PREVALENCE OF DIABETES IN HIV INFECTED PATIENTS AND HIV PATIENTS RECEIVING ANTI RETROVIRAL THERAPY .

- CROSS SECTIONAL STUDY.

Dissertation submitted for

MD Degree (Branch I) General Medicine
March 2008

The Tamil Nadu Dr.M.G.R.Medical University
Chennai, Tamil Nadu.

CERTIFICATE

This is to certify that this dissertation "PREVALENCE OF DIABETES IN HIV INFECTED PATIENTS AND HIV PATIENTS RECEIVING ANTI RETROVIRAL THERAPY" -CROSS SECTIONAL STUDY submitted by **DR. S.SELVARAJU** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

Dr P. Selvaraj MD,
Professor of Medicine ,
Chief II Medical unit ,
Department of Medicine ,
Madurai Medical College,
Madurai.

Dr. Ayyappan MD,
Professor and Head,
Department of Medicine,
Madurai Medical College,
Madurai.

DECLARATION

I, **Dr.S.Selvaraju** solemnly declare that the dissertation titled **"PREVALENCE OF DIABETES IN HIV INFECTED PATIENTS AND HIV PATIENTS RECEIVING ANTIRETROVIRAL THERAPY"-CROSS SECTIONAL STUDY** has been prepared by me.

This is submitted to the Tamil Nadu, Dr. M.G.R. Medical University Chennai, in partial fulfilment of the regulations for the award of MD degree Branch I (General Medicine).

Place : Madurai

Date :

Dr. S.SELVARAJU

ACKNOWLEDGEMENT

I express my sincere thanks to **Dean, Govt Rajaji Hospital and Madurai Medical College** for permitting me to use the facilities of Madurai Medical College and Govt. Rajaji Hospital to conduct this study.

I will ever remain in gratitude to my chief **Dr. P. Selvaraj M.D.,** Prof of Medicine, not only for guiding me through the study, but also for being my mentor and source of inspiration during the period of my post graduate training.

I express my sincere thanks to Our professor and Head of the Department of Medicine Prof **Dr. A. Ayyappan** and my beloved teachers **Dr.M. Kamaraj MD., Dr.Moses K Daniel MD., Dr.S.Vadivel Murugan MD., Dr.D.Venkatraman MD., Dr.M.Muthiah MD.**.

I express my sincere thanks to our former Head of the Dept. of Medicine, Prof **Dr. P.Thirumalaikolundu Subramanian MD** for his guidance and valuable advice to conduct this study successfully.

I express my sincere thanks to Professor of diabetology , Prof **Dr. J.Asirvatham MD** for his guidance and valuable advice.

I express my heart felt thanks to my Assistant professors **Dr. M. Natarajan MD., Dr.P.Purushothaman MD., Dr.R.Prabaharan MD.,**for their valuable support and guidance through out my study.

I express my sincere thanks to Medical Officer in Anti Retroviral Therapy Centre **Dr.S. Parthasarathy,** and also staffs in the ART centre **S.Prabhu, V.Raja mahendravarman, P.Mani, P.Aruna, M.Umadevi, R.Kayalvizhi, M.Ayyappan** for their valuable support through out my study.

My family and friends have stood by me during my times of need. Their help and support have been valuable to the study.

I would grossly fail in my duty if I fail to mention here of my patients who have ungrudgingly borne the pain and discomfort of investigations. I cannot but pray for their speedy recovery and place this study as a tribute to them and to the numerous others likely affected.

CONTENTS

INTRODUCTION

Many non-communicable diseases are set to increase dramatically during the 21st century. In particular, the prevalence of diabetes mellitus may double from 124 millions people worldwide in 1997 to 220 millions by 2010. More than 97% of these patients will have type II diabetes. The projected increase in the number of diabetic patients will strain the capabilities of healthcare providers the world over. Thus it is of paramount importance to revisit the causes and epidemiology of diabetes mellitus. [Ref 1]

Diabetes mellitus is caused by both environmental and genetic factors. The environmental factors that may lead to the development of diabetes mellitus include physical inactivity, drugs and toxic agents, obesity, viral infection, and location. While type I diabetes is not a genetically predestined disease, an increased susceptibility can be inherited. Genetic susceptibility plays a crucial role in the etiology and manifestation of type II diabetes, with concordance in monozygotic twins approaching 100%. Genetic factors may have to be modified by environmental factors for diabetes mellitus to become overt. An individual with a susceptible gene may become diabetic if environmental factors modify the expression of these genes .

Diabetes is a disease where the body does not produce enough, or dose not respond to the hormone insulin. This affects the regulation of the amount of glucose in the blood . Abnormalities in glucose metabolism (insulin resistance, hyperglycaemia, and diabetes mellitus) are a concern because persistently high

blood glucose is associated with an increased risk of cardiovascular , renal diseases. The worldwide prevalence of DM has risen dramatically over the past two decades. With the greatest potential increases are Asia and Africa—precisely the areas with the greatest potential increases in the prevalence of HIV infection and AIDS . Likewise, prevalence rates of IFG are also increasing. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is expected to rise more rapidly in the future because of increasing obesity and reduced activity levels. DM increases with aging. Type 2 DM is preceded by a period of IGT2, and a number of life-style modifications and pharmacologic agents prevent or delay the onset of DM.

The Diabetes Prevention Program (DPP) demonstrated that intensive changes in life-style (diet and exercise for 30 min/day five times/week) in individuals with IGT prevented or delayed the development of type 2 diabetes by 58% compared to placebo. This effect was seen in individuals regardless of age, sex, or ethnic group. In the same study, metformin prevented or delayed diabetes by 31% compared to placebo. For the prevention of diabetes we need to address the risk factors associated with the development of diabetes mellitus.

[Ref23]

Hyperinsulinemia and insulin resistance may be an intrinsic component of many disorders, such as hypertension, hyperlipidemia, and atherosclerosis.

Medications that also alter the glucose insulin homeostasis include Thiazide Diuretics , Beta-Blockers , Calcium-Channel Blockers , Corticosteroids and so on.

Numerous studies have associated the HIV infection and the Anti retroviral agents with various metabolic complications, including diabetes. . More effective treatment in recent years has greatly increased the life span of people with HIV/AIDS. As patients live longer, we are placing more emphasis on enhancing the *quality* of their lives by treating HIV/AIDS as a long-term chronic condition .

In considering these facts a study was conducted in Govt Rajaji Hospital , Madurai to estimate the prevalence of diabetes in HIV patients and those receiving Anti Retroviral Therapy.

REVIEW OF LITERATURE

HISTORICAL ASPECTS

The best early evidence of a description of the symptoms of diabetes in the world's literature is recorded in the Ebers papyrus that appears to date from 1550 B.C. This links the description of polyuria to Imhotep, a man of medicine, architecture, and magic, who was a high priest and minister to the Pharaoh Zosser in 3000 B.C.

The following masterly description of severe diabetes by Arateus from about A.D. 150 represents the sum of our knowledge up until the second half of the 17th century.[ref 17]

Diabetes is a wonderful affection, not very frequent amongmen, being a melting down of the flesh and limbs into urine. Its course is of a cold and humid nature, as in dropsy. The course is the common one, namely, the kidneys and the bladder; for the patients never stop making water, but the flow is incessant, as if from the opening of aqueducts. The nature of the disease then, is chronic, and it takes a long period to form: but the patient is short-lived, if the constitution of the disease be completely established; for the melting is rapid, the death speedy.

In 1674, Thomas Willis, a physician, an anatomist discovered (by tasting) that the urine of individuals with diabetes was sweet. It was Matthew Dobson of Manchester, England, who demonstrated, in 1776, that persons with diabetes actually excrete sugar in the urine.

After boiling urine to dryness, he noted that the residue, a crystalline material, had the appearance and taste of “brown sugar” .[ref 17]

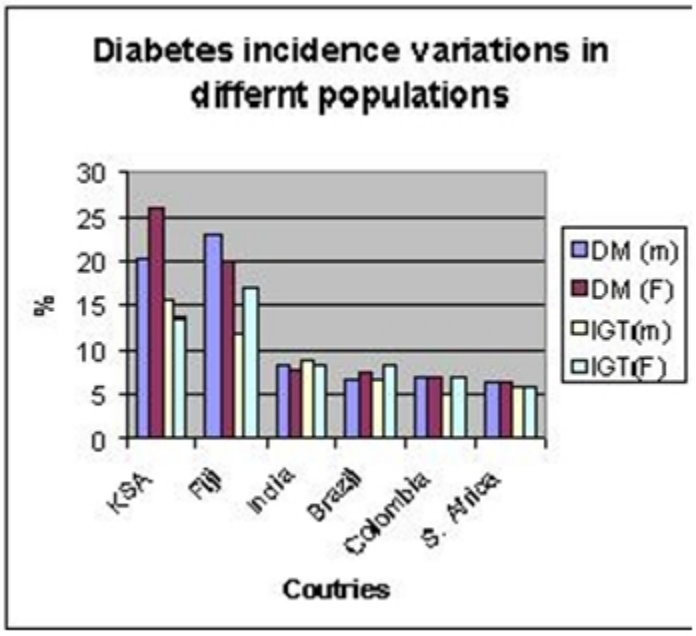
Banting, Best, Collip, and Macleod demonstrated the new extract corrected the metabolic acidosis in the first person to receive the substance in January 1922 called insulin.

EPIDEMIOLOGY

At a glance

All diabetes and IGT	2003	2025
Total world population (billions)	6.3	8.0
Adult population (billions) (20-79 years)	3.8	5.3
Number of people with diabetes (millions) (20-79 years)	194	333
World diabetes prevalence (%) (20-79 years)	5.1	6.3
Number of people with IGT (millions) (20-79 years)	314	472
IGT prevalence (%) (20-79 years)	8.2	9.0

[Ref16]



[ref 5]

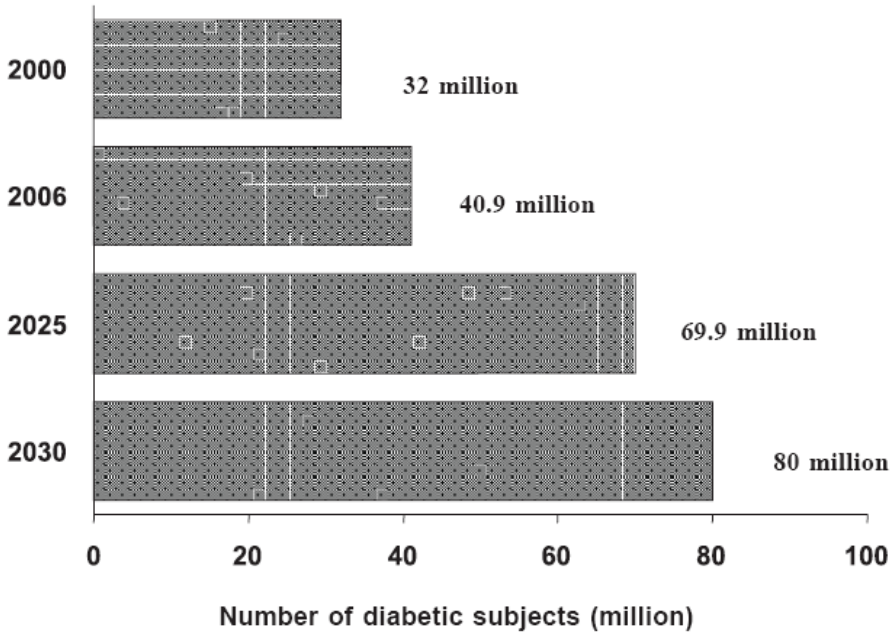
Diabetes mellitus is one of the most common endocrine disorders affecting almost 6% of the world's population. The number of diabetic patients will reach 300 millions in 2025 (International Diabetes Federation, 2001). More than 97% of these patients will have type II diabetes. The projected increase in the number of diabetic patients will strain the capabilities of healthcare providers the world over. Thus it is of paramount importance to revisit the causes and epidemiology of diabetes mellitus. Diabetes mellitus is caused by both environmental and genetic factors.

The incidence of type I diabetes ranged from 1.9 to 7.0/100,000/yr in Africa, 0.13 to 10/100,000/yr in Asia, ~4.4/100,000/yr in Australasia, 3.4 to 36/100,000/yr in Europe, 2.62 to 20.18/100,000/yr in the Middle East, 7.61 to 25.7/100,000/yr in North America, and 1.27 to 18/100,000/yr in South America.

The epidemiology of type II diabetes is equally bleak. The prevalence of type II diabetes ranged from 0.3 to 17.9% in Africa, 1.2 to 14.6% in Asia, 0.7 to 11.6% in Europe, 4.6 to 40% in the Middle East, 6.69 to 28.2% in North America, and 2.01 to 17.4% in South America. [ref 1]

The prevalence of type 2 DM and its harbinger, IGT2, is highest in certain Pacific islands, intermediate in countries such as India and the United States, and relatively low in Russia and China. This variability is likely due to genetic, behavioral, and environmental factors.

