kaniyambadi block, North Arcot Ambedker district in Tamil Nadu. This Panchayath union is adjacent to the Vellore town and has a population of 102,629 (2000CHAD census). The Community Health Department of

Christian Medical College; Vellore has been carrying out an Integrated Community health and development programme in this block since 1960. The villages included in this study are highlighted in the **figure5.1.** The villages under study are of same social, demographic and cultural characteristics with farming as the main occupation of the residents.

5.2. Baseline survey

Baseline data for the cohort study came from a cross sectional study on coronary heart disease performed by Christian Medical College as a part of Indian Council of Medical Research collaborative study on coronary heart disease between 1991and 1993. This multicentric study was done by Delhi and Vellore centres in both urban and rural areas

5.3 Baseline survey methodology

- Twenty three clusters of villages were selected using cluster sampling (probability proportionate to size.).
- All individual between the ages of 30 and 60 were enumerated and invited for the study. The response rate was 71%.That is 4693 individuals were studied.
- Cross sectional data was obtained on several risk factors including socio-demographic, biochemical, clinical, anthropometric and lifestyle related risk factors.
- Among the respondents, biochemical parameters were obtained for 3,108 individuals.

5.4 Baseline biochemical measurement

Important biochemical measurements done in the baseline survey were- fasting plasma glucose, total cholesterol and lipid profile. Fasting plasma glucose was measured in the baseline survey after ensuring overnight fasting.. The method used for plasma

glucose measurement was glucose oxidase peroxidase (GOD/POD) method.. Oral glucose tolerance test was not done in the baseline survey.

5.5 Measurement of risk factors at the baseline study

A structured interview schedule was used to obtain information on potential risk factors for coronary heart disease and diabetes at the baseline survey like history of smoking, alcohol, socioeconomic status. Standard methods were used to measure height, weight, and waist and hip circumference. Both systolic and diastolic BP were measured in the right arm after making the participant sit comfortably in a chair.

5.6 Current study

5.6.1 Study design

Non concurrent cohort study.

5.6.2 Study period

March 2006 – June 2006.

5.6.3 Study population

Study population consists of an eligible cohort selected from the baseline cohort after applying certain inclusion and exclusion criteria**.**

5.6.4 Methodology

Detailed data of the Participants in the baseline survey were collected. A follow up survey was performed retrospectively between March 2006 and June 2006. Of the initial cohort, 325 subjects had moved out of the Kaniyambadi block, 310 people were dead and 51 could not be traced.

Participants at the baseline survey were grouped according to baseline fasting plasma glucose. Those who were having fasting plasma glucose value of 80-126mg/dl with complete individual clinical biochemical and household data were eligible for the

present study. Those who were dead, migrated or not traceable were excluded from the study. The population who fitted in the inclusion criteria were considered eligible to participate in the present study and formed the eligible cohort which was 1852.

5.6.5 Sample size determination

Table 5.1

Sample size calculation for each sub group of fasting plasma glucose

Baseline FPG group	Cumulative incidence(%)	precision	95%confidence interval	Sample size
80-89mg/dl	4	2.5	1.5-6.5	246
90-99mg/dl	11	4.5	6.5 -15.5	193
100-109mg/dl	25	9	16 -34	93
110-125 mg/dl	50	13	37 -63	59

Due to constraints in time and money, all people in the eligible cohort were not included in the follow up study. Participants in the eligible cohort were stratified into four groups according to baseline fasting glucose (FPG) level as given below.

1. FPG value of 80 mg/dl - 89mg/dl.
2. FPG value of 90mg/dl - 99mg/dl
3. FPG value of 100-109mg/dl
4. FPG value of 110-125mg/dl

The sample size was determined using the formula for each group

$$n = 4pq/d^2$$

1. For the baseline FPG of 80mg/dl to 89mg/dl

Assuming the cumulative incidence for this group is 4% with 95% confidence interval and precision of 2.5%

$$\mathbf{n_1 = 4x4x96/2.5^2 = 246}$$

95% confidence interval 1.5 - 6.5

2. For the baseline FPG of 90mg/dl to 99mg/dl

Assuming the cumulative incidence for this group is 11% with 95% confidence interval and precision of 4.5 %

$\mathbf{n_2 = 4x11x89/4.5^2 = 193}$ **95% confidence interval 6.5 -15.5**

. 3. For the baseline FPG of 100mg/dl to 109mg/dl

Assuming the cumulative incidence for this group is 25% with a confidence interval of 95% and precision of 9%

$\mathbf{n_3 = 4x25x75/9^2 = 93}$ **95% confidence interval 16 - 34**

4. For baseline FPG of 110mg/dl to 126mg/dl

Assuming the cumulative incidence for this group is 50% with a confidence interval of 95% and precision of 13%

$\mathbf{n_4 = 4x50x50/13^2 = 59}$ **95% confidence interval 37 - 63**

Total sample size required = 246+193+93+59 = 591

Assuming 90% response rate, the sample size needed was

80-89mg/dl	270
90-99mg/dl	212
100-109 mg/dl	102
110-125 mg/dl	65

To achieve a sample size of 591 assuming 90% response rates a total of 649 people were needed .A sub cohort of 649 people were selected from the eligible cohort by

stratified random sampling. The lowest cut point of FPG for the study group was 80 to 89 mg/dl and highest cut of FPG was 110-125 mg/dl.

5.6.6. Data collection

5.6.7 Blood glucose measurement

A. Fasting plasma glucose measurement

All participants in the study cohort were asked to attend a survey site in their village between 7 am 8 am after an overnight fasting. The procedure and purpose of this study were explained to the patient and verbal consent was obtained. The blood sample were collected in tubes containing sodium fluoride. To ensure that venous fasting blood sugars were reliably determined fasting blood samples were delivered to the laboratory within one hour of collection.

B.Oral glucose tolerance test

Before giving oral glucose, a separate verbal consent was taken from participants and the procedure was explained to them .. 75 gram of anhydrous glucose in 250-m1of water was given and the blood samples were collected 2 hours later in tubes containing sodium fluoride. Samples were delivered to the laboratory within one hour of collection Biochemical analysis of blood was performed on fresh samples by glucose oxidase method using Hitachi 912 Auto analyzer. For comparative purpose same biochemical test was used for both the baseline study and the follow up study. Both the baseline and the follow up survey plasma glucose was tested in the CMC biochemistry laboratory.

5.6.8 Measurement of risk factors at present study

A large number of risk factors were measured during the baseline survey.

. A selected number of risk factors were measured in the present survey including weight, height, abdominal circumference and blood pressure, with the same method as described

in the baseline study in order to minimize biases. Height and weight were measures using standard measuring scales. Waist circumference was measured using ordinary measuring tape at the level of umbilicus. Body mass index was calculated using the formula - weight divided by the square of the height (kg/m^2).

Variables to assess the socio economic status (SES) of the subject were-Type of the house, owner ship of house, land ownership, occupation of the head of the household and highest education of the house hold. Physical activity was assessed as perceived by the subject about his work related as well as leisure time activity.

5.6.9. Statistical analysis of the data

The raw data was entered into Microsoft excel and was verified by the investigator..Statistical analysis was carried out using SPSS 12

6. STATISTICAL PROCEDURES

Outcome definition

Since there is considerable controversy regarding diagnostic criteria of Type 2 diabetes, two different criterias were used for diagnosis of diabetes

1. Fasting plasma glucose value of 126mg/dl or more

This criteria WAS put forward by American Diabetes Association in 1997

2 Either FPG>=126mg/dl or OGTT>=200mg/dl (WHO 1999 criteria)

The WHO prefers OGTT over FPG and has specified that if circumstances were not allowing for oral glucose tolerance test to be done then fasting plasma glucose could be used for the diagnosis of diabetes.

6.1 Incidence of diabetes

. Calculation of Incidence can be

A. Cumulative incidence

B Incidence density

B. Annual incidence of infection

Cumulative incidence (CI) reflects the probability that an individual develops a disease during a given time period.

$$\textbf{Cumulative incidence} = \frac{\textbf{Number of new cases of a disease during a given time period}}{\textbf{Total population at risk}}$$

Incidence density it is the number of people diagnosed newly as diabetic/total follow up years multiplied by 1000. In this cohort study mean year of follow up was 14.16years.

Since our study couldn't collect the data about the exact period in which cases develop we assumed that people progressed to diseased state exactly in the middle of the study period. Mean follow up period for the cases was taken as 7.06 years and mean follow up period for non cases was 14.12 years

$$\text{Incidence density} = \frac{\text{New cases of the disease during a period of time}}{\text{Total person-time of observation}}$$

Annual risk of infection It is calculating from cumulative incidence

$$CI = 1 - e^{-it}$$

CI = Cumulative incidence.

t = Time period of the study.

i=Annual incidence of infection

e = exponential

i=ln (1-CI)/t ln is the natural log

6.2 Calculation of relative risk

Relative risk and 95% confidence interval are calculated to determine the strength of association between selected risk factors and annual incidence of diabetes. Relative risk was calculated using the formula.

RR= Incidence of disease among exposed / incidence of disease among nonexposed

95% confidence interval calculated using epi info6.

6.3 Logistic regression

The present study out come was defined as whether progressed to diabetes or not .since outcome of the study were measured as dichotomous variable, logistic regression was used.

6.3.1 Univariate analysis

Univariate analysis was done to calculate strength of association between baseline fasting blood sugar and other selected risk factors of future diabetes. Those facters found significant in the univariate analysis were included in the multivariate analysis.

6.3.2 Multivariate analysis

To assess the independent effect of baseline risk factors associated with diabetes multivariate logistic regression was used for analysis..It permits control for confounding and evaluation of interaction for a host of variable with great statistical efficiency. The risk factors included for analysis were sex, age, baseline FPG, baseline cholesterol, baseline blood pressure BMI and abdominal circumference

7. RESULTS

7.1 Baseline cohort

7.1.1Age sex specific prevalence of diabetes in baseline cohort according to FPG>=126 mg/d l(1997 ADA criteria)

Table 7.1 showed that the prevalence of type 2 diabetes in baseline cohort as per ADA criteria was 2.96%. Prevalence of diabetes increases with age and .highest prevalence was for the age group 51-60 years. Males had higher prevalence than females.

Table 7.1.1

Age sex specific prevalence of diabetes in baseline cohort according to FPG>=126mg/dl

AGE GROUP	FREQUENCY			FPG>= 126MG/DL			PREVALENCE PER 100		
	Male	Female	Total	Male	Female	total	Male	Female	Total
30-40	667	924	1591	15	17	32	2.2	1.8	2.01
41-50	385	542	927	17	13	30	4.4	23..9	3.23
51-60	290	299	589	16	14	30	5.5	4.7	5.09
Total	1342	1765	3107	48	44	92	3.6	2.5	2.96

7.1.2. Descriptive statistics of the baseline cohort according to the FPG

Table 7.1.1 showed that 58.5% of the baseline cohort accepting study criteria were females and 41.5% were males. 13.08% of the people belonged to the impaired fasting glucose category according to the American diabetes association's (ADA) revised category.(100-125mg/dl)

Table 7.1.2

Classification of baseline cohort above 80mg/dl and below 126mg/dl

BASELINE FPG	MALE (%)	FEMALE (%)	TOTAL (%)
80-89	551(55.2)	770(54.7)	1321(54.9)
90-99	309(30.9)	462(32.8)	771(32)
100-109	98(9.8)	132(9.4)	230(9.6)
110-125	41(4.1)	44(3.1)	85(3.5)
Total	999(100)	1408(100)	2407(100)

7.2 Descriptive statistics of study cohort

7.2.1. Age and sex distribution of study cohort

Table 7.2.1 showed that 47.5% of the study cohort belonged to the 40-50 age group. Male and female distribution of study cohort was 38.6% and 61.4% respectively. Table 7.2.1 showed that male and female population were uniformly distributed in each age group.

Table 7.2.1

Age and sex distribution of study cohort

AGE GROUP AT PRESENT SURVEY (YEARS)	MALE (%)	FEMALE (%)	ALL (%)
40-50	107(46.94)	173(47.79)	280(47.5%)
51-60	67(29.38)	129(35.64)	196(33.2%)
61-70	54(23.68)	60(16.57)	114(19.3%)
Total	228(100)	362(100)	590(100)

7.2.2Classification of study cohort according to the Baseline glucose

The total number subjects studied were 590. The planned sample size in FPG of group110-125mg/dl could not be achieved .Proportion of participants in each group of baseline FPG is comparable with that of baseline cohort.

Table 7.2.2 Classification of study cohort according to baseline FPG

BASELINE FPG	MALE (%)	FEMALE (%)	TOTAL (%)
80-89	109(47.8)	154(42.5)	263(44.4)
90-99	63(27.6)	121(33.4)	184(31)
100-109	37(16.3)	62(17.2)	99(16.7)
110-125	19(8.3)	25(6.9)	44(7.4)
Total	228(100)	362(100)	590(100)

7.2.3 Baseline characteristics of people in the study cohort according to the baseline FPG

Table 7.2.3 showed that mean of the baseline systolic and diastolic blood pressure at the study cohort remained same for all categories of baseline glucose. Mean cholesterol, mean age, and mean waist circumferences were increasing along with each category of baseline fasting glucose.

Table 7.2.3

Baseline characteristics of participants in the study cohort according to baseline FPG

Baseline glucose (mg/d)l		cholesterol	Systolic BP	Diastolic BP	Study age	BMI	Waist circumference
80-89	Mean	153.1	127.1	80.2	41.41	20.4	70.8
	N	263	263	262	263	260	260
	Std. Deviation	35	25.6	9.1	8.3	3.1	8.3
90-99	Mean	162.7	126	80.4	43.8	21.5	72.
	N	184	184	182	184	184	182
	Std. Deviation	35.16	25.3	7.8	8.1	3.8	11.6
	Mean	172.4	128.1	80.7	43.6	21.9	74.5

100-109	N	99	99	97	99	97	98
	Std. Deviation	37.3	19.6	6.7	7.9	3.8	10.9
110-125	Mean	175.3	128.9	80.9	45.5	22.9	75.6
	N	44	44	44	44	43	44
	Std.	39.6	24.5	10.3	8.123	3.90926	16.338
	Total	590	589	585	590	584	584

7.3 Incidence of type2 diabetes in study cohort

As described earlier three different methods were used for calculation of Incidence

A. Cumulative incidence

B Incidence density

B. Annual incidence of infection

Cumulative incidence (CI) reflects the probability that an individual develops a disease during a given time period.

$$\text{Cumulative incidence} = \frac{\text{Number of new cases of a disease during a given time period}}{\text{Total population at risk}}$$

$$\text{Incidence density} = \frac{\text{New cases of the disease during a period of time}}{\text{Total person-time of observation}}$$

Mean follow up years for the study were 14.16 Mean follow up years for cases were considered as 7.08 years assuming that the participants progressed to cases exactly at the middle of the follow up years.

Annual incidence was calculated by the formula

i= ln (1-CI)/t where i is the annual incidence, t time period of the study and CI is the cumulative incidence.

Annual incidence and incidence density measures the incidence rate where as the cumulative incidence measures the risk. of developing the disease.