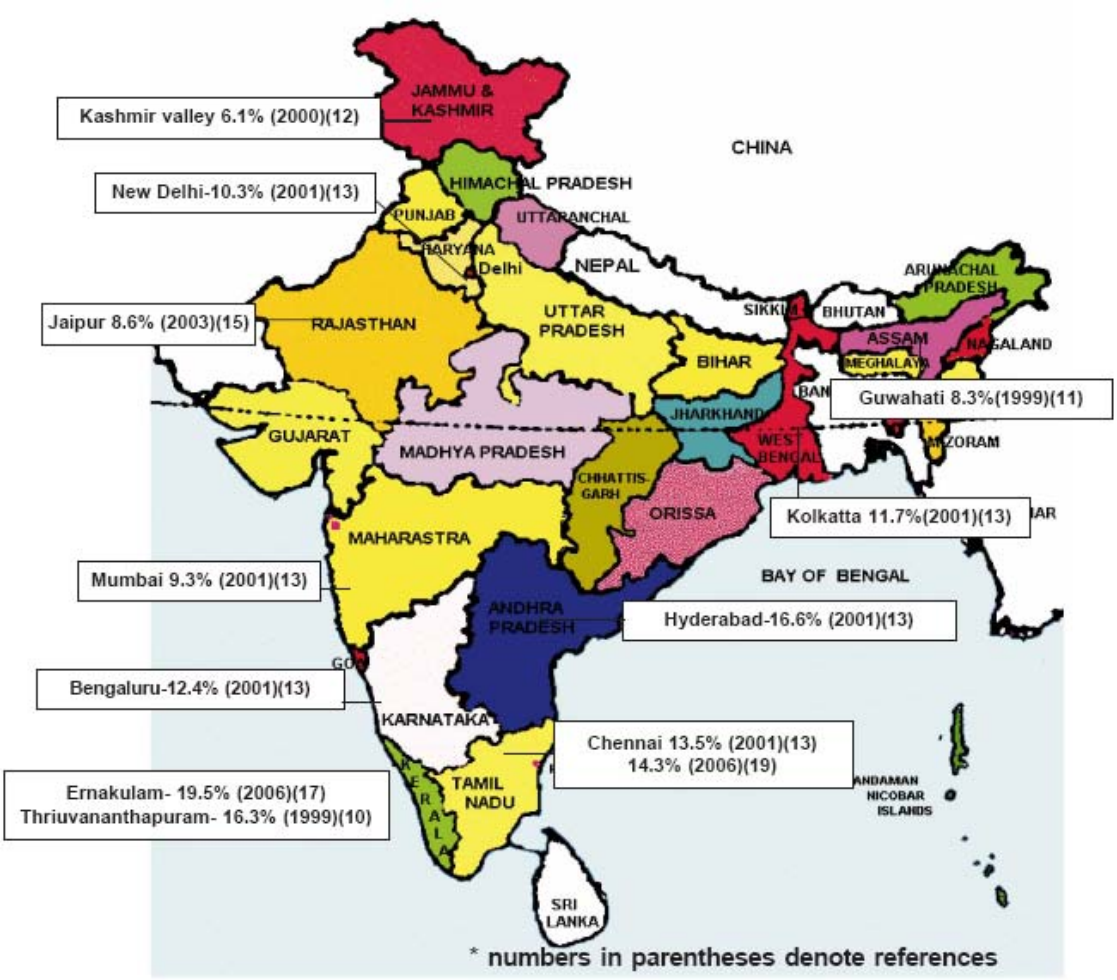
Evolution of the diabetes epidemic in India [ref 12]



Estimated number of diabetic subjects in India.

The National Urban Diabetes Survey (NUDS), a population based study was conducted in six metropolitan cities across India and recruited 11,216 subjects aged 20 yr and above representative of all socio-economic strata.. The study reported that the age standardized prevalence of type 2 diabetes was 12.1 per cent. This study also revealed that the prevalence in the southern part of India to be higher-13.5 per cent in Chennai, 12.4 per cent in Bangalore, and 16.6 per cent in Hyderabad; compared to eastern India (Kolkatta) ,11.7 per cent; northern India (New Delhi), 11.6 per cent; and western India (Mumbai), 9.3 per cent. [ref12]

The study also suggested that there was a large pool of subjects with impaired glucose tolerance (IGT), 14 per cent with a high risk of conversion to diabetes. [ref12]



Prevalance of Diabetes. [ref 12,25,26,27,28,29.]

DIAGNOSIS

The Diabetes Expert Committee criteria

The Diabetes Expert Committee criteria

	Normal Glucose Tolerance	Impaired Glucose Tolerance	Diabetes Mellitus[2]
Fasting plasma glucose (mg/dL)	< 110	110–125	>/= 126
Two hours after glucose load (mg/dL)	< 140	140–199	>/=200

[ref 7]

PATHOGENESIS;

TYPE 1 DM

Type 1 DM develops as a result of the synergistic effects of genetic, environmental, and immunologic factors that ultimately destroy the pancreatic beta cells. Features of diabetes do not become evident until a majority of beta cells are destroyed (~80%). At this point, residual functional beta cells still exist but are insufficient in number to maintain glucose tolerance.

GENETIC CONSIDERATIONS

The major susceptibility gene for type 1 DM is located in the HLA region on chromosome 6. Most individuals with type 1 DM have the HLA DR3 and/or DR4 haplotype. In addition to MHC class II associations, at least 17 different genetic loci contributes susceptibility to type 1DM. The risk of developing type 1 DM is increased tenfold in relatives of individuals with the disease

AUTOIMMUNE FACTOR

The following abnormalities in both the humoral and cellular arms of the immune system have identified.

(1) islet cell autoantibodies;

(2) activated lymphocytes in the islets, peripancreatic lymph nodes, and systemic circulation;

(3) T lymphocytes that proliferate when stimulated with islet proteins; and

(4) release of cytokines within the insulitis.

Pancreatic islet molecules targeted by the autoimmune process include insulin, glutamic acid decarboxylase (GAD, the biosynthetic enzyme for the neurotransmitter GABA), ICA-512/IA, and phogrin. Transplanted islets are destroyed by a recurrence of the autoimmune process of type 1A DM. .[ref3]

ENVIRONMENTAL FACTORS

Putative environmental triggers include viruses (coxsackie and rubella most prominently), bovine milk proteins, and nitrosourea compounds. .[ref3]

TYPE 2 DM

Insulin resistance and abnormal insulin secretion are central to the development of type 2 DM. Although controversy remains regarding the primary defect, most studies support the view that

insulin resistance precedes insulin secretory defects and that diabetes develops only if insulin secretion becomes inadequate

.

GENETIC CONSIDERATIONS

Type 2 DM has a strong genetic component. Major genes that predispose to this disorder have yet to be identified, but it is clear that the disease is polygenic and multifactorial. Various genetic loci contribute to susceptibility, and environmental factors (such as nutrition and physical activity) further modulate phenotypic expression of the disease. The concordance of type 2 DM in identical twins is between 70 and 90%. Individuals with a parent with type 2 DM have an increased risk of diabetes; if both parents have type 2 DM, the risk approaches 40%. Insulin resistance, as demonstrated by reduced glucose utilization in skeletal muscle, is present in many nondiabetic, first-degree relatives of individuals with type 2 DM.[ref3]

METABOLIC ABNORMALITIES;

INSULIN RESISTANCE

The decreased ability of insulin to act effectively on peripheral target tissues (especially muscle and liver) is a prominent feature of type 2 DM and results from a combination of genetic susceptibility and obesity. Insulin resistance is relative, however, since supernormal levels of circulating insulin will normalize the plasma glucose.

Insulin resistance impairs glucose utilization by insulin-sensitive tissues and increases hepatic glucose output; both effects contribute to the hyperglycemia. Increased hepatic glucose output predominantly accounts for increased FPG14 levels, whereas decreased peripheral glucose usage results in postprandial hyperglycemia .[ref3]

The pathogenesis of insulin resistance is currently focused on a PI-3-kinase signaling defect, which reduces translocation of GLUT4 to the plasma membrane.

OBESITY

Obesity is generally associated with abdominal distribution of fat, producing an abnormally high waist-to-hip ratio. This "visceral" obesity, due to accumulation of fat in the omental and mesenteric regions, correlates with insulin resistance; subcutaneous abdominal fat seems to have less of an association with insulin insensitivity .Exercise may affect the deposition of visceral fat as suggested by CT scans of Japanese wrestlers, whose extreme obesity is predominantly subcutaneous. Their daily vigorous exercise program prevents accumulation of visceral fat, and they have normal serum lipids and euglycemia despite daily intakes of 5000–7000 kcal and development of massive subcutaneous obesity.

Several **adipokines**, secreted by fat cells, can affect insulin action in obesity. Two of these, **leptin** and **adiponectin**, seem to increase sensitivity to insulin, presumably by increasing hepatic responsiveness. Two others **tumor necrosis factor-**which inactivates insulin receptors, and the newly discovered peptide **resistin**—interfere with insulin action on glucose metabolism and have

been reported to be elevated in obese animal models. Mutations or abnormal levels of these adipokines may contribute to the development of insulin resistance in human obesity. [ref 4]

IMPAIRED INSULIN SECRETION

Insulin secretion initially increases in response to insulin resistance to maintain normal glucose tolerance. Initially, the insulin secretory defect is mild and selectively involves glucose-stimulated insulin secretion. The response to other nonglucose secretagogues, such as arginine, is preserved. Eventually, the insulin secretory defect progresses to a state of grossly inadequate insulin secretion.

The reason(s) for the decline in insulin secretory capacity in type 2 DM is unclear. Islet amyloid polypeptide or amylin is cosecreted by the beta cell and likely forms the amyloid fibrillar deposit found in the islets of individuals with long-standing type 2 DM. Whether such islet amyloid deposits are a primary or secondary event is not known. The metabolic environment of diabetes may also negatively impact islet function. For example, chronic hyperglycemia paradoxically impairs islet function ("glucose toxicity") and leads to a worsening of hyperglycemia. Improvement in glycemic control is often associated with improved islet function. In addition, elevation of free fatty acid levels ("lipotoxicity") and dietary fat may also worsen islet function. .[ref3]

INCREASED HEPATIC GLUCOSE PRODUCTION

In type 2 DM, insulin resistance in the liver reflects the failure of hyperinsulinemia to suppress gluconeogenesis, which results in fasting hyperglycemia and decreased glycogen storage by the liver in the postprandial state. Increased hepatic glucose production occurs early in the course of diabetes, though likely after the onset of insulin secretory abnormalities and insulin resistance in skeletal muscle. .[ref3]

INSULIN RESISTANCE SYNDROMES

The insulin resistance condition comprises a spectrum of disorders, with hyperglycemia representing one of the most readily diagnosed features. The metabolic syndrome, the insulin resistance syndrome, or syndrome X are terms used to describe a constellation of metabolic derangements that includes insulin resistance, hypertension, dyslipidemia [low high-density lipoprotein (HDL) and elevated triglycerides], central or visceral obesity, type 2 diabetes or IGT2/IFG and accelerated cardiovascular disease.[ref3]

These associations have now been expanded to include small, dense, low-density lipoprotein (LDL), hyperuricemia, , prothrombotic state with increased levels of plasminogen activator inhibitor type 1 (PAI-1), and proinflammatory state.

OTHER SPECIFIC TYPES OF DIABETES MELLITUS

MATURITY-ONSET DIABETES OF THE YOUNG (MODY)

This subgroup is a relatively rare monogenic disorder characterized by non–insulin-dependent diabetes with autosomal dominant inheritance and an age at onset of 25 years or younger. Patients are nonobese, and their hyperglycemia is due to impaired glucose-induced secretion of insulin. Six types of MODY have been described. Except for MODY 2, in which a glucokinase gene is defective, all other types involve mutations of a nuclear transcription factor that regulates islet gene expression.

MODY 2 is quite mild, associated with only slight fasting hyperglycemia and few if any microvascular diabetic complications. It generally responds well to hygienic measures or low doses of oral hypoglycemic agents. MODY 3—the most common form—accounts for two-thirds of all MODY cases. The clinical course is similar to that of idiopathic type 2 diabetes in terms of microangiopathy and failure to respond to oral agents with time. . [ref 4]

HYPERGLYCEMIA SECONDARY TO SPECIFIC CAUSES

Hyperglycemia due to tissue insensitivity to insulin
Hormonal tumors (acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma)
Pharmacologic agents (corticosteroids, sympathomimetic drugs, niacin)
Liver disease (cirrhosis, hemochromatosis)
Muscle disorders (myotonic dystrophy)
Adipose tissue disorders (lipodystrophy, truncal obesity)
Insulin receptor disorders (acanthosis nigricans syndromes, leprechaunism)
Hyperglycemia due to reduced insulin secretion
Hormonal tumors (somatostatinoma, pheochromocytoma)
Pancreatic disorders (pancreatitis, hemosiderosis, hemochromatosis)
Pharmacologic agents (thiazide diuretics, phenytoin, pentamidine)

.

[ref 4]

DRUG-INDUCED DISORDERS OF GLUCOSE TOLERANCE *[ref 2]*

The association of medication with alterations in glucose-insulin homeostasis is not new. Polypharmacy enhances the risk for drug-drug interactions and adverse drug effects.