Present study diagnosed diabetes based on two different diagnostic criteria

1. Fasting blood sugar >=126mg/dl alone. (ADA 1997)

2. Either FPG >=126mg/dl or OGTT>=200mg/dl. (WHO-1999)

Table 7.3.1A showed that Incidence of diabetes of study cohort was 12.86 per 1000 PY using the criteria of FPG alone and 18.65 per1000 PY when defined by either FPG >=126mg/dl or OGTT>=200mg/dl. Incidence density of diabetes using FPG alone as criteria was 13.65 per person years and either FPG or OGTT was 19.63 per1000 person years .

Both approaches should yield similar results.The minor differences of the results in the annual incidence of the diabetes and incidence density weredue to the differences in the computational methods used..The annual incidence rate calculated from the cumulative incidence assumes a constant rate of incidence through out the time period resulting in the survivors demonstrating a negative exponential curve.in general estimate arrived in this method will be slightly smaller than the incidence rate obtained through using person years as the denominator.

As shown in the table7.3.1 diabetes defined by the either fasting plasma glucose (FPG) or oral glucose tolerance (OGTT)prodces a higher estimate for incidence of the diabetes.

Table 7.3.1A

Incidence of diabetes in study cohort according to Two different criteria

DIAGNOSTIC CRITERIA	NUMBER OF PEOPLE	NUMBER OF CASES	CUMULATIVE INCIDENCE	FOLLOW-UP (PERSON-YEARS)	INCIDENCE DENSITY PER1000PY	ANNUAL INCIDENCE PER 1000PY
FPG>=126mg/dl	590	104	17.6%	7620.86	13.65	12.86
FPG>=126mg/dl or OGTT>=200mg/dl	590	144	24.4%	7336.32	19.63	18.65

7.4 Association between risk factors and incidence of type2 diabetes

7.4.1 Age and incidence of diabetes

Table 7.4.1Aand 7.4.1B showed that annual incidence of diabetes increased with age. Relative risk was calculated from the cumulative incidence considering 30-40 age group as the reference category.

Table 7.4.1A Association between age and type2 diabetes (FPG>=126mg/dl)

AGE GROUP AT BASE LINE SURVEY	FREQUENCY	PROGRESSION TO FPG>=126MG/DL	CUMULATIVE INCIDENCE	ANNUAL INCIDENCE PER1000	RR(CI)
30-40	280	38	13.6	9.72	1
41-50	196	36	18.4	13.38	1.32
51-60	114	30	26.3	20.15	1.93

Table7.4.1B Association between age and type2 diabetes (either FPG>=126mg/dlor OGTT>=200mg/dl)

AGE GROUP	FREQUENCY	PROGRESSION TO FPG>= 126 OR OGTT>=200	CUMULATIVE INCIDENCE	ANNUAL INCIDENCE PER 1000PY	RR(95% CI)
30-40	280	52	18.6	13.7	1
41-50	196	50	25.5	19.64	1.37
51-60	.114	42	36.8	30.64	1.97

7.4.2 Baseline Fasting plasma glucose and annual incidence of type2 diabetes

Table7.4.2A and table7.4.2B, showed that as baseline glucose increased risk of future diabetes also increased. This result is in agreement with western longitudinal studies especially Pima Indian studies and Hoorn study in Dutch population.

Table 7.4.2A

Annual incidence when diabetes defined by FPG alone

Base line FPG	frequency	Progression to FPG>=126mg/dl	Cumulative Incidence (%)	Annual incidence per 1000	RR(ci)

80-89	263	24	9.1	6.38	1
90-99	184	29	15.8	11.43	1.74
100-109	99	29	29.3	23.11	3.22
110-125	44	22	50	46.21	7.24

Table7.4.2 B

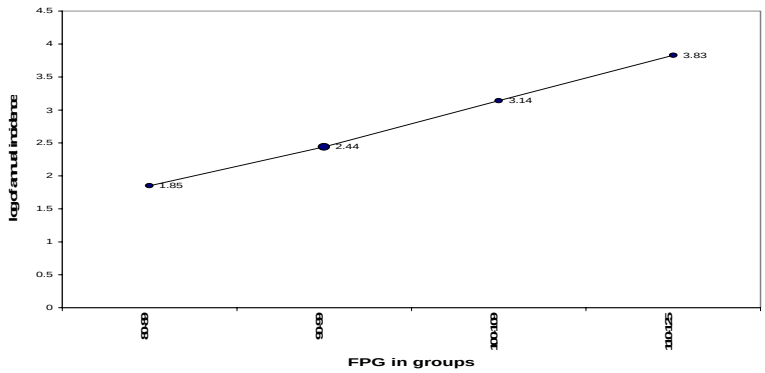
Annual incidence when diabetes defined by FPG>=126 or OGTT>=200mg/dl

Base line FPG	Frequency	Progression to FPG>= 126 or OGTT>=200	Cumulative Incidence (%)	Annual incidence per 1000PY	CI
80-89	263	39	14.8	10.7	1
90-99	184	43	23.4	17.74	1.58
100-109	99	38	38.4	32.28	2.59
110-125	44	24	54.5	52.56	4.91

7.4.3 Log of annual incidence and diabetes as defined by either FPG criteria

Fig 7.4.3 showed that when log of annual incidence plotted against baseline glucose the graph described a linear relation

Fig 7.4.3 Log of annual incidence and diabetes as defined by either FPG criteria



7.4.4Linear regression for log of annual incidence

Using the regression equation

$$y = a + bx$$

where a is the constant

b-regression coefficient

y-dependant or outcome variable (log of annual incidence)

x - Is the independent or predictor variable

y=1.85

a= 1.168

b=0.655

7.4.5 Projected annual incidence of baseline FPG below 80mg/dl

Assuming the FPG group 60- 69mg/dl and70-79mg/dl follows the linear relation log annual incidence is calculated for these groups

Log annual incidence of FPG of 70-79mg/dl group **1.85 -0.655 = 1.195**

Log annual incidence of FPG of 70-79mg/dl group **1.195-0.655 = 0.54**

Antilog of this values will give the annual incidence of that group

Projected annual incidence of 60-69mg/dl group **1.71per 1000PY**

Projected annual incidence of 70-79mg/dl group **3.303 per 1000PY**

7.4.6Incidence of type2 diabetes in baseline cohort

Incidence of diabetes in the study cohort cannot be applied to baseline cohort since study cohort is lacking the population representative of the baseline glucose value less than 80mg/dl.Since log of annual incidence plotted against baseline FPG followed linear relation .Annual incidence of FPG 60-69 group and 70-79 were calculated from extrapolated results.

It would be interesting to apply baseline FPG specific incidence rate to the entire baseline cohort to estimate the expected 15 year cumulative incidence in the group.

Table7.4.6 projected Incidence of type2 diabetes in baseline cohort as defined by FPG>=126mg/dl or OGTT >=200mg/dl

BASELINE FPG	TOTAL	ANNUAL INCIDENCE PER1000	EXPECTED INCIDENCE
60-69	91	1.71	0.16

70-79	518	**3.303**	1.71
80-89	1321	**6.38**	8.43
90-99	771	**11.43**	8.81
100-109	230	**23.11**	5.31
110-125	85	46.21	3.93
Total	3016	-	28.35

Projected annual incidence in the baseline cohort

28.35/3016*1000 = 9.4 per 1000 PY

Cumulative incidence = $1-e^{-it}$ **i = 0.0094**

t = 14.16

it = 0.0094 x 14.16 = 0.1331

-it = - 0.1331

e^{-it} **= 0.875**

Cumulative incidence = 1 - 0.875 = =12.5%

Assuming baseline cohort also followed the annual incidence of study cohort

The cumulative incidence of baseline cohort 12.5%

Comparison of the projected cumulative incidence of baseline cohort to the baseline prevalence in 1991 survey (2.9%) showed that there has been currently atleast 4.3

fold increase in burden of diabetes if the baseline cohort followed the same incidence rate.

7.4.7. Cumulative incidence of type2 diabetes according to baseline fasting plasmaglucose

The present study participants are classified according to baseline fasting plasma glucose and measured risk of diabetes across each category. Below an FPG of 85 mg/dl less than 7% participants progressed to diabetes. Incidence of diabetes started to rise in those with FPG 95mg/dl and above. Incidence of diabetes was highest in the group with FPG 110-125mg/dl. 52.54% of the study participants in the group with FPG 110-125mg/dl became progressed to diabetes when using FPG or OGTT as diagnostic criteria.

Fig7.4.7A.Diabetes defined by FPG>=126 mg/dl

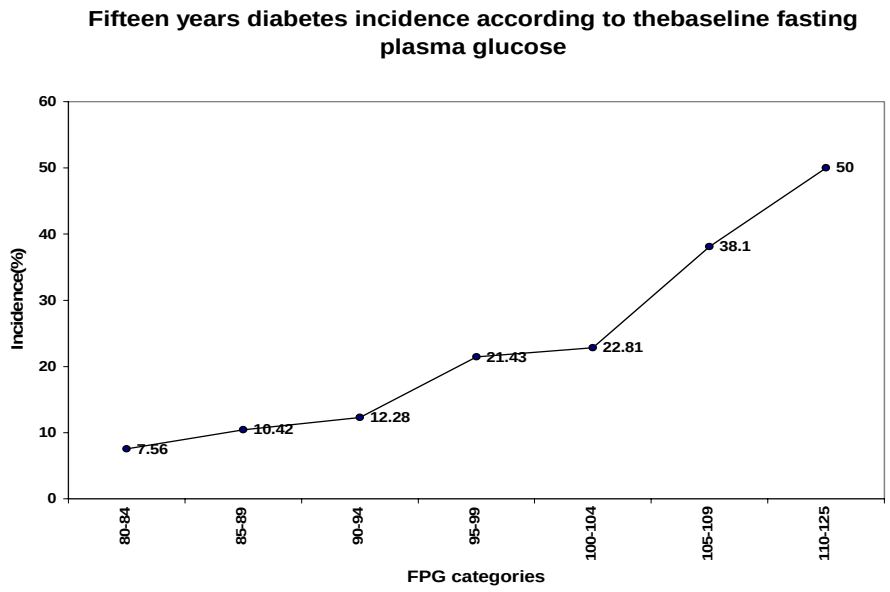
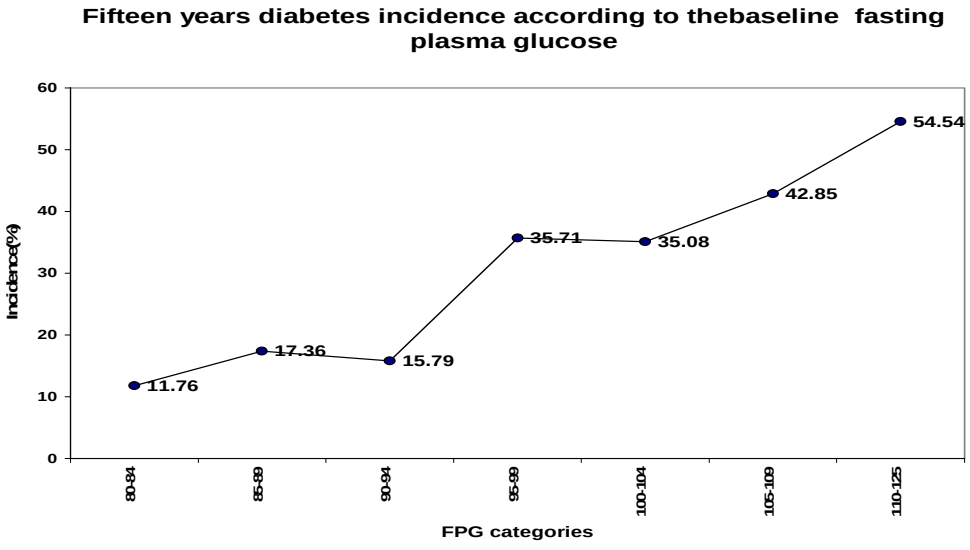


Table 7.4.7B Diabetes defined by either FPG or GTT>=200mg/dl



7.4.8 Association between sex and type2 diabetes

Annual incidence of diabetes as defined by two criteria (table7.4.4A& 7.4.4.) in males and females were calculated separately and relative risk was estimated.it showed that males were having higher risk of diabetes than females..Global estimate of diabetes also showed that India male sex is more at risk than female for type 2 diabetes

Table 7.4..8A.

Annual incidence of diabetes as defined by FPG alone

SEX	Frequency	FPG>=126MG/DL	Cumulative Incidence (%)	ANNUAL INCIDENCE PER1000	RR(95%CI)
Female	362	49	13.53	9.70	1
Male	228	55	24.12	18.40	1.78(1.15-2.77)

Table 7.4.8.B

Annual incidence of diabetes as defined by either FPG or OGTT

SEX	Frequency	BY FPG>=126 OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
female	362	79	21.81	16.41	1
Male	228	65	28.50	22.37	1.31(0.81-1.92)

7.4.9 Baseline blood pressure and incidence of diabetes

As shown in 7.4.9A to 7.4.9 B tables those with hypertention had nearly two times higher risk of developing future diabetes compared to the reference category. This difference was statistically significant

Table 7.4.9.A Incidence of diabetes as defined by FPG alone

BLOOD PRESSURE	Frequency	FPG>=126MG/DL	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
SBP<140 or DBP<90	461	67	14.53	10.54	**1**

SBP>=140 or DBP>=90	132	37	28.03	21.93	**1.93(1.21-3.08)**

Table 7.4.9B

Incidence of diabetes as defined by either FPG or OGTT

BLOOD PRESSURE	Frequency	FPG>=126 OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
SBP<140 or DBP<90	461	93	20.17	15.13	1
SBP>=140 or DBP>=90	132	51	38.63	32.56	1.92(1.27-2.89)

7.4.10. Annual incidence of diabetes according to baseline cholesterol

7.4.6A to 7.4.6D showed that baseline cholesterol above 150mg/dl annual incidenc seems to be increased. A cholesterol value of >=200mg/dl had 3-4 times higher risk of getting diabetes compared to cholesterol value <=150mg/dl

Table 7.4.10.A

Annual incidence of diabetes as defined by FPG alone

TQTAL CHOLESTROL	Frequency	FPG>=126MG/DL	)	ANNUAL INCIDENCE PER1000	RR(95%CI)
<=150	243	27	11.11	7.85	1
151-200	258	50	19.37	14.36	1.74(1.03-2.96)
>=201	89	27	30.33	24.10	2.73(1.46-5.11)

Table7.4.10.B Annual incidence of diabetes according to baseline cholesterol as defined by either FPG or OGTT

TQTAL CHOLESTROL	Frequency	FPG>=126MG/DL OGTT>=20OMG/	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
<=150	243	38	15.63	11.33	1
151-200	258	68	26.35	20.4	1.68(1.07-2.66)
>=201	89	38	42.69	37.12	2.73(1.59-4.70)

7.4.11 Physical activity at baseline survey and Annual incidence of diabetes

Table7.4.7A & 7.4.7B showed that heavy physical activity had a protective effect on type2 diabetes. People who were heavy workers had low incidence of diabetes.