Hyperglycemia	Hypoglycemia
Thiazide and loop diuretics	Salicylates
Beta-blockers	Beta-blockers
Calcium-channel blockers	Beta agonists
Central alpha blockers	Pentamidine
Minoxidil	Quinine and quinidine
Diazoxide	ACE inhibitors
Corticosteroids and ACTH	Disopyramide
Oral contraceptive	Fibric acid derivatives
Nicotinic acid	Streptozotocin
Beta-2 agonists	MAOI
Cyclosporine	Acetaminophen
Thyroid hormones	Tricyclics
Pentamidine	Trimethoprim-sulphamethoxyzole
Isoniazid	Propoxyphene
Phenytoin	Octreotide
Phenothiazines	Tetracycline
Nalidixic acid	Mebendazole
Asparaginase	Cibenzoline
Dapsone	Stanozolol
Morphine	Flouxetine
Encainide	Ethanol
Lithium	Sertaline
L-Dopa	Tromethamine
Theophylline	Ganciclovir
Acetazolamide	Lithium
Rifampicin	Temafloxacillin
Indomethacin	
Dopamine	
Chlordiazepoxide	
Amoxapine	
Droperidol	
Doxapram	
Octreotide	
Quinathazone	
Ethanol	
Amiodarone (?)	

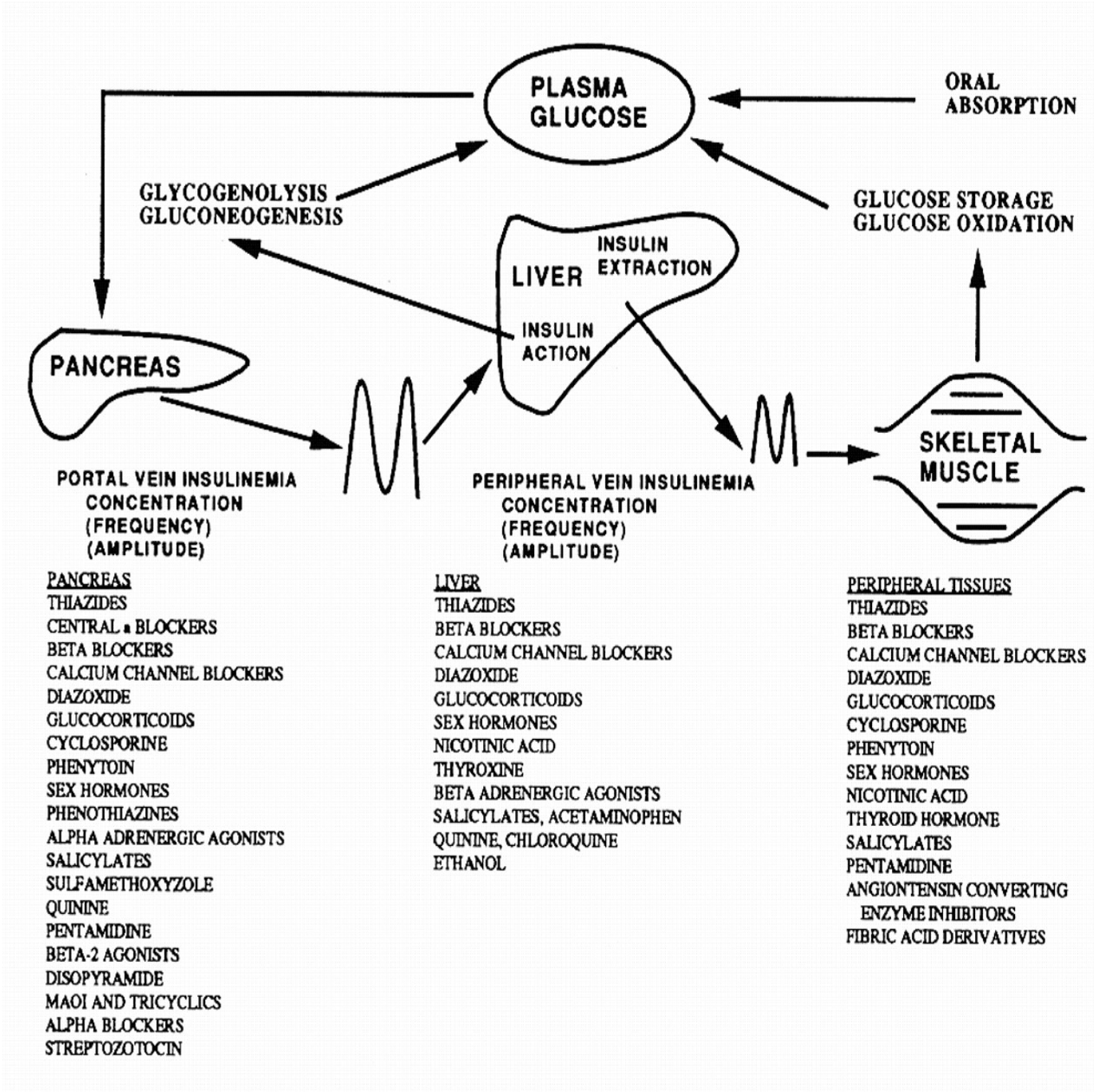
* ACE = angiotensin-converting enzyme; ACTH = adrenocorticotropic hormone; MAOI = monoamine oxidase inhibitor.

[ref 2]

In patients with impaired glucose tolerance, medication can induce frank diabetes, which may manifest as hyperosmolar nonketotic coma. Discontinuation of diabetogenic medication may result in normal glucose tolerance with an improved quality of life for many patients. Furthermore, the reductions in plasma insulin levels and insulin resistance that often accompany improved glucose tolerance will retard the development of hyperlipidemia, coronary artery disease, and hypertension. It is particularly important to avoid combinations of drugs that may induce abnormalities in glucose insulin homeostasis. A commonly encountered example is the combination of ß-blockers and thiazides in hypertensive patients**.** [ref 2]

In many cases, the mechanisms are not clearly recognized and need further evaluation. Recent evidence indicates that insulin pulsatility may be an important physiologic determinant of insulin action; however, few studies have examined the influence of pharmacologic agents on hormone pulsatility. Furthermore, it is probable that drugs may act at multiple sites to induce aberrations in glucose metabolism, as shownbelow. Medications such as ß-blockers may cause both hyper- and hypoglycemia. This apparent paradox may reflect factors such as dose, nutritional state, concomitant ingestion of other medication, severity of illness, patient age, and pancreatic islet cell reserve. The formulation of the medication (for example, sustained compared with regular release) should also be considered. Moreover, alcohol ingestion may influence**.**hepatic drug metabolism. In addition

to its hypoglycemic effect, heavy alcohol use may result in glucose intolerance. It is prudent to monitor plasma glucose values when it is not possible to avoid medication with known effects on carbohydrate metabolism. [ref 2]



. [ref 2]

CLINICAL FINDINGS

	Type 1 Diabetes	Type 2 Diabetes
Polyuria and thirst	++	+
Weakness or fatigue	++	+
Polyphagia with weight loss	++	–
Recurrent blurred vision	+	++
Vulvovaginitis or pruritus	+	++
Peripheral neuropathy	+	++
Nocturnal enuresis	++	–
Often asymptomatic	–	++

While many patients with type 2 diabetes present with increased urination and thirst, many others have an insidious onset of hyperglycemia and are asymptomatic initially. This is particularly true in obese patients, whose diabetes may be detected only after glycosuria or hyperglycemia is noted during routine laboratory studies. Occasionally, type 2 patients may present with evidence of neuropathic or cardiovascular complications because of occult disease present for some time prior to diagnosis. Chronic skin infections are common. Generalized pruritus and symptoms of vaginitis are frequently the initial complaints of women. Diabetes should be suspected in women with chronic candidal vulvovaginitis as well as in those who have delivered large babies (> 9 lb, or 4.1 kg) or have had polyhydramnios, preeclampsia, or unexplained fetal losses. . [ref 4]

Obese diabetics may have any variety of fat distribution; however, diabetes seems to be more often associated in both men and women with localization of fat deposits on the upper segment of the body (particularly the abdomen, chest, neck, and face) and relatively less fat on the appendages, which may be quite muscular. Standardized tables of waist-to-hip ratio indicate that ratios of "greater than 0.9" in men and "greater than 0.8" in women are associatedwith an increased risk of diabetes in obese subjects. Mild hypertension is often present in obese diabetics. Eruptive xanthomas on the flexor surface of the limbs and on the buttocks and lipemia retinalis due to hyperchylomicronemia can occur in patients with uncontrolled type 2 diabetes who also have a familial form of hypertriglyceridemia. . [ref 4]

HUMAN IMMUNODEFICIENCY VIRUS DISEASE

INTRODUCTION

AIDS was first recognized in 1981, when the unexplained occurrence of Pneumocystis carinii pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) in 26 previously healthy homosexual men in New York and Los Angeles. Within months, the disease became recognized in male and female injection drug users (IDUs) and soon thereafter in recipients of blood transfusions and in hemophiliacs. .[ref6]

In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was

demonstrated clearly to be the causative agent of AIDS. In 1985, a sensitive enzyme-linked immunosorbent assay (ELISA) was Developed. .[ref6]

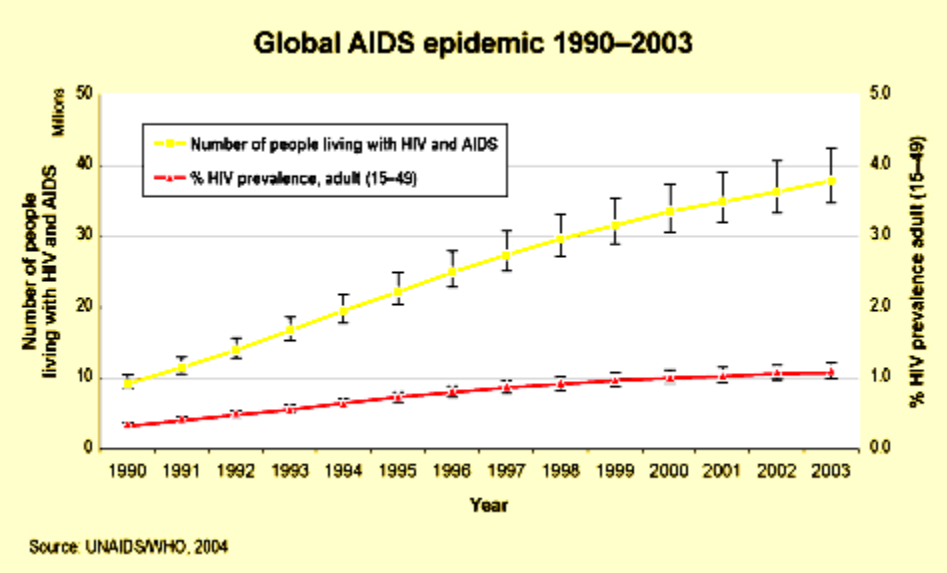
DEFINITION

Using the current CDC3 classification system , any HIV-infected individual with a CD4+ T cell count of <200/uL has AIDS by definition, regardless of the presence of symptoms or opportunistic diseases.[ref6]

EPIDEMIOLOGY

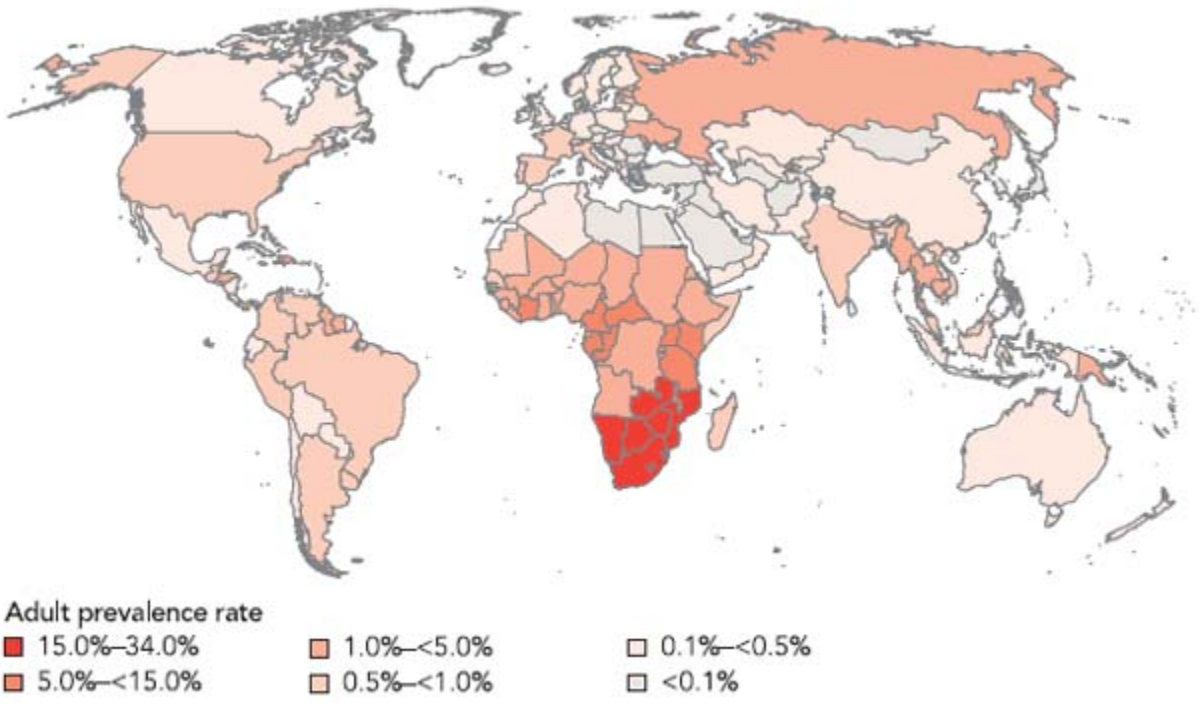
HIV Incidence and Prevalence 2004 [ref 8]