Table7.4.11A Diabetes defined by FPG alone

PHYSICAL ACTIVITY	Frequency	PROGRESSION TO FPG>=126	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Mild to moderate	336	70	20.83	15.57	1
Heavy	254	34	13.39	9.58	0.642(40-1.02)

Table 7.4.11.B Annual incidence of diabetes as defined by either FPG or OGTT

PHYSICAL ACTIVITY	Frequency	PROGRESSION TO FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Mild to moderate	336	95	28.27	22.15	1
Heavy	256	49	19.14	14.29	0.677(0.45_1.01)

7.4.12 Body mass index at baseline survey and annual incidence of diabetes

Table 7.4.8A to shows that as compared to the reference category (<=20kg/m^2 the group with BMI 21kg/m2-24kg/m2 had two fold risk of getting diabetes. This risk

increases to 5 times when BMI increases>=25kg/m2.This showed that risk of future diabetes started at a lower BMI compared to the western countries.

Table 7.4.12.A

Diabetes defined by FPG alone

BMI	Frequency	PROGRESSION TO FPG>=126	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
<=20kg/m^2	306	26	8.49	5.92	1
21-24 kg/m^2	194	43	22.16	16.72	2.61(1.51-4.53)
>=25 kg/m^2	80	32	40	34.06	4.71(2.56-8.69)

Table 7.4.12.B

Diabetes as defined by either FPG or OGTT

BMI	Frequency	PROGRESSION TO EITHER FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
<=20 kg/m^2	306	41	13.39	9.59	1
21-24 kg/m^2	194	61	31.44	25.16	2.34(1.49-3.71)
>=25 kg/m^2	80	38	47.5	42.96	3.54(2.07-6.06)

7.4.13 Socio economic status annual incidence

Table7.4.9 shows that people from higher socioeconomic status are at higher risk of getting diabetes than lower socioeconomic status**.**

Table 7.4.14A

Diabetes defined by FPG alone

SES	Frequency	PROGRESSION TO FPG>=126ALONE	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Low	91	11	12.08	8.59	1
Middle	421	70	16.6	12.12	1.37(0.67-2.87)
High	78	23	29.4	23.29	2.43(1.05-5.73)

Table 7.4.14.B

Diabetes as defined by either FPG or OGTT

SES	Frequency	PROGRESSION TO EITHER FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE	RR(95%CI)
Low	91	14	15.38	11.13	1
Middle	421	104	24.70	18.91	1.6(0.85-3.08)
High	78	26	33.33	27.03	2.16(1.00-4.72)

7.4.15 Annual incidence of diabetics according to baseline waist circumference

For definition of abdominal obesity cut off used was males >=85cm of waist circumferences and females>=80cm. These measurements were done at the level of umbilicus using ordinary measuring tape.

Table 7.4.15.A

Diabetes defined by FPG alone

WAIST CIRCUMFERENCE	Frequency	PROGRESSION TO FPG>=126 ALONE	Cumulative Incidence (%)	ANNUAL INCIDENCE	RR(95%CI)
Non obese	492	66	13.41	10.10	1
Obese	98	38	38.77		2.89(1.79-4.66)

Table 7.4.15.B

Diabetes as defined by either FPG or OGTT

WAIST CIRCUMFERENCE	Frequency	PROGRESSION TO EITHER FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Non obese	492	94	19.10	15.23	1
Obese	98	50	51.02	49.08	2.67(1.74-4.09)

7.5 Association between selected risk factors at present survey and type 2 diabetes

7.5.1 Association between obesity at present survey and type 2 diabetes

Table 7.5.1A&B showed that people who progressed to obesity during 15 years time period have higher risk of diabetes than nonobese people**.**

Table 7.5.1A

Diabetes defined by >=126mg/dl

WAIST CIRCUMFERENCE	Frequency	PROGRESSION TO FPG>=126 ALONE	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Non obese	354	42	11.86	8.41	1
Obese	138	24	17.39	12.73	1.46(0.83-2.59)

Table7.5.1B

Diabetes as defined by either FPG>=126mg/dlor OGTT>=200mg/dl

WAIST CIRCUMFERENCE	Frequency	PROGRESSION TO EITHER FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
Non obese	354	61	17.23	15.56	1
Obese	138	33	23.9	18.21	1.38(0.85-2.27)

7.5.2 Association between BMI at present survey and type 2 diabetes

The results showed that people who were converted to BMI>=20 were having higher risk of diabetes than reference category(<=20kg/dl)

Table 7.5.2A

Diabetes defined by FPG alone

BMI	Frequency	PROGRESSION TO FPG>=126	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
<=20kg/m^2	144	12	8.33	5.8	1
21-24 kg/m^2	226	37	16.37	12.03	1.96(0.95-4.13)
>=25 kg/m^2	120	17	14.16	11.38	1.69(0.74-3.96)

Table 7.5.2.B

Diabetes as defined by either FPG or OGTT

BMI	Frequency	PROGRESSION TO EITHER FPG>=126OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
<=20 kg/m^2	144	19	9.95	9.43	1

21-24 kg/m^2	226	55	19.15	18.21	1.92(1.02-3.37)
>=25 kg/m^2	120	27	17.71	16.83	1.78(0.87-3.38)

7.5.3 Association between blood pressure at present survey and type 2 diabetes

Diabetes defined by FPG alone showed that incidence of diabetes and incidence of blood pressure are not associated**.**

Table7.5.3A

Present blood pressure and Diabetes as defined by either FPG or OGTT

BLOOD PRESSURE	Frequency	FPG>=126MG/DL	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR 95%CI)
SBP<140 or DBP<90	381	56	14.7	10.59	1
SBP>=140 or DBP>=90	77	11	14.29	10.27	0.97(0.46-2.02)

Table 7.5.3B

Present blood pressure and diabetes defined by either FPG or OGTT

BLOOD PRESSURE	Frequency	FPG>=126 OR OGTT>=200	Cumulative Incidence (%)	ANNUAL INCIDENCE PER 1000	RR(95%CI)
SBP<140 or DBP<90	4893	72	18.9	13.96	1
SBP>=140 or DBP>=90	943	21	27.27	21.23	1.44(0.81-2.57)

7.6 Univariate analysis of selected variables

Univariate analysis of selected risk factors with risk of diabetes was done by using both criteria.It was seen from this analysis that basline glucose above 90mg/dl,sex, age above 50 years, baseline BP>=140/90mmof Hg ,cholesterol mg/dl, physical activity at baseline ,BMI>=21kg/m^2 **and** waist circumference of 85 or above for males and 80 or above for females were associated with risk of future diabetes.

t**Table 7.6.1B**

Univariateanalysis Diabetes defined by FPG>= 126 mg/dl or OGTT>=200mg/dl

RISK FACTOR	ODDS RATIO	CONFIDENCE INTERVAL	P VALUE
Baseline FPG 80-89 90-99 100-109 110-125	1 1.811 4.045 9.680	- 1.023-3.208 2.213-7.396 4.711-19.891	- 0.042* 0.000* *0.000*
Sex Female male	1 1.527	- 0.997--2.341	- 0.052 .
Age 30-40 41-50 51-60	1 1.363 2..158	- 0.823-2.256 1.269-3.668	- 0.191 0.000*
Cholesterol <=150 151-200 >=200	1 1.923 3.484	- 1.160-3.188 1.905-6.371	- 0.011* 0.000*
Blood pressure SBP<140/DBP<90 SBP>=140/DBP>=90	1 2.273	- 1.435-3.60	- 0.000*
Physical activity Mild to moderate Heavy	1 0.631	- 0.355-1.121	0.116
BMI <=20 21-24 >=25	1 2.084 5.979	- 1.236-3.512 3.276-10.912	- 0.006* .000*
SES Low High	1 2.43	- 1.05-5.73	0.04*
Abdominal obesity Non Obese Obese	1 4.088	- 2.524-6.620	.004*
Abdominal obesity Non obese obese	1 1.564	- (0.906-2.698)	0.108

RISK FACTOR	ODDS RATIO	CONFIDENCE INTERVAL	P VALUE
BaselineFPG			
80-89	1	-	
90-99	1.730	1.071-2.793	.025*
100-109	3.619	2.126-6.160	.000*
110-125	6.807	3.442-13.463	.000*
Sex			
Female	1	-	-
male	1.429	.976-2.090	0.06
Age			
30-40	1	-	
41-50	1.348	.862-2.11	.191
51-60	2.489	1.549-4	.000*
Cholesterol			
<=150	1	-	-
151-200	1.930	2.332-6.925	.000*
>=200	4.019	1.239-3.007	.004*
Blood pressure			
SBP<140/DBP<90	1	-	-
SBP>=140/DBP>=90	2.471	1.627-3.753	0.000*
Physical activity	1	-	
Mild to moderate	0.645	.0.388-1.070	-
Heavy			.089
BMI	1	-	-
<=20	2.282	1.456-3.576	0.000*
21-24	5.552	3.189-9.667	0.000*
>=25	2.529		
Abdominal obesity	1	-	-
Non Obese	4.410	2.797-6.954	0.000*
Obese	1.959		
Abdominal obesity in present survey	1	-	-
Non Obese	1.509	.935-2.436	.092
Obese			

7.6.2 Multivariate analysis

The present study measures the outcome as dichotomous variable, like diabetes present or absent .So independent risk analysis logistic regression was used.

Multi variate logistic regression

The risk factors that had shown significance in univariate analysis were included in multivariate analysis. After adjusting with other selected risk factors baseline fasting plasma glucose group of 110-125mg/dl was the powerful predictor of future diabetes. In both criteria. It also had shown that risk of FPG in predicting future diabetes started with the FPG of 110-125mg/dl . Other predictors when diabetes defined by either FPG or OGTT were sex ,baseline blood pressure>=140/90mm of Hg, baseline cholesterol above 200mg/dl, BMI>=21kg/m^2, waist circumference of 85 and above for males and 80 and above for females. But when used FPG alone only sex and BMI >=25kg/m^2 were shown significant.

Table7.6.2.A

Multivariate logistic regression diabetes defined by FPG>=126 mg/dl

RISK FACTOR	ODDS RATIO	CONFIDENCE INTERVAL	P VALUE
Baseline			
80-89	1.573	0.865-2.861	0.138
90-99	3.091	1.605-5.953	0.001*
100-109	6.336	2.875-13.963	0.000*
Sex			
Female	1	-	-
male	1.725	1.053-2.827	0.030*

Age 30-40 41-50 51-60	1 1.145 1.460	- 0.650-2.018 0.795-2.683	- 0.639 0.223
Cholesterol <=150 151-200 >=200	1 1.369 1.620	1 0.776-2.413 0.807-3.252	- 0.278 0.175
Blood pressure SBP<140/DBP<90 SBP>=140/DBP>=90	1 1.412	- 0.805-2.478	- 0.229
Physical activity Mild to moderate Heavy	1 0.646	- 0.338-1.235	- 0.186
BMI <=20 21-24 >=25	1 1.754 3.331	- 0.970-0.3.173 1.482-7.484	- 0.063 0.004*
SES Low High	1 1.2	- .770-2.4	.315
Abdominal obesity Non Obese Obese	1 1.510	- .733-3.109	- 0.264
Abdominal obesity in present survey Non Obese Obese	1 1.119	- 0.607-2.064	- 0.719

* statistically significant

Table 7.6.2B

.Diabetes defined by either FPG>=126 mg/dl or OGTT>=200mg/dl

RISK FACTOR	ODDS RATIO	CONFIDENCE INTERVAL	P VALUE
BaselineFPG 80-89 90-99 100-109 110-125	1 1.467 2.734 4.096	- .881-2.442 1.518-4.924 1.917-8.753`	- 0.141 0.001* 0.000*

Sex Female male	 1 1.576	 - 1.015-2.447	 - 0.043*
Age 30-40 41-50 51-60	 1 1.077 1.682	 - 0.650-1.784 0.981-2.885	 - 0.774 0.059
Cholesterol <=150 151-200 >=200	 1 1.382 2.045	 - 0.841-2.269 1.099-3.805	 - 0.202 0.024*
Blood pressure SBP<140/DBP<90 SBP>=140/DBP>=90	 1 1.628	 - .0.982-2.698	 - 0.059
Physical activity Mild to moderate Heavy	 1 0.661	 - .0.371-1.177	 - 0.160
SES **Low** **High**	 1 1.1	 - 0.654-1.43	 - .646
BMI <=20 21-24 >=25	 1 1.877 2.529	 - 1.124-3.133 1.201-5.326	 - 0.016* 0.015*
Abdominal obesity Non Obese Obese	 1 1.959	 - 1.013-3.788	 - 0.046*
Abdominal obesity in present survey Non Obese Obese	 1 1.060	 - 0.617-1.821	 - 0.832

* statistically significant

8.**Discussion**

The rural population in Kaniyambadi block was studied for the prevalence of coronary heart disease and its risk factors by ICMR-CMC group in 1991-1993. The present study made use of this situation and considered the 1991 study as the baseline survey for the follow-up study. Main objective of the study is to determine predictive validity of fasting blood glucose in risk of developing future diabetes This study selected a sub cohort from the baseline survey after applying certain inclusion and exclusion criteria .The sample size required was 591. Assuming 90%

response rate 649 people were invited for the follow up study. The overall response rate was 91%. Even though response rate was high it was not uniformly distributed among the sub groups. The Required sample size for the FPG of 90-99mg/dl group and FPG of 110-125mg/dl wasn't adequate.

The study population consisted of 228 men and 362 women with a mean age of 41.99(SD 8..27) years at the baseline, who were followed up after 14.16 years (SD 0.83).. To determine predictive validity of fasting blood glucose baseline FPG were classified into different groups .The lowest group was 80-89mg/dl and highest group was 110-125mg/dl. Other selected risk factors at baseline survey like age ,sex, cholesterol blood pressure BMI, and abdominal circumference on the risk of type2 diabetes were also studied. Risk factors measured at present survey were blood pressure, BMI, waist circumference etc.

Incidence of diabetes

The cumulative incidence of diabetes was 17.6 % according to the ADA criteria. and 24.4% according to the WHO-1999 criteria: The annual incidence was 11.16 per1000PY when calculated by fasting plasma glucose criteria by ADA and 18.65per 1000 PY when calculated by either fasting or 2hr OGTT. .It appears that WHO criteria increases the overall sensitivity of the study but with the present data one may not be able to say that specificity has decreased. As a general rule this increase in sensitivity can decrease the specificity. It can be seen that the values of annual incidence and incidence density were almost equal. The slight difference is because in the annual incidence, occurrence of new cases were at a constant rate ,whereas in the incidence density the study assumed that new cases had occurred at the half period of the follow up time .

Predictive validity of fasting plasma glucose in detecting future diabetes.

The baseline fasting plasma glucose of study population varied from 80 to 125 mg/dl. Of the 447 participants with normal fasting glucose (80-99mg/dl) at the baseline,53 participants(11.9%) developed diabetes(ADA criteria) at a mean follow-up period of 14.16 years . Of the 143 participants with impaired fasting glucose at the baseline (110-125mg/dl), 51 participants (35.7%) had diabetes at follow-up (ADA criteria) According to the WHO criteria, the cumulative incidence

was 18.5% for participants with normal fasting glucose and 43.3.% for those with impaired fasting glucose.

To measure the distribution of risk of future diabetes in baseline glucose the present study categorized the baseline glucose into different groups and measured strength of association between baseline glucose and type2 diabetes by both univariate analysis and multivariate analysis Univariate analysis showed that when the base line glucose level increased. the risk of future type2 diabetes also increased. Incidence of diabetes started to rise in those with FPG 90-99mg/dl group and was highest in the group with baseline glucose of 110-125mg/dl.Attempt was made to arrive at level of blood sugar above which the risk of diabetes is notifiably higher.Eventhough there is an incremental risk of developing diabetes with any increase in FPG level, above 95mg/dl this risk appears to increase higher.. The same trend was seen in the ADA and WHO diabetes criteria. Multiple logistic regression showed that risk started with 100-110mg/dl category of FPG and FPG group with 110-125mg/dl had 4-5 times higher risk of developing future diabetes than reference category (80mg/dl-89mg/dl). The results of this study showed that fasting glucose category of 100-125 mg/dl is an independent predictor of future diabetes for a follow up period of 14.16 years.