Region	Living With HIV	New Infections	Adult Prevalence	Deaths
Sub-Saharan	25.4 million	3.1 million	7.4%	2.3 million
N. Africa, Middle East	540,000	92,000	0.3%	28,000
South and Southeast Asia	7.1 million	890,000	0.6%	490,000
East Asia	1.1 million	290,000	0.1%	51,000
Latin America	1.7 million	240,000	0.6%	95,000
Caribbean	440,000	53,000	2.3%	36,000
East Europe	1.4 million	210,000	0.8%	60,000
Western/Central Europe	610,000	21,000	0.3%	6500
North America	1.0 million	44,000	0.6%	16,000
Total	**39.4 million**	**4.9 million**	**1.1%**	**3.1 million**



[ref 9]

HIV infection/AIDS is a global pandemic, with cases reported from virtually every country. The current estimate of the number of cases of HIV infection among adults worldwide is ~37 million, two-thirds of whom are in sub-Saharan Africa; 50% of cases are women. In addition, an estimated 2.5 million children younger than age 15 are living with HIV/AIDS. [ref 6]

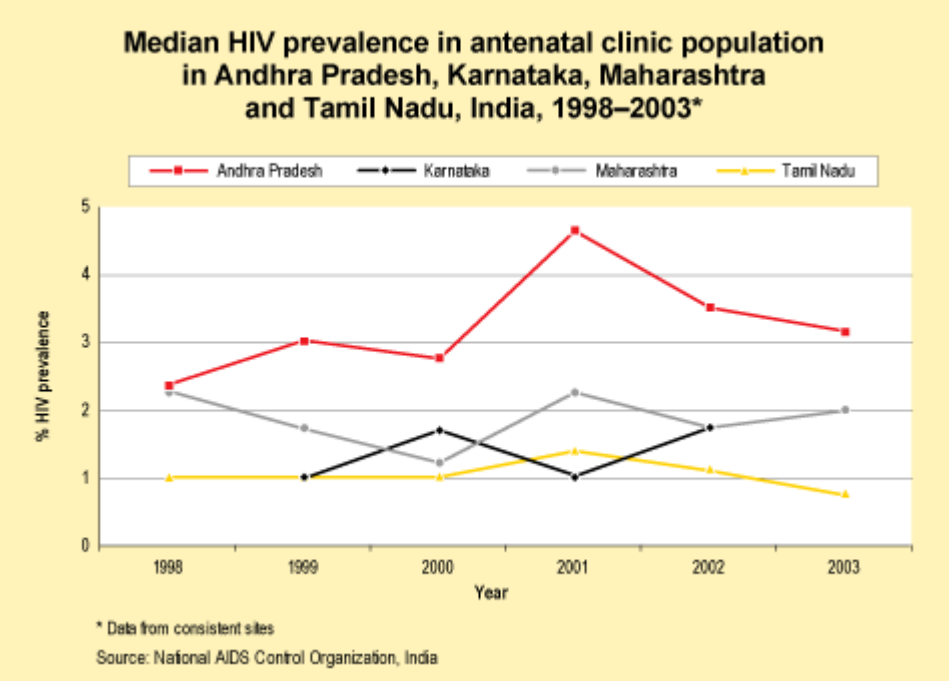


[ref 11]

A global view of HIV infection

India has the largest number of people living with HIV outside South Africa—estimated at 4.6 million in 2002. Most infections are acquired sexually, but a small proportion is acquired through injecting drug use.

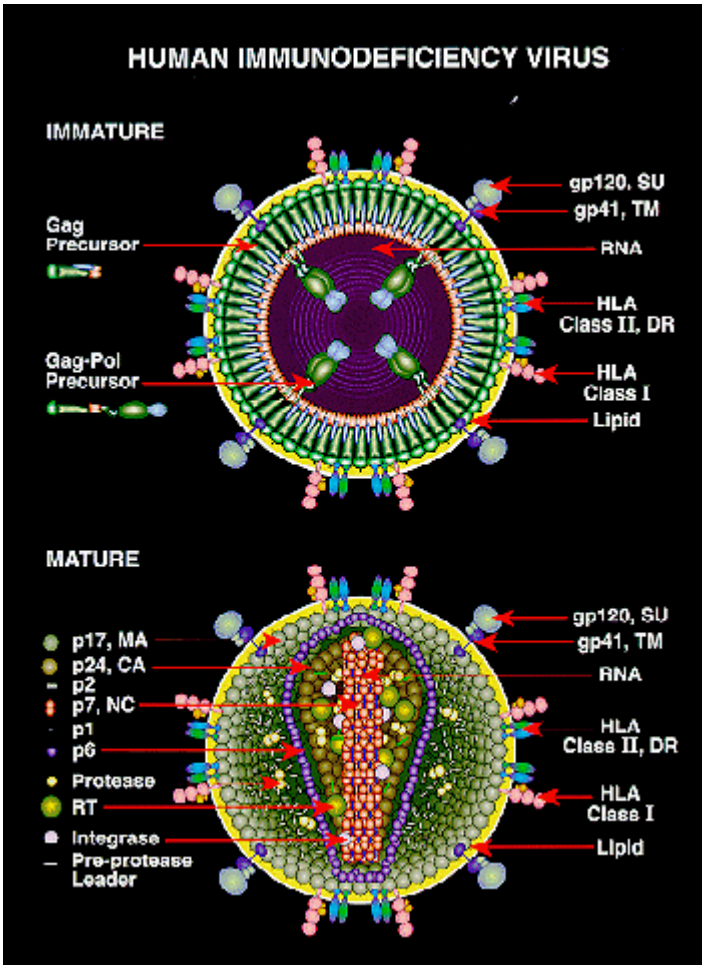
In the southern states of Andhra Pradesh, Karnataka, Maharashtra, and Tamil Nadu, HIV is transmitted mainly through heterosexual sex, and is largely linked to sex work. Indeed, according to selected surveys, more than half of sex workers have become infected with HIV.



[ref 9]

In India, knowledge about HIV is still scant and incomplete. In a 2001 national behavioural study of nearly 85000 people, only 75% of respondents had heard of AIDS and awareness was particularly low among rural women in Bihar, Gujarat and West Bengal. Less than 33% of all respondents had heard of sexually transmitted infections and only 21% were aware of the links between sexually transmitted infections and HIV.

ETIOLOGIC AGENT



- **Gag Proteins and Precursor (p55)**
  - Capsid Structural Protein (CA, p24)
  - Matrix Protein (MA, myristylated, p17)
  - RNA Binding Protein (p9)
  - RNA Binding Protein (proline-rich, p7)
  - Other Gag Proteins(p6, p2, p1)
- **Viral Encoded Enzymes**
  - Polymerase (p61,p55)
    - Reverse Transcriptase
    - Rnase H
  - Protease (p10)
  - Integrase (p32)
- **Envelope Proteins**
  - Surface Glycoprotein (gp120)
  - Transmembrane Glycoprotein (gp41)
- **Accessory and Regulatory Proteins**
  - Tat
  - Rev
  - Nef
  - Vif (Viral Infectivity Factor)
  - Vpr
  - Vpu
  - Vpx
  - Tev
- **Nucleic Acids**
  - HIV RNA

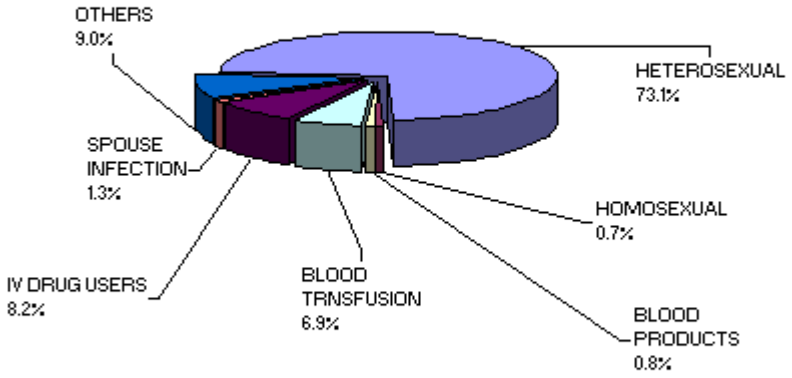
[ref 13]

The etiologic agent of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses.the HIV virion is an icosahedral structure containing numerous external spikes formed by the two major envelope proteins, the external gp120 and the transmembrane gp41.

TRANSMISSION

Figure - 4

PROBABLE SOURCE OF INFECTION IN AIDS CASES



Source: NACO

[ref 12]

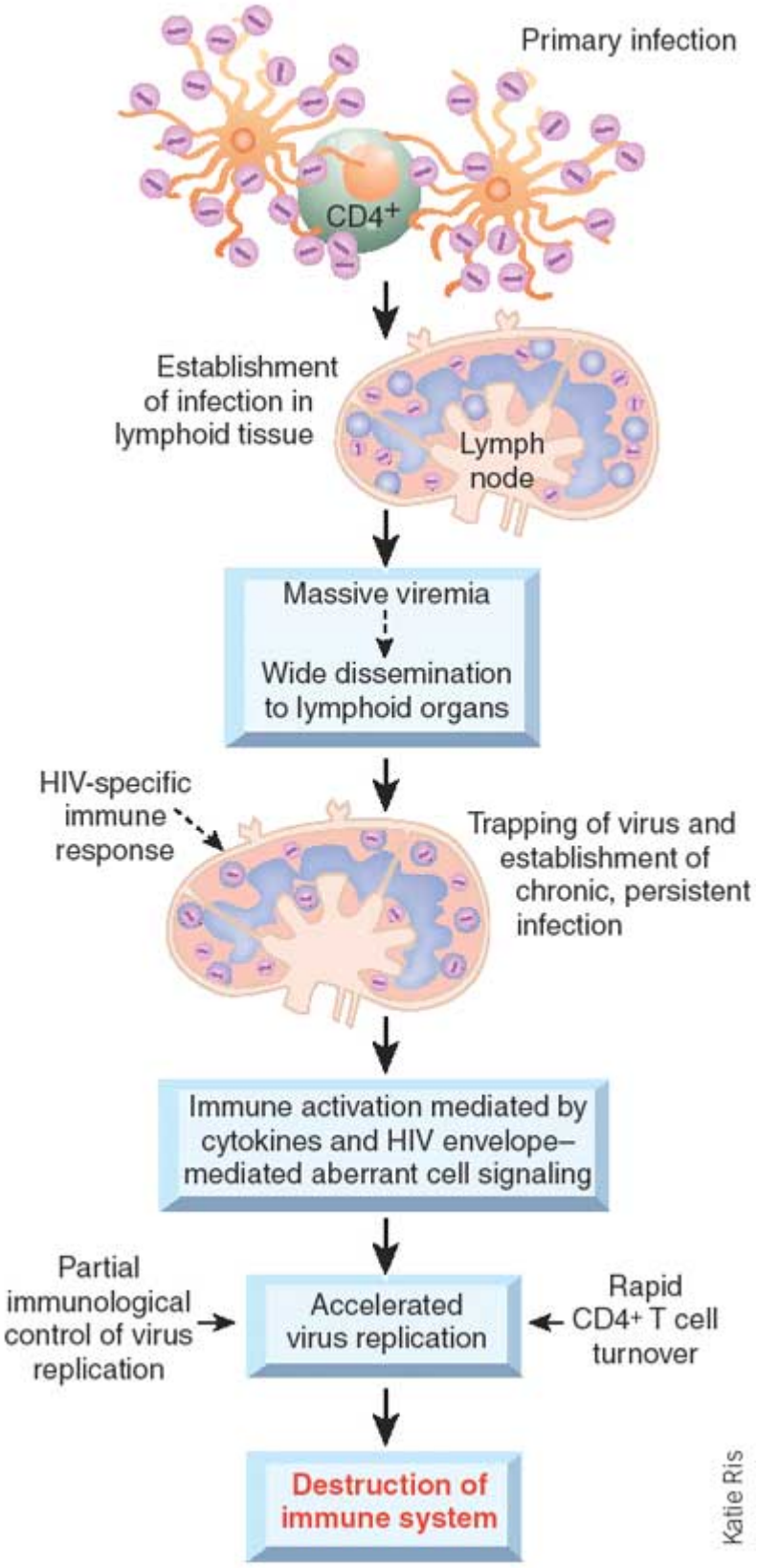
HIV2 is transmitted by both homosexual and heterosexual contact; by blood and blood products; and by infected mothers to infants either intrapartum, perinatally, or via breast milk.

PATHOPHYSIOLOGY AND PATHOGENESIS

The hallmark of HIV disease is a profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as helper T cells

When the number of CD4+ T cells declines below a certain level, the patient is at high risk of developing a variety of opportunistic diseases, particularly the infections and neoplasms that are AIDS-defining illnesses. Some features of AIDS, such as KS and neurologic abnormalities ,cannot be explained completely by the immunosuppressive effects of HIV, since these complications may occur prior to the development of severe immunologic impairment. [Ref6]

The combination of viral pathogenic and immunopathogenic events that occurs during the course of HIV disease from the moment of initial (primary) infection through the development of advanced-stage disease is complex and varied. It is important to appreciate that the pathogenic mechanisms of HIV disease are multifactorial and multiphasic [ref6]


Primary infection
CD4+
Establishment of infection in lymphoid tissue
Lymph node
Massive viremia
Wide dissemination to lymphoid organs
HIV-specific immune response
Trapping of virus and establishment of chronic, persistent infection
Immune activation mediated by cytokines and HIV envelope–mediated aberrant cell signaling
Partial immunological control of virus replication
Accelerated virus replication
Rapid CD4+ T cell turnover
Destruction of immune system
Katie Ris

[ref14]

ENDOCRINOLOGIC MANIFESTATIONS

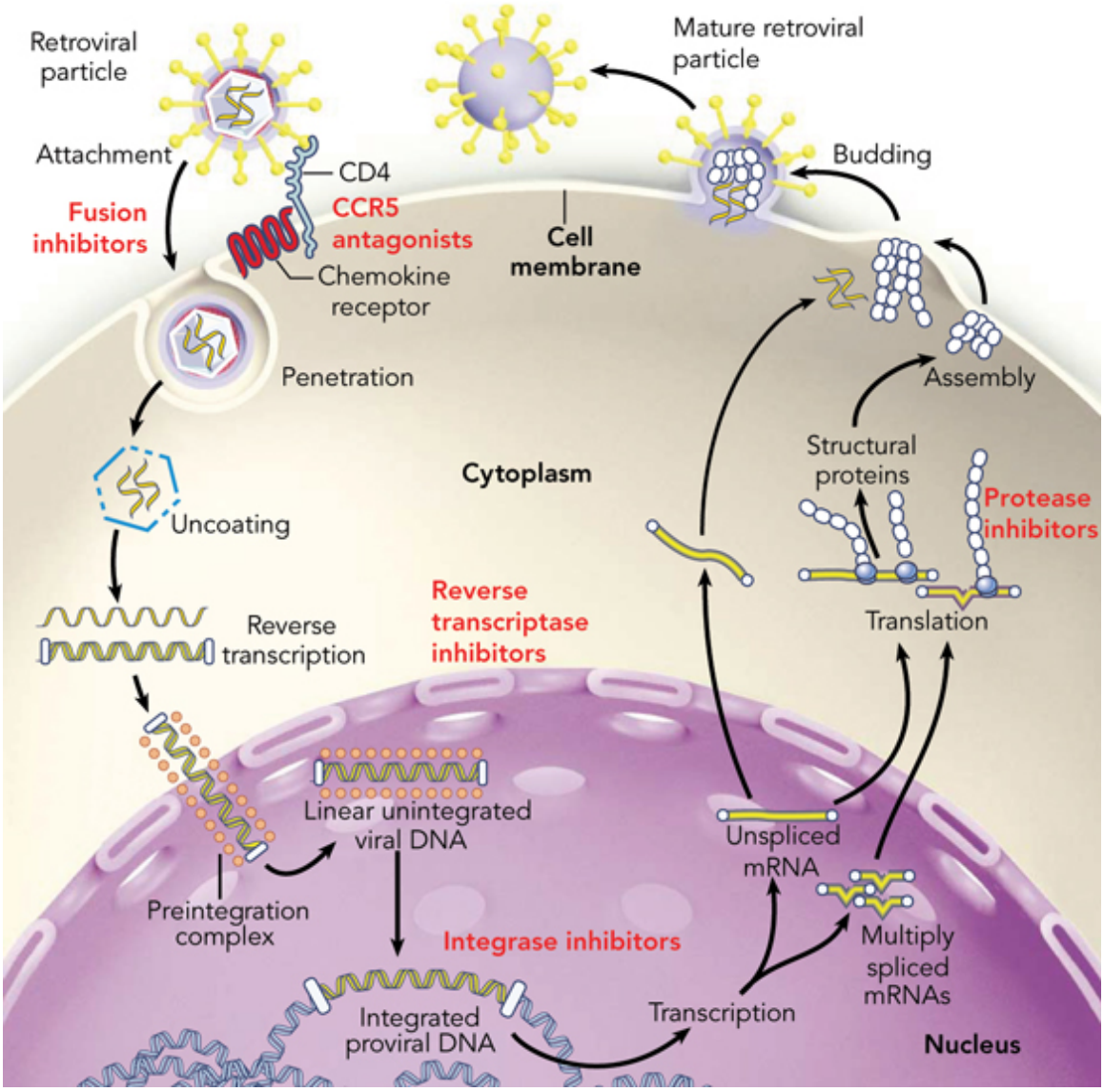
Hypogonadism is probably the most common endocrinologic abnormality in HIV-infected men.

The adrenal gland is also a commonly afflicted endocrine gland in patients with AIDS. Abnormalities demonstrated on autopsy include infection (especially with CMV and *M avium* complex), infiltration with Kaposi's sarcoma, and injury from hemorrhage and presumed autoimmunity. The prevalence of clinically significant adrenal insufficiency is low. Patients with suggestive symptoms should undergo a cosyntropin stimulation test. [ref7]

Although frank deficiency of cortisol is rare, an isolated defect in mineralocorticoid metabolism may lead to salt-wasting and hyperkalemia.

AIDS patients appear to have abnormalities of thyroid function tests different from those of patients with other chronic diseases. AIDS patients have been shown to have high levels of triiodothyronine (T_3), thyroxine (T_4), and thyroid-binding globulin and low levels of reverse triiodothyronine (rT_3). The causes and clinical significance of these abnormalities are unknown. [ref7]

ANTIRETROVIRAL THERAPY



The best time to initiate antiretroviral treatment remains controversial. It is best to weigh the benefits of viral suppression against the side effects of the drugs for each patient. In general, treatment for asymptomatic HIV disease should be initiated when the CD4 cell count drops below 350 cells/mcL or symptomatic HIV disease. Patients with rapidly dropping CD4 counts or very high viral loads (>100,000/mcL) should be considered for earlier treatment. For those patients who

might have difficulty adhering to treatment or who are at higher risk for toxicity (eg, underlying liver disease), waiting until the CD4 count nears 200 cells/mcL may be a better strategy.

. Antiretroviral therapy.

Drug	**Common Side Effects**
Zidovudine (AZT)	Anemia, neutropenia, nausea, malaise, headache, insomnia, myopathy granulocytopenia , lactic acidosis , hepatomegaly with steatosis.
Didanosine (ddI)	Peripheral neuropathy, pancreatitis, dry mouth, hepatitis, , abnormalities on liver function tests, lactic acidosis, hepatomegaly with steatosis.
Zalcitabine (ddC)	Peripheral neuropathy, aphthous ulcers, hepatitis, pancreatitis, lactic acidosis, hepatomegaly with steatosis
Stavudine (d4T))	Peripheral neuropathy, hepatitis, pancreatitis , lactic acidosis, hepatomegaly with steatosis, ascending neuromuscular weakness, lipodystrophy.
Lamivudine (3TC)	Rash, peripheral neuropathy
Emtricitabine	Skin discoloration palms/soles (mild)
Abacavir	Rash, fever—if occur, rechallenge may be fatal
Tenofovir	Gastrointestinal distress
Saquinavir	Gastrointestinal distress
Ritonavir	Gastrointestinal distress, peripheral paresthesias, nausea, abdominal pain, hyperglycemia, fat redistribution, lipid abnormalities.
Indinavir	Kidney stones, , hyperglycemia, fat redistribution, lipid abnormalities
Nelfinavir	Diarrhea
Amprenavir	Gastrointestinal, rash, nausea, vomiting, diarrhea, oral paresthesias, elevated liver function tests, hyperglycemia, fat redistribution, lipid abnormalities.

Fosamprenavir	Same as amprenavir
Lopinavir/ritonavir	Diarrhea
Atazanavir	Hyperbilirubinemia, hyperglycemia, fat maldistribution
Tipranavir/ritonavir	Gastrointestinal, rash
Nevirapine)	Rash
Delavirdine	Rash
Efavirenz	Neurologic disturbances
Enfuvirtide	Injection site pain and allergic reaction

[ref7]

AIDS-related opportunistic infections and Treatment

Treatment of AIDS-related opportunistic infections and malignancies.

Infection or Malignancy	**Treatment**	**Complications**
Pneumocystis jiroveci infection	Trimethoprim-sulfamethoxazole	Nausea, neutropenia, anemia, hepatitis, drug rash, Stevens-Johnson syndrome.
	Pentamidine	Hypotension, hypoglycemia, anemia, neutropenia, pancreatitis, hepatitis.
	Trimethoprim, with dapsone,	Nausea, rash, hemolytic anemia in G6PD[3]-deficient patients. Methemoglobinemia (weekly levels should be < 10% of total hemoglobin).
	Primaquine, and clindamycin,	Hemolytic anemia in G6PD-deficient patients. Methemoglobinemia, neutropenia, colitis.

	Atovaquone,	Rash, elevated aminotransferases, anemia, neutropenia.
Mycobacterium avium complex infection	Clarithromycin,	Clarithromycin: hepatitis, nausea, diarrhea; ethambutol: hepatitis, optic neuritis.
	Rifabutin,	Rash, hepatitis, uveitis.
Toxoplasmosis	Pyrimethamine combined with sulfadiazine,	Leukopenia, rash.
Lymphoma	Combination chemotherapy (eg, modified CHOP, M-BACOD, with or without G-CSF or GM-CSF).	Nausea, vomiting, anemia, leukopenia, cardiac toxicity (with doxorubicin).
Cryptococcal meningitis	Amphotericin B	Fever, anemia, hypokalemia, azotemia.
	Fluconazole,	Hepatitis.
Cytomegalovirus infection	Valganciclovir,	Neutropenia, anemia, thrombocytopenia.
	Ganciclovir,	Neutropenia (especially when used concurrently with zidovudine), anemia, thrombocytopenia.
	Foscarnet,	Nausea, hypokalemia, hypocalcemia, hyperphosphatemia, azotemia.
Esophageal candidiasis or recurrent vaginal candidiasis	Fluconazole,	Hepatitis, development of imidazole resistance.
Herpes simplex infection	Acyclovir,	Resistant herpes simplex with chronic therapy.
	Valacyclovir,	Nausea.
	Foscarnet	See above.
Kaposi's sarcoma		
Limited cutaneous disease	Observation, intralesional vinblastine.	Inflammation, pain at site of injection.

Abnormalities in glucose metabolism have been described with increasing frequency in patients with HIV in many studies and may result from both direct and indirect effects of highly active antiretroviral therapies (HAART).

Prevalence and Incidence of Pre-diabetes and Diabetes in the Multicenter AIDS Cohort Study showed HIV+ men with HAART exposure have an increased prevalence and incidence of pre-diabetes and DM. [ref 10]

AIMS AND OBJECTIVES

1. To determine the prevalence of diabetes mellitus in HIV infected Patients.

2. To determine the prevalence of diabetes mellitus in HIV patients receiving highly active anti retroviral therapy.

MATERIALS AND METHODS

Setting : All HIV patients who were attending anti retroviral therapy centre. GRH, Madurai.

Collaborating Departments **:A**nti retroviral therapy centre
Madurai Medical College
Madurai.
Department of Diabatology
Madurai Medical College
Madurai

Design of the study **:** cross sectional study

Period of study **:** 01.09.2006 – 31.10.2007

Sample size **:** 128

Ethical committee approval **:** Obtained

Consent **:** Informed consent was obtained

Financial support **:** Nil

Conflict of interest **:** Nil

Selection and Details of Study subjects

128 HIV patients who were attending Anti Retro Therapy Centre Govt Rajaji Hospital, during the period from 01.09.2006 – 31.10.2007 were included in the study.

Inclusion criteria

All HIV patients attending Anti Retro Therapy Centre were taken.

Exclusion criteria

1. Patients on medications other than ART [Beta-Blockers, ThiazideDiuretics, Corticosteroids, Phenytoin,OralContraceptives and Sex Hormones, Phenothiazines and all the drugs mentioned in (ref2)] which are likely to produce glucose intolerance were excluded.

2. Conditions that are likely to produce transient hyperglycemia like ,patients with fever , Pneumonia, acutely ill patients were excluded.

The total number of cases screened were 140. Of which 12 cases were excluded from the study. After exclusion of these patients, the total number of patients who were taken into account for our study was128.

128 patients who were included in the study were divided into 5 groups

1.Patients on D4T(30)+3TC+NVP were included in **Group 1**,

2.Patients on D4T(30)+3TC+EFVwere included in **Group2**,

3.Patients on ZDV+3TC+NVP were included in **Group 3**,

4.Patients on ZDV+3TC+EFVwere included in **Group 4**,

5.Patients not on any drugs were included in **Group 5**.

The prevalence of DM was determined, defined as fasting glucose concentration of 126 mg/dL or more or 2 hour post prandial glucose concentration of 200 mg/dL or higher on two subsequent days , self-reported DM, or self reported use of an anti diabetic medication (ie, insulin, sulfonylureas, thiazolidinediones, biguanides, meglitinides, or -glucosidase inhibitors).

The prevalence of IGT AND IFG were also determined,

IFG - was defined as FPG >/= 110 mg/dL but < 126 mg/dL .

IGT - which was defined as plasma glucose levels between 7.8 and 11.1 mmol/L (140 and 200 mg/dL) 2 hours after meal. [ref3]

RESULTS AND OBSERVATIONS

The collected data was analysed using Epidemiological information package 2002 developed by Centre for Disease Control (CDC) Atlanta in Collaboration with WHO. CHI square test was used for test of significance. These data was compared with published literature.

In our study, 128 HIV patients were studied.

A. CHARECTERISTICS OF CASES INCLUDED IN THE STUDY

Table 1: Total cases

Group	**Cases**	
	No.	**%**
1	50	39.1
2	24	18.8
3	18	14.1
4	8	6.3
5	28	21.9
Total	128	100

128 patients were included in the study and they were divided into 5 groups. Patients on D4T(30)+3TC+NVP were included in **Group 1(50)**, Patients on D4T(30)+3TC+EFVwere included in **Group2(24)**, Patients on ZDV+3TC+NVP were included in **Group 3(18)**, Patients on ZDV+3TC+EFV were included in **Group 4(8)**, Patients not on any drugs were included in **Group 5(28)**.

Table 2 :Age

Age group in years	*Cases*	
	No.	**%**
< 10	3	2.3
10-19	2	1.6
20-29	34	26.6
30-39	56	43.8
40-49	26	20.3
50 & Above	7	5.4
Total	128	100
Mean	33.9 yrs	
S.D.	9.2 yrs	

2.3% of patients belong to < 10 years of age, 1.6% of belong to 10 - 19 years of age, 26.6%of patients belong to 20-29 years of age, 43.8 % of patients belong to 30-39 years of age, 26%of patients belong to 40-49 years of age and 7% of patients belong to 50 & Above years of age.

Table 3: sex

Sex	**Cases**	
	No.	**%**
Males	77	60.2
Females	51	39.8
Total	128	100

In our patients 60.2%were males and 39.8% were females.

Table 4: Marital status

Marital status	**Cases**	
	No.	**%**
Married	106	82.8
Unmarried	22	17.2
Total	128	100

Among 128 study patients 82.8% were married and 17.2 were unmarried.

Table 5: Marital status: BMI

Parameter	Mean	S.D.
Height	163.7 cms	11.9 cms
Weight	56.6 kg.	8.5 kg
B.M.I.	21.02	1.88

In our patients mean height was 163.7 cms , mean weight was 56.6 kg and BMI was 21.

B. RELATIONSHIP OF CHARACTERISTICS OF CASES AND PREVALANCE OF D.M. & IGT/IFG

Table 6: Age and Prevalance

Age in years	D.M.		*IGT/IFG*	
	Present	**Absent**	**Present**	**Absent**
Mean	37.7	33.4	38.1	33.6
S.D.	10.4	8.9	6	9.4
'p'	**0.005 Significant**		**0.0474 Significant**	

In diabetes and IGT/IFG patients ,the mean age was 37.7 and 38.1 respectively. Whereas in non glucose intolerance patients the mean agewas 33 with significant' p' value showed increased prevalence of glucose intolerance with increasing age.

Table 7: **Sex and Prevalance**

Sex	**D.M.**				***IGT/IFG***			
	Present(17)		**Absent(111)**		**Present(10)**		**Absent(118)**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Males	11	64.7	66	59.5	6	60	71	60.2
Females	6	35.3	45	40.5	4	40	47	39.8
'p'	0.8843 Not significant				0.6199 Not significant			

Out of 17 diabetic patients, males were 64.7% and females were 35.77%.In 10 IGT/IFG patients males were 60% while females were 40% with insignificant 'p' value showed the prevalence of glucose intolerance in our study was equal in both the sexes.

Table 8 : BMI and **Prevalance**

B.M.I.	**D.M.**				***IGT/IFG***			
	Present(17)		**Absent(111)**		**Present(10)**		**Absent(118)**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Below normal < 18.5	-	-	12	10.8	1	10	11	9.3
Normal 18.5 – 24.9	17	100	94	84.7	9	90	102	86.4
Overweight > 24.9	-	-	5	4.5	-	-	5	4.2
'p'	0.6786 Not significant				0.2967 Not significant			

Among 128 patients 10.8% had BMI of < 18.5 , 84.7% had BMI of 18.5 – 24.9 and 5% had BMI of > 24.9. All the 17 diabetic cases were within the range of 18.5 – 24.9. In 10 IGT/IFG patients 90% were within the range of 18.5 – 24.9 and 10% were BMI of < 18.5, with insignificant 'p' value shows glucose intolerance in our study was not associated with high BMI value.

Table 9:Prevalence of D.M./ IGT/IFG

Group	D.M.				*IGT/IFG*			
	Present		Absent		Present		Absent	
	No.	%	No.	%	No.	%	No.	%
1(50)	7	14	43	86	4	8	46	92
2 (24)	4	16.7	20	83.3	2	8.3	22	91.7
3 (18)	2	11.1	16	88.9	1	5.6	17	94.4
4 (8)	1	12.5	7	87.5	1	12.5	7	87.5
5 (28)	3	10.7	25	89.3	2	7.1	26	92.9
Total (128)	17	13.3	111	86.7	10	7.8	118	92.2

The prevalence of diabetes mellitus was 13.3 % .In group 1 the prevalence was 14%.In group 2 it was16.7%.In group 3 it was 16%.In group 4 the prevalence was 12.5%. In group 5 it was 10.7%. The prevalence of IGT/IFG was 7.8% with 8%, 8.3%, 5.6%, 12.5% 7.1% in group1,2,3,4&5 respectively.

Prevalence of D.M & IGT/IFG

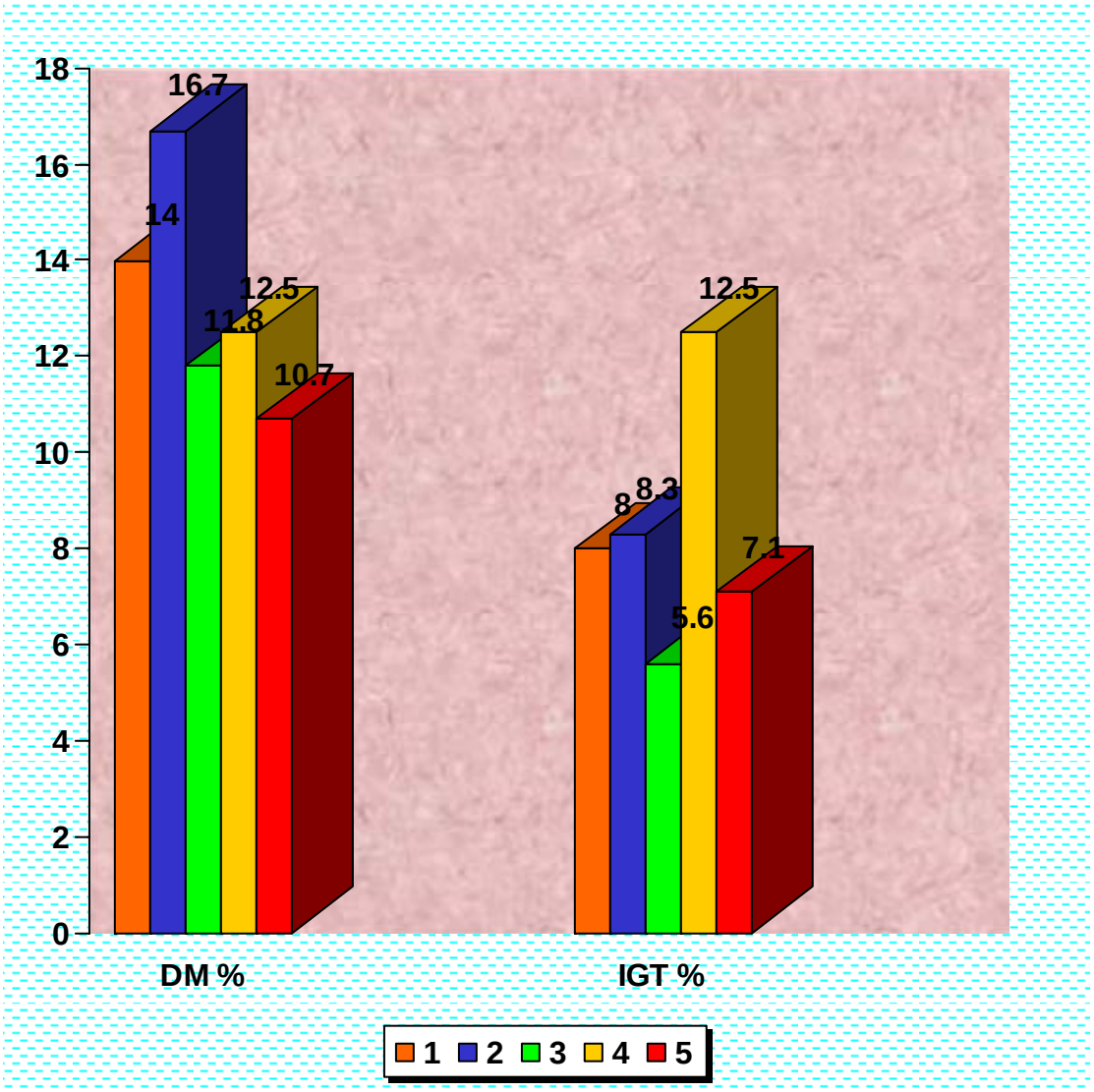


Table 10 :Prevalence of D.M./ IGT/IFG in HIV patients on HAART and Not on HAART

Group	Prevalence of D.M. in %			*Prevalence of IGT/IFG in %*		
	On HAART	**Not on HAART Group 5**	**'p'**	**On HAART**	**Not on HAART**	**'p'**
1	14	10.7	**0.0249 Significant**	8	7.1	0.4983 (Not Significant)
2	16.7	10.7	**0.0001 Significant**	8.3	7.1	0.3562(Not Significant)
3	11.1	10.7	0.4792 (Not Significant)	5.6	7.1	0.1992 (Not significant)
4	12.5	10.7	0.2352 (Not Significant)	12.5	7.1	**0.0001 Significant**
Total	14	10.7	**0.0249 Significant**	8	7.1	0.4983 Not Significant

Prevalance of diabetes mellitus among HIV patients not receiving HAART [group 5] was 10.7% and prevalence among HIV patients on HAART was 14%.There was increased prevalence of diabetes in patients on HAART than patients not on HAART with significant 'p' value.

Considering individual groups , patients on Stavudine+Lamivudine +Nevirapine **Group1**& patients on Stavudine+Lamivudine +Efavirenzwere **Group2**, had higher prevalence with significant ‘p’ value.

Prevalance of IGT/IFG among HIV patients not on HAART [group 5] was 7.1% .Among patients on HAART it was 8% with insignificant ‘p’ value. Considering individual groups Group 4 had higher prevalence with significant ‘p’ value. But the number of IGT/IFG patients in group 4 was only one made it insignificant.

DISCUSSION & COMPARATIVE ANALYSIS

All the patients who were attending anti retroviral therapy centre, GRH, Madurai were considered for the study. patients on medications other than ART [Beta-Blockers, ThiazideDiuretics, Corticosteroids, Phenytoin,OralContraceptives and Sex Hormones, Phenothiazines and all the drugs mentioned in (ref2)] and Conditions that are likely to produce transient hyperglycemia like patients with fever , Pneumonia, acutely ill patients were excluded.. Finally 128 patients were selected and divided into 5 Groups based on treatment they have received.

Patients on Stavudine+Lamivudine+Nevirapine were included in **Group1**, patients on Stavudine+Lamivudine +Efavirenz were included in **Group2**,Patients on Zidovudine+ Lamivudine +Nevirapine were included in **Group 3**, Patients on Zidovudine+ Lamivudine +Efavirenz were included in **Group 4**, and Patients not on any drugs were included in **Group 5**.

Dose of drugs used in HAART was Stavudine 30mg, Lamivudine -150 mg , Nevirapine-200mg, Zidovudine-300mg and Efavirenz-600mg.

Adherence to antiretroviral therapy was assessed by response to interviewer query, "On average, how often did you take your medication as prescribed?" All our patients were 100% adherent to HAART

Urine analysis, Fasting blood sugar after atleast 8 hours fasting , Post prandial blood sugar 2 hours after meal , Blood urea, S.creatinine , CD4 count, liver function test, ECG were done for all the patients.

Those patients with abnormal glucose value , the Fasting blood sugar and Post prandial blood sugar were repeated on the next day.

BMI was calculated for all the patients using their height and weight.

128 patients were included in our study and prevalence of diabetes and prediabetes were determined through cross sectional pattern.

In our study the prevalence 0f diabetes was 13.3%. Many studies were conducted in india to determine the prevalence of diabetes in the general population.. In Raman kutty et al study the prevalence was 12.4 % in Thiruvananthapuram .In 2001 Misra et al study the prevalence was 10.3 in New Delhi . In Mohan et al study the prevalence was 12 % in Chennai. Another study in the same year was conducted by Ramachandran et al , National Urban diabetes Survey showed the pravalance of 12.1% . [ref 11] .Compared to these studies which were conducted in the the general population the pravalance was higher in our study i.e, 13.3%which was conducted among HIV seropositive patients and those receiving antiretroviral therapy.

Prevalance of diabetes in urban India [ref 11,13,14,15,16,18,19,20,21]

Year	Author	Place	prevalance (%)
1972	Ahuja	ICMR Multicentre Study	2.1
1979	SR Iyer *et al.*	Bardoli	4.4
1988	Ramachandran	Kudremukh	5.0
1992	Ramchandran	Chennai	8.2
2000	Raman kutty	Thiruvananthapuram	12.4
2001	Iyer	Dombivli	7.5
2001	Misra	New Delhi	10.3
2001	Mohan	Chennai	12.0
2001	Ramachandran	National Urban diabetes Survey(Six Cities)	12.1
2002	Gupta [17]	Jaipur	12.7

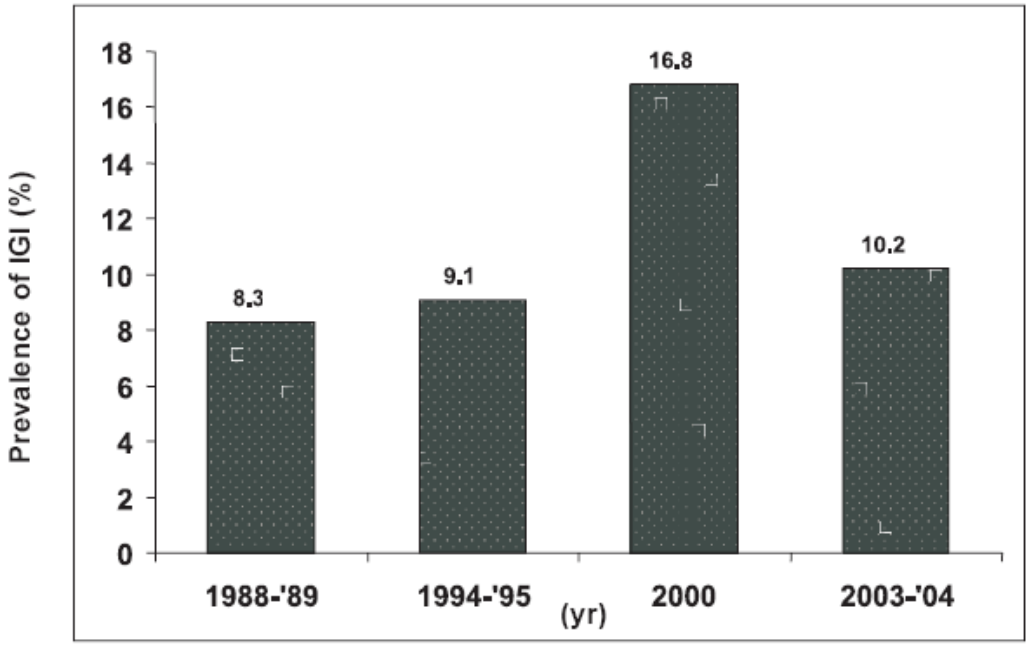
Looking at the region-wise prevalance of diabetes, in a recent study conducted among urban subjects [National Urban diabetes Survey(NUDS)] the prevalance of diabetes in the southern part of India was found to be higher -13.5% among Chennai residents, in Bangalore 12.4% and Hyderabad 16.6% than eastern India 11.7% (Kolkatta), northern India 11.6% (New Delhi) and western India 9.3% (Mumbai).Thus it is clear that in the last two decades, there has been a marked increase in the prevalance of diabetes among urban Indians.

All the diabetic cases in our study were within the range of BMI i.e., 18.5 – 24.9. Majority of the diabetic subjects in India are LBW type 2 DM. There are several publications on this subject. The pathogenesis of this disorder is not clear

Prediabetes- the harbinger of future diabetes

Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) collectively called as prediabetic states, have a high risk of conversion to diabetes. Several studies have shown that these prediabetic states are also high risk stages for cardiovascular disease. Hence data on IGT and IFG are also urgently needed as they are indicators of future diabetes prevalence and burden on the nation.

The National Urban Diabetes Survey (NUDS) results indicate the prevalence of IGT was 16.8 per cent in Chennai, 14.9 per cent in Bengaluru (formerly Bangalore), 29.8 per cent in Hyderabad, 10 per cent in Kolkatta, 10.8 per cent in Mumbai and 8.6 per cent in New Delhi. The ADEPS done in Kerala showed that 11.2 per cent of the subjects had either IFG or IGT.



Prevalence of Impaired glucose tolerance at Chennai.

A recent study has reported a decreased prevalence of IGT in an urban population compared to earlier studies done in Chennai (16.8% in 2000 to 10.2% in 2004). In our study also the prevalence of IFG/ IGT was 7.8% much lower than the general population. This could suggest that the diabetes epidemic in urban India may be slowing down or it may also suggest that there could be a rapid progression from the normal state through IGT to diabetes, which could imply a rapid increase in the diabetes epidemic or a worsening diabetogenic environment.

In the Multicenter AIDS Cohort Study in which the prevalence of diabetes and prediabetes was determined among the HIV seropositive persons and those receiving HAART. IN this study 1107 men were included and the prevalence of DM and prediabetes was determined at the index visit .

In our study only the HIV infected patients and the patients receiving HAART were included and they were divided into 5 groups. Comparison was made between these groups. In the Multicenter AIDS Cohort Study along with HIV infected patients and the patients receiving HAART, HIV seronegative participants also were included.

In our study,out of 128 patients 100 patients were on HAART. 28 patients were not on any drugs. In the Multicenter AIDS Cohort Study 563 were HIV seronegative , 121 were HIV infected but not on any drugs and 423 were on HAART.

In our study both males and females were included. Out of 128 patients 60.2%were males and 39.8% were females. In the Multicenter AIDS Cohort Study all the participants were males.

In our study both fasting and postprandial blood glucose were taken for two consecutive days to find out the glucose intolerance.. In the Multicenter AIDS Cohort Study only single fasting glucose value was taken to define. glucose intolerance.

The other two criterias to define the glucose intolerance were same in both our study and in the Multicenter AIDS Cohort Study i.e, use of anti-diabetic medication and self-reported diagnosis of DM.

In our study patients did not receive protease inhibitors. In the Multicenter AIDS Cohort Study protease inhibitors were used in HAART.

In the Multicenter AIDS Cohort Study the prevalence of diabetes mellitus was 14% in HIV positive group on HAART , 11% in HIV positive group not on HAART and the prevalence of DM was 5% in the HIV seronegative group. In our study also the prevalence of diabetes mellitus was 14% in HIV positive group on HAART, 10.7% in HIV positive group not on HAART .The overall prevalence of diabetes mellitus was 13.3 % .

In comparing HIV seropositive patients on HAART with HIV seropositive not on any drugs , the prevalence of diabetes was significantly higher among patients on HAART . Considering individual groups ,patients in group 1 & 2 i.e, those on Stavudine+Lamivudine+Nevirapine **&** Stavudine + Lamivudine + Efavirenz had higher prevalence with significant ‘p’ value.

SUMMARY

The study **"PREVALENCE OF DIABETES IN HIV INFECTED PATIENTS AND HIV PATIENTS RECEIVING ANTIRETROVIRAL THERAPY"** Was done in 128 patients who were attending the anti retroviral therapy centre. GRH, Madurai .selected patients were divided into 5 Groups based on treatment they have received. Most of the patients were males. Patients on Stavudine+Lamivudine+Nevirapine were included in **Group1**, patients on Stavudine+Lamivudine +Efavirenz were included in **Group2**, Patients on Zidovudine+ Lamivudine +Nevirapine were included in **Group 3**, Patients on Zidovudine+ Lamivudine +Efavirenz were included in **Group 4**, and Patients not on any drugs were included in **Group 5**.

Urine analysis, Fasting blood sugar after atleast 8 hours fasting , Post prandial blood sugar 2 hours after meal , Blood urea, S.creatinine , CD4 count, Liver function test, ECG were done for all the patients.

Those patients with abnormal glucose value , the Fasting blood sugar and Post prandial blood sugar were repeated on the next day.

Out of 128 patients, 2.3% of patients belong to < 10 years of age, 1.6% of patients belong to 10-19years of age, 26.6% of patients belong to 20-29 years of age, 43.8 % of patients belong to 30-39 years of age, 26% of patients belong to 40-49 years of age and 7% of patients belong to 50 & Above years of age.

60.2%were males and 39.8% were females.

10.8% had BMI of < 18.5 , 84.7% had BMI of 18.5 – 24.9 and 5% had BMI of > 24.9. All the 17 diabetic cases were within the range of 18.5 – 24.9. In IGT/IFG patients 90% were within the range of 18.5 – 24.9 and 10% were BMI of < 18.5.

CONCLUSION

1. Prevalence of diabetes mellitus was 14% in HIV positive group on HAART, 10.7% in HIV positive group not on HAART. The overall prevalence of diabetes mellitus was 13.3 % in HIV patients.

2. Prevalence of IGT/IFG was 8% in HIV positive group on HAART, 7.1% in HIV positive group not on HAART .The overall prevalence was 7.8 % in HIV patients.

3. The prevalence of diabetes in HIV patients in our study was comparable to general population.

4. The prevalence of diabetes was significantly higher in HIV patients receiving HAART than HIV patients not on HAART.

5.Among HAART received patients ,those on Stavudine+Lamivudine+Nevirapine **&** Stavudine+Lamivudine +Efavirenz showed higher prevalence with significant 'p' value.

6. Among HAART drugs, protease inhibitors are well known to produce hyperglycemia. In our study those on Stavudine + Lamivudine+Nevirapine **&** Stavudine+Lamivudine +Efavirenz also showed higher prevalence of Diabetes.

7. So HIV patients on HAART should be periodically checked for blood glucose level.

8. The prevalence of IGT/IFG in HIV patients was slightly lower than the general population.

Limitations: In our study only small number of [128] patients were involved and since it was a prevalence study the causal relationship was not able to obtained. It needs longitudinal study.

BIBLIOGRAPHY

1. Diabetes Mellitus and its Complications: Molecular Mechanisms, Epidemiology, and Clinical Medicine Volume 1084 published November 2006 . Ann. N.Y. Acad. Sci. 1084: 1–29 (2006). doi: 10.1196/annals.1372.029.

2..Manjula K. Pandit; John Burke; Anthony B. Gustafson; Anil Minocha; and Alan N. Peiris drug-induced Disorders of Glucose Tolerance . 1 April 1993 | Volume 118 Issue 7 | Pages 529-539.

3. Alvin C. Powers . DIABETES MELLITUS - Harrison's Principles of Internal Medicine 16th Edition.

4. Diabetes Mellitus & Hypoglycemia *Current Medical Diagnosis & Treatment* 2007.

5. Mohamad Said Maani Takrouri: Diabetes Mellitus Is A Global Problem. *The*

Internet Journal of Health. 2007. Volume 6 Number 1.

6. Anthony S. Fauci, H. Clifford Lane -HUMAN IMMUNODEFICIENCY VIRUS DISEASE: AIDS AND RELATED DISORDERS 1036-1139 Harrison's Principles of Internal Medicine 16th Edition.

7.Infectious Diseases: HIV >*Current Medical Diagnosis & Treatment* 2007

8. . John G. Bartlett, MD : Global HIV Epidemiology, Research, and Care 3rd IAS Conference on HIV Pathogenesis and Treatment .

9. 2004 Report on the global AIDS epidemic-unaids.

10. Brown TT, Cole SR, Li X, Kingsley LA, Palella FJ, Riddler SA, Visscher BR, Margolick JB, Dobs AS. Prevalence and Incidence of Pre-diabetes and Diabetes in the Multicenter AIDS Cohort Study.-*11th Conf Retrovir Opportunistic Infect Febr 8 11 2004. San Franc CA Conf Retrovir Opportunistic Infect 11th 2004 San Franc Calif.* 2004 Feb 8-11; 11: abstract no. 73.

11. V Mohan Why Are Indians More Prone to diabetes? Vol. 52 • June 2004.

12. V. Mohan, S. Sandeep, R. Deepa, B. Shah* & C. Varghese Epidemiology of type 2 diabetes: Indian scenario *Madras Diabetes Research Foundation & Dr Mohan's Diabetes Specialities Centre, Chennai.*Indian J Med Res 125, March 2007, pp 217-230.

13. Ramachandran A, Jali MV, Mohan V, Snehalatha C,Viswanathan M. High prevalence of diabetes in an urban population in south India. *BMJ* 1988; *297* : 587-90.

14 Ramachandran A, Snehalatha C, Latha E, Vijay V,Viswanathan M. Rising prevalence of NIDDM in an urban population in India. *Diabetologia* 1997; *40* : 232-7.

15. Raman Kutty V, Joseph A, Soman CR. High prevalence oftype 2 diabetes in an urban settlement in Kerala, India. *Ethn Health* 1999; *4* : 231-9.

16. Ramachandran A, Snehalatha C, Latha E, Manoharan M, Vijay V. Impacts of urbanisation on the lifestyle and on the prevalence of diabetes in native Asian Indian population. Diabetes Res Clin Pract 1999; 44:207-213.

17. Joslin ‘s Diabetes Mellitus - 14th Edition

18. Iyer SR, Iyer RR, Upasani SV, et al. Diabetes mellitus in Dombivli—an urban population study. J Assoc Physicians India 2001;49:713-716.

19. Mohan V, Shanthirani S, Deepa R, et al. Intra urban differences in the prevalence of the metabolic syndrome in southern India - The Chennai Urban Population Study (CUPS). Diabet Med 2001; 18; 280-287.

20. Misra A, Pandey RM, Rama Devi J, et al. High prevalence of diabetes, obesity and dyslipidaemia in urban slum population in northern India. Int J Obes 2001; 25: 1-8.

21. Misra A, Vikram NK. Insulin resistance syndrome(metabolic syndrome) and Asian Indians. Current Sci 2002;83:1483-96.

22. Ramachandran A, Snehalatha C, Dharmaraj D, Viswanathan M. Prevalence of glucose intolerance in Asian Indians, Urban rural difference, and significance of upper body adiposity. *Diabetes Care* 1992;15:1348-55.

23. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *NEJM* 2000;346:393-403.

24. King H, Aubert RE, Herman WH. Global burden of diabetes,1995-2025. Prevalence numerical estimates and projections. *Diabetes Care* 1998;21:1414-31.

25. Shah SK, Saikia M, Burman NN, Snehalatha C, Ramachandran A. High prevalence of type 2 diabetes in

urban population in north eastern India. *Int J Diabetes Dev Countries* 1999; *19* : 144-7.

26. Zargar AH, Khan AK, Masoodi SR, Laway BA, Wani AI, Bashir MI, *et al*. Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in the Kashmir Valley of the Indian subcontinent. *Diabetes Res Clin Pract* 2000; *47* : 135-6.

27. Gupta A, Gupta R, Sarna M, Rastogi S, Gupta VP, Kothari K. Prevalence of diabetes, impaired fasting glucose

and insulin resistance syndrome in an urban Indian population. *Diabetes Res Clin Pract* 2003; *61* : 69-76.

28. Menon VU, Kumar KV, Gilchrist A, Sugathan TN, Sundaram KR, Nair V, *et al*. Prevalence of known and undetected diabetes and associated risk factors in central Kerala - ADEPS. *Diabetes Res Clin Pract* 2006; *74* : 289-94.

29. Mohan V, Deepa M, Deepa R, Shantirani CS, Farooq S, Ganesan A, *et al*. Secular trends in the prevalence of diabetes and glucose tolerance in urban South India - the Chennai Urban Rural Epidemiology Study (CURES-17).

Diabetologia 2006; *49* : 1175-8.

30. Joshi SR. Metabolic syndrome—emerging clusters of theIndian phenotype. J Assoc Physicians India 2003; 51:445 -446.

Web References

1. http://www.japi.org

2 **.**www.niaid.nih.gov/daids/dtpdb/VIRTARG.asp

3. planningcommission.nic.in/.../vol2/v2c3-4-2.htm

4 http://www.eatlas.idf.org/Prevalence/

5. *http://www.nejm.org*

GLOSSARY

AIDS	-Acquired Immuno Deficiency Syndrome
BMI	- Body Mass index
DM	- Diabetes Mellitus
D4T(30)	- Stavudine
EFV	- Efavirenz
GRH	- Government Rajaji Hospital
HT	- Hypertension
HAART	-Highly Active Anti Retroviral Therapy
IGT	-Impaired Glucose tolerance
IFG	-Impaired Fasting Glucose
NVP	- Nevirapine
3TC	- Lamivudine
ZDV	- Zidovudine

PROFORMA

Name: Age: Sex :

IP/OP No : Occupation :

Marital status: WHO stage :

Educational status :

Clinical status :

Polyuria : Y/N

Polydipsia : Y /N

Polyphagia: Y/N

Pruritus : Y/N

Past History :

Diabetes : Hypertension :

IHD :

Drug History : Y/N Allopathic/ Ayurvedic / Others (For HIV)

Anti Diabetic Agents

Personal History :

Smoking: Y/N Duration: Packs/ Day

Alcohol : Y/N Duration:

Diet : Veg/ Non veg

Family History ;

Diabetes : Y/N

Father / Grand parents / Brother / Son

Mother / Sister / Daughter

Examination :

Height Weight BMI

Vital signs

(a) Pulse rate (b) Respiratory rate

(c) Blood pressure

Systems :

Cardio vascular status

Respiratory status

Neurological status

Treatment ;

1 . Lamivudine / Stavudine / Nevirapine

2 . Lamivudine / Stavudine / Efavirenz

3. Lamivudine / Zidovudine / Nevirapine

4 . Lamivudine / Zidovudine / Efavirenz

5. Not on drugs

Investigations:

Urine albumin :

Sugar :

Deposit :

Blood sugar :

day	Fasting [mg]	Postprandial [mg]
1		
2		

Blood Urea :

Ser Creatinine :

Lipid profile :

Liver Function Test

CD4 Count / ul :

Percentage :

E.C.G.

Ophthal evaluation :

MASTER CHART

SN	age	sex	M	HT	WT	BMI	S	HTN	G	DM	IGT/IFG	N	CAD
1	33	F	1	16O	41	16	2	2	2	2	2	2	2
2	35	F	1	160	43	17	2	2	2	2	2	2	2
3	30	F	1	166	48	17	2	2	1	2	2	2	2
4	50	M	1	163	47	18	1	1	1	2	2	2	2
5	24	F	2	168	50	18	2	2	1	2	2	2	2
6	29	F	1	156	43	18	2	2	3	2	2	2	2
7	42	F	1	159	45	18	2	2	1	2	2	2	2
8	29	F	1	160	46	18	2	2	3	2	2	2	2
9	32	F	1	156	44	18	2	2	2	2	2	2	2
10	45	M	1	163	48	18	2	2	2	2	2	2	2
11	40	M	1	166	50	18	2	1	5	2	1	1	2
12	33	M	1	169	52	18	2	2	5	2	2	2	2
13	29	F	1	161	48	19	2	2	1	2	2	2	2
14	26	F	1	161	48	19	2	2	1	2	2	2	2
15	28	F	1	165	51	19	2	2	1	1	2	2	2
16	31	F	1	163	50	19	2	1	2	2	1	1	2
17	37	F	1	161	49	19	2	2	1	2	1	2	2
18	43	M	1	170	55	19	2	2	2	2	2	2	2
19	48	M	1	167	53	19	2	1	2	1	2	1	1
20	35	F	1	162	50	19	2	2	1	2	2	2	2
21	39	M	1	168	54	19	2	2	2	2	2	2	2
22	33	M	1	168	54	19	2	2	2	2	2	2	2
23	35	F	1	163	51	19	2	2	1	2	2	2	2
24	42	M	1	174	58	19	2	2	1	1	2	2	2
25	33	F	1	154	46	19	2	2	1	2	2	2	2
26	35	F	1	159	49	19	2	2	2	1	2	2	2
27	37	F	1	157	48	20	2	2	3	2	2	2	2
28	32	M	1	169	56	20	2	2	1	2	2	2	2
29	25	M	2	169	56	20	1	2	1	2	2	2	2
30	25	M	1	173	59	20	2	2	1	2	2	2	2
31	15	F	2	167	55	20	2	2	5	2	2	2	2
32	35	M	2	168	56	20	2	2	3	2	2	2	2
33	25	F	2	160	51	20	2	2	1	2	2	2	2
34	4	M	2	88	16	21	2	2	4	1	2	2	2
35	9	M	1	116	28	21	2	2	2	2	2	2	2
36	22	F	1	153	47	20	2	2	1	2	2	2	2
37	40	F	1	164	54	20	2	2	5	2	1	2	1
38	31	F	1	168	57	20	2	2	5	2	2	2	2
39	32	M	1	168	57	20	2	2	5	2	2	2	2
40	30	M	1	167	57	20	2	2	1	2	2	2	2
41	25	F	2	158	51	20	2	2	1	2	2	2	2
42	35	F	1	158	51	20	2	2	3	1	2	2	2
43	42	M	1	171	60	21	2	2	2	2	1	2	2

44	28	M	1	168	58	21	1	2	2	2	2	2	2
45	47	M	1	172	61	21	2	2	1	2	2	2	2
46	50	M	1	160	53	21	2	1	1	2	1	2	1
47	35	M	2	169	59	21	2	2	2	2	2	2	2
48	42	M	1	166	57	21	1	2	3	2	2	2	2
49	26	M	2	163	55	21	1	2	5	2	2	2	2
50	38	F	1	164	56	21	2	1	1	1	2	1	1
51	36	M	1	170	60	21	2	2	1	2	2	2	2
52	30	M	1	170	60	21	2	2	3	2	2	2	2
53	26	F	2	164	56	21	2	2	5	2	2	2	2
54	29	F	1	170	60	21	2	2	4	2	2	2	2
55	42	M	1	170	60	21	1	2	5	1	2	2	2
56	36	M	1	168	59	21	2	2	1	2	1	2	2
57	32	M	1	168	59	21	2	1	1	2	2	1	2
58	23	F	1	166	58	21	2	2	5	2	2	2	2
59	4	M	1	82	13	19	2	2	1	2	2	2	2
60	36	M	1	166	58	21	2	2	5	2	2	2	2
61	31	M	1	170	61	21	1	2	2	2	2	2	2
62	28	M	1	160	54	21	2	2	5	2	2	2	2
63	32	M	1	171	62	21	1	2	1	2	2	2	2
64	44	M	1	164	57	21	2	2	5	2	2	2	2
65	50	M	1	171	62	21	2	2	1	2	2	1	2
66	29	M	1	167	59	21	2	2	1	2	2	2	2
67	40	M	1	167	59	21	2	2	3	1	2	2	2
68	27	F	1	161	55	21	2	2	2	2	2	2	2
69	47	M	1	168	60	21	1	2	1	1	2	2	2
70	37	F	1	165	58	21	2	2	4	2	1	2	2
71	30	M	1	169	61	21	1	2	1	2	2	2	2
72	45	M	1	169	61	21	2	2	1	2	2	2	2
73	34	M	1	169	61	21	2	2	4	2	2	2	2
74	44	M	1	169	61	21	2	1	5	1	2	1	1
75	35	M	1	174	65	22	2	1	2	1	2	1	1
76	51	F	1	160	55	22	2	2	2	1	2	2	2
77	46	M	1	170	62	22	2	2	2	2	2	2	2
78	35	F	1	167	60	22	2	2	5	2	2	2	2
79	42	M	1	171	63	22	2	2	2	2	2	2	2
80	34	M	1	158	54	22	2	2	1	2	2	2	2
81	22	F	2	158	54	22	2	2	3	2	2	2	2
82	40	M	1	169	62	22	1	1	1	1	2	1	1
83	31	M	1	165	59	22	2	2	2	2	2	2	2
84	35	M	1	169	62	22	2	2	1	2	2	2	2
85	32	M	1	169	62	22	1	2	3	2	2	2	2
86	35	F	1	163	58	22	2	2	5	2	2	2	2
87	47	M	1	166	60	22	2	2	4	2	2	2	2
88	45	M	1	166	60	22	2	1	4	2	2	2	2
89	31	F	1	166	60	22	2	2	4	2	2	2	2
90	19	F	2	167	61	22	2	2	5	2	2	2	2
91	32	F	1	171	64	22	2	2	4	2	2	2	2
92	50	M	1	165	60	22	1	1	5	2	2	2	1

93	26	F	2	165	60	22	2	2	1	2	2	2	2
94	57	M	1	165	60	22	2	2	5	2	2	2	2
95	27	M	1	168	62	22	2	2	3	2	2	2	2
96	30	M	1	168	62	22	2	2	3	2	2	2	2
97	25	F	2	152	51	22	2	2	1	2	2	2	2
98	30	F	1	166	61	22	2	2	5	2	2	2	2
99	40	M	1	170	64	22	2	1	1	1	2	2	2
100	32	M	1	170	64	22	2	2	2	2	2	2	2
101	39	M	1	171	65	22	2	2	3	2	2	2	2
102	38	M	1	168	63	22	1	1	5	2	2	2	2
103	27	M	2	164	60	22	1	2	5	2	2	2	2
104	35	M	1	168	63	22	2	2	1	2	2	2	2
105	28	M	2	160	57	22	2	2	5	2	2	2	2
106	40	M	1	165	61	22	2	1	1	2	1	2	2
107	32	M	1	165	61	22	1	2	1	2	2	2	2
108	36	F	1	161	58	22	2	2	3	2	2	2	2
109	33	M	1	172	67	23	2	2	3	2	2	2	2
110	29	F	1	165	62	23	2	2	1	2	2	2	2
111	25	M	2	170	66	23	2	2	2	2	2	2	2
112	47	M	1	170	66	23	2	2	1	2	2	2	2
113	66	M	1	171	67	23	2	1	1	2	2	2	2
114	37	M	1	171	67	23	1	2	1	1	2	2	2
###	35	F	1	160	59	23	2	2	5	1	2	2	2
116	26	M	2	158	58	23	2	2	5	2	2	2	2
117	36	F	1	162	61	23	2	2	1	2	2	2	2
118	35	M	1	176	72	23	1	2	3	2	2	2	2
119	27	M	2	171	68	23	2	2	1	2	2	2	2
120	24	F	2	168	66	23	2	2	1	2	2	2	2
121	40	M	1	157	60	24	1	2	5	2	2	2	2
122	28	M	1	159	63	25	2	2	3	2	1	2	2
123	23	F	2	158	64	26	2	2	2	2	2	2	2
124	28	F	1	161	67	26	2	2	1	2	2	2	2
125	36	F	1	160	66	26	2	2	3	2	2	2	2
126	33	M	1	158	65	26	1	2	5	2	2	2	2
127	27	F	2	160	68	27	2	2	1	2	2	2	2
128	46	F	1	166	60	22	2	2	5	2	2	2	2

Sex: M-Male, F-Female

M-Marital status : 1-married , 2-Unmarried

S – Smoking : 1 –Yes , 2 – No

HT: 1-Present, 2-Absent

G – Group :1,2,3,4&5

DM: 1-Present, 2-Absent

HT: 1-Present, 2-Absent

IGT/IFG : 1-Present, 2-Absent

CAD: 1-Present, 2-Absent

N – Nephropathy : 1-Present, 2-Absent