There are a number of longitudinal studies done by western countries with similar results [38] ,but there is no longitudinal study done in India to measure whether impaired fasting glucose is a real risk factor or not..Hoorn study[63] showed that of those with normal fasting at baseline, 4.5% had diabetes at the follow-up examination and 64.5% of the participants who had both impaired fasting at baseline progressed to diabetes.. Even in western countries, very few studies are done about predictive validity of fasting blood sugar and future diabetes Most of the studies were based on impaired glucose tolerance and risk of future diabetes.

This result strongly supports the revised criteria of lowering the cut off for impaired fasting glucose from 110 to 100mg/dl by ADA. In fact the result of the present study suggests that lowest cut point of the impaired fasting glucose that predict future diabetes can be lowered from 100 to 95mg/dl.

To estimate the incidence of the whole baseline cohort the present result was not sufficient since the study population was lacking FPG below 80mg/dl.Since log annual incidence according to the baseline FPG followed the linear relation , FPG of

60-69mg/dl group and 70-79mg/dl group can be calculated by extrapolating the present result. The projected annual incidence and cumulative incidence for the disease free baseline cohort was calculated. The projected cumulative incidence was 12.5% and annual incidence was 9.4 per 1000 PY.

Thus it appears that if one were to start with nondiabetic(based on the ADA criteria)population of 3016 individual with a mean fasting blood glucose of 87.21(sd 10.1) and mean age of 41.2(sd 8.7) 12.5% would have progressed to the diabetes stage (ADA criteria) during a period of 14.16 years . This indeed would be underestimating the true prevalence as it excludes those who were diabetic in the baseline survey and survive for the duration of the study.

The prevalence of diabetes in the baseline study based on the ADA criteria (reclassified during the present survey) showed 2.9%.and current burden of the disease estimated to be at least four times high. Thus there is adequate evidence to conclude that overall susceptibility to diabetes has been increased during last 15 years. The villages enrolled in this study are more or less representative of an average south Indian village, these result clearly foresee the disease burden that much of rural south India is going to face.

Prior studies have highlighted the escalating problem of diabetes in urban India however; high quality information about type2 diabetes in rural areas is scarce. Even though longitudinal studies are lacking in India, there is more evidence to suggest that prevalence of type 2 diabetes is increasing in rural areas based on cross sectional studies. A study on the prevalence of diabetes in the rural population of South India was conducted in the year 1990, and the prevalence rate was reported to be 2.4%.[31]. Another study conducted by the Diabetes Research Center (DRC) in Chennai, India, reported a prevalence of 5.9% in semi urban areas, which is midway between the urban (11.6%) and the rural (2.4%) figures.[32]The sample population resembled rural population for some features, but had access to certain urban facilities. A recent survey in a rural area in 2003 showed indications of the transition in the lifestyle of the rural population, and a striking increase in the rate of prevalence of diabetes was noted (6.3%). In a developing area of Andhra Pradesh, about 13 per cent of adults aged 30 or above were found to have diabetes and another 16 per cent with symptoms of pre-diabetes[19] The rapid increase in population, increased longevity and high ethnic susceptibility to diabetes, coupled

with rapid urbanization and changes from traditional lifestyles, will most likely trigger a diabetes epidemic in the rural India also.

Analysis of other selected risk factors

Sex and diabetes

This study showed that males had more risk for future diabetes than females Global diabetes study results shows that there is a male excess in India (11 vs. 8 million)[2]

Age and diabetes

Univariate analysis showed that as age increased risk of future diabetes also increased. After adjusting with other risk factors it was found that age wasn't a significant predictor of future diabetes**.**

The baseline study showed that prevalence of diabetes increases with age. The DECODA study group[26]pointed that the prevalence of diabetes reached its peak at 60–69 years of ages followed by a decline at 70–79 years of age in Indian cohorts and mean FPG increased with age and reached a peak at 60–69 years of age then started to decline ..Analysis of the baseline characteristics of the present study population showed that like DECODA study here also mean FPG increased with age. So one need to examine whether age or mean FPG is the real predictor of future diabetes

Baseline blood pressure and diabetes.

Univariate analysis and multivariate analysis revealed that hypertension as defined by SBP>=140 mm of Hg and DBP>=90mm of Hg at baseline study is significantly associated with diabetes (WHO criteria). This finding is in agreement with earlier studies done in the west.

Cholesterol and diabetes

The association between baseline cholesterol and diabetes remained even after adjusting many other variables. Cholesterol baseline value of 150-200mg/dl in the

univariate and above 200mg/dl in the multivariate analysis showed a strong association. Previous longitudinal studies from western countries had similar results and were explained in terms of metabolic syndrome.

BMI and diabetes

The strong association between BMI and diabetes remained even after adjusting for many other variables. Univariate analysis showed the lower limit of BMI for risk of developing diabetes started with the group of BMI 21-24kg/m^2 This lower limit of risk remained in the multivariate analysis using WHO diagnostic criteria for diabetes.

The results of the DECODA study group[60] showed that The effect of BMI on the age-adjusted prevalence of Type 2 diabetes was modified by ethnicity with considerably lower thresholds in Indian subjects compared to those from the rest of Europe. The risk starting at a BMI between 15 and 20 kg/m^2 in Indian populations compared to 25 kg/m^2 in Europeans.. . Cross sectional studies from South India also proved that BMI>=23 kg/m^2 associated with risk of diabetes[31]. This difference should be reflected in national and international recommendations regarding "optimal" BMI

Abdominal obesity and diabetes.

Multivariate analysis showed that an abdominal circumference of 85cm or above for males and 80cm or above for females is a real predictor of future diabetes. According to the International Diabetes Federation (IDF)) central obesity for south Asian population was defined as waist circumference >=90 cm for males and >=80cm [67]for females .

Previous studies from south East Asian countries showed that central adiposity is a real risk factor for diabetes and the risk starts a little earlier than western countries[30,31]

Excess body fat appears to play a strong role in insulin resistance, but the way the fat is distributed is also significant. Weight concentrated around the abdomen and in the upper part of the body (apple-shaped) is associated with insulin resistance and diabetes, heart

disease, high blood pressure, stroke, and unhealthy cholesterol levels. Abdominal obesity is also common among people in countries where weights tend to be low, such as Asia or India..

The results showed that, at relatively low abdominal circumference, the Kaniyambadi rural cohort experience elevated levels of risks for the future diabetes.. These findings points the need to revise the WHO cut-off values for the various indices of obesity and fat distribution like BMI and waist circumference. The present study showed that after adjusting all other risk factors abdominal obesity at the baseline survey had 1-3 times risk for getting future diabetes over a period of 15 years. Clustering of risk factors for future type2 diabetes like abdominal obesity, cholesterol, blood pressure and prediabetes stage were seen in this study and all can be explained in terms of the metabolic syndrome.[22] Symptoms and features are:

- Fasting hyperglycemia - Diabetes mellitus type 2 or impaired fasting glucose
- High blood pressure
- Central obesity also known as visceral adiposity.
- Elevated triglycerides
- Decreased HDL cholesterol

The metabolic syndrome is not benign; it is associated with a substantially elevated risk of type 2 diabetes (5-fold) and of cardiovascular disease (CVD) (2–3-fold)[22]

The present study couldn't include HDL and triglycerides for the analysis

Socioeconomic status and diabetes

Univariate analysis showed a significant positive association of SES with the type 2 diabetes.It lost its significance after adjusting with other variables.

Chennai Urban population study showed that subjects belonging to higher socio-economic status (SES) had greater prevalence of glucose intolerance compared to subjects from lower socioeconomic status.[72]. This was probably related to the physical activity of the low income group (LIG) as most of them were involved in moderate to strenuous physical activity at work. Prevalence of diabetes and IGT were significantly lower in the LIG than in the high-income group (HIG). The finding of lower prevalence of diabetes in the socially deprived urban Indians was in contrast to the positive association of diabetes and social deprivation in western countries.[71]

Physical activity and diabetes

The present study showed that even though annual incidence is less in people with high physical activity it couldn't show any significant protective effect both in univariate and multivariate analysis.

A number of selected risk factors at present survey like incidence of blood pressure, BMI, abdominal obesity and diabetes were also studied. But none showed significance for risk of developing future diabetes

The main objective of this study was to find the predictive validity of fasting blood glucose in detecting future diabetes in rural south India over a period of 15 years. The results of the study proved that baseline fasting plasma glucose is a real predictor of future diabetes .The results of the study also highlights the importance of the impaired fasting glucose in detecting future type 2 diabetes .After adjusting with all variables Selected risk factors at baseline survey like cholesterol, blood pressure ,body mass index,sex and ,waist circumference were significant predictors of diabetes when diabetes was defined by the WHO diagnostic criteria.

Studies of patients with IGT or IFG had shown success for lifestyle interventions in delaying or preventing the development of diabetes.[68,69,70]There is strong evidence that

a structured program of diet and exercise can reduce the risk of progression to type 2 diabetes in patients with prediabetes. Patients with IFG and IGT should be advised on the benefits of modest weight loss, good dietary habits, and regular physical activity.

The results of the present study points to the urgent need for intervention studies in the Kaniyambadi block. With overall development in the Tamilnadu state and specific economic developmental inputs by Community Health Department of Christian Medical College it is considerable life style changes has increased the diabetic proneness of the community. We are yet to completely control the infectious disease problem in this region, this new threat of diabetes epidemic can add considerable disease burden to the community.

. Since diabetes is a disease of slow progression, early detection of the intermediate stages like impaired fasting glucose and impaired glucose tolerance and appropriate intervention starting at this stage will definitely decrease the future burden of the disease .

9. SUMMARY AND CONCLUSION

The objective of this cohort study was to estimate the predictive validity of fasting plasma glucose in risk of future type 2 diabetes. Some selected risk factors for future diabetes was also studied. The annual incidence of diabetes in the study cohort by ADA criteriea FPG>=126mg/dl was studied and by WHO criteria that is either FPG>=200mg/dl or OGTT>= 200mg/dl was also studied. This study shows that males are at higher risk of developing future diabetes than females. This study also shows that age is not a significant predictor of future diabetes as baseline prevalence study has shown. After simultaneous adjustments for confounders using multivariale analysis baseline fasting plasma glucose remained as a significant predictor of future type 2 diabetes in a rural population aged 30-60. The risk associated withFPG increases from 100ml/dl and highest risk is for the group with FPG 110-125 mg/dl. The result of this study strongly supported ADA's concept of impaired fasting glucose. This study also showed that the revised classification of impaired fasting glucose [100 mg/dl-125 mg/dl] is applicable for a south Indian rural population aged 30-60 years. The present study calculated projected cumulative incidence of the baseline cohort and it showed at least four fold increase in the burden.of the disease.Other significant predictors were sex,

baseline cholesterol >=200 mg/dl and systolic blood preasure >=140mg./dl,diastolic blood pressure >=90mg/dl ,BMI>=25kg/m^2 and abdominal obesity(male>=85cm and female>=80cm.) .Risk factrors like physical activity, socioeconomic statusand age were proved as nonsignificant in multivariate analysis.

10 LIMITATIONS

- As 2hr OGTT was not done in baseline survey it was not possible to compare with risk of future type2 diabetes by FPG and future type2 diabetes by 2hrOGTT.
- All people in eligible cohort were not able to be followed up because of limited resources. Even though total sample size calculated was achieved required sample size could not be achieved for subgroupof FPG 110-125 mg/dl
- The exact point of time at which the participants progressed to diabetes was not found since there was no serial follow up of the people in the baseline cohort. So for analysis purpose the present study assumed that at exactly half of the follow up period conversion of normoglycemia to diabetes stage occurred.

11.RECOMMENDATIONS

It is necessary to

- Increase the public health awareness about type2 diabetes. The study results showed that fifteen years cumulative incidence was about four fold higher than baseline prevalence.
- We should Screen the public for risk factors for diabetes and blood glucose investigations should be done on high risk approach.
- Since most of the risk factors are modifiable, early intervention studies are recommended to find out whether progression to type2 diabetes can be prevented at an earlier stage.

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APPENDIX -1

OPERATIONAL DEFINITIONS

1. Types of house

Hut – a one-room construction of mud walls with a thatched roof.

Kutcha – construction with more than one room with mud walls and thatched roof.

Mixed – a house, which has one or two of the following, cement or mortar used for plastering of wall or floor with the tiled roof.

Pucca – one which is built with a foundation using stone or bricks with mortar and cement and having a stone laid roof or tiled roof.

Mansion – a large house containing more than 5 rooms (excluding kitchen and toilet).

2. OCCUPATION

I-Agriculture related

1.1-land owner

1.2–cultivator owner

1.3–cultivator tenant

1.4–cultivator labourer

II-Non agriculture (general)

2.1-Business man/factory owner
2.2-White collar job/clerk/teacher/malaria worker
2.3-Armed forces/police
2.4-Skilled labourer/electrician/mechanic/driver
2.5-Petty business
2.6-Manual labourers
2.7-Domestic workers
2.8-Attender/peon

III-Traditional non-agriculture (rural)

3.1-Blacksmith

3.2-Goldsmith

3.3-Potter

3.4-Masonry

3.5-Basket weaving

3.6-Craft-centre employee

3.7-Barber

3.8-Shepherd

3.9-Dhobi

IV-Person not employed gainfully

4.1-House wife

4.2-House hold work

V-High prestige-low income

5.1-PTCHW

5.2-Balwadi teacher

5.3-Temple priest

3. SES SCORING

Education

No education-0, Primary (1-5)-1, Middle (6-8)-2, High (9-10)-3,

Higher sec-4, Above 12^{th}-5

Land owner :(In wet lands)

1 Acre of wet land = 5 acres of dry land.

No land – 0, <1 Acre – 1, 1-4 Acre -2, 5-9 Acre -3, >=10Acre – 4,

Occupation

1.4, 2.6, 2.7 – agric labor, Unskilled – 1

3.1-3.9, 2.7-skilled – 2

2.5- Small business – 3

5.1-5.3,2.8- independent profession – 4

1.1 -1.3 – Cultivator – 5

2.1 – 2.3 – Govt/Private/Exservice - 6

4. Physical activity

1. Sedentry- Retired people, Unemployed, Businessman ECT.

2. Mild-Clerical jobs, Teachers ECT

3. Moderate- Peons, Artisans, Postman, Mechanic, Shepherd, Drivers ECT.

4. Heavy- Farmers, Blacksmith, Manual labours ECT.

APPENDIX-2

STUDY ON TYPE 2 DIABETES MELITUS

SNO

IDNO

NAME

HEIGHT (m)

WEIGH(kg)

BMI(kg/m$^{2)}$

WAIST CIRCUMFERENCE (cm)

BLOOD PRESSURE(mm of Hg)

DATE OF SURVEY

FASTING BLOOD SUGAR(mg/dl)

2HOUR ORAL GLUCOSE TOLERENCE TEST(mg/dl